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Biomarkers and Imaging

O-49

PLASMA PROTEOMICS REVEALS TISSUE-SPECIFIC RESPONSE IN PATIENTS WITH MYOSITIS

Yue-Bei Luo[1,2], Josefin Kenrick[3], Antonella Notarnicola[1,4], Angeles Galindo-Feria[1,4], Ana D.U. Navas[5], Irene P. Garcia[1,4], Orane Demuynck[6], Valerie Leclair[7,8], Karin Lodin[1,4], Eveline Van Gompel[1,9], Andrea Kemp[1,4], Lara Dani[1,4], Maryam Dastmalchi[1,4], Lina-Marcela Diaz-Gallo[1], Charlotta Preger[3], María B. Alvez[3], Mathias Uhlén[3], Peter Nilsson[3], Fredrik Edfors[3], Elisa Pin[3], Ingrid E. Lundberg[1,4], Begum Horuluoglu[1]

[1]Division of Rheumatology, Center for Molecular Medicine, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden, [2]Department of Neurology, Xiangya Hospital, Central South University, Changsha, China, [3]Department of Protein Science, SciLifeLab, KTH Royal Institute of Technology, Stockholm, Sweden, [4]Department of Gastro, Dermatology and Rheumatology, Karolinska University Hospital, Stockholm, Sweden, [5]Vall d'Hebron University Hospital, Barcelona, Spain, [6]Département de Médecine Interne et Immunologie Clinique, Centre Hospitalier Universitaire Lille, Centre de référence des Maladies Auto-Immunes Systémiques rares du Nord et Nord-Ouest, Lille, France, [7]Department of Medicine, McGill University, Montreal, Canada, [8]Division of Rheumatology and Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, Canada, [9]Laboratory of Tissue Homeostasis and Disease, Skeletal Biology and Engineering Research Center, Department of Development and Regeneration, KU Leuven, Leuven, Belgium

Objective. Circulation serves as a central conduit allowing signal communication of tissues as well as facilitating clearance and recycling of tissue-derived proteins. Reliable and tissue-specific biomarkers that are associated with clinical manifestations of myositis are lacking. We aimed to apply a dual antibody-based proximity extension assay to profile the plasma protein changes in patients with myositis.

Methods. Plasma from 201 patients diagnosed with myositis at Karolinska University Hospital were analyzed using the Olink Explore1536 assay. Disease activity measurements and laboratory results were collected. Differential abundance analysis was performed using the limma algorithm. Proteins with adjusted p-values <0.01 were considered differentially abundant. Tissue scores were calculated based on tissue protein lists curated from GTEx database. Interferon and complement pathway scores were calculated according to relevant Gene Ontology and Reactome terms.

Results. Plasma of patients with DM was enriched with IFN signaling and skin associated (IFNλ1, BST2, KRT5), ASyS with lung associated (SFTPD, MSLN), IMNM with muscle associated (CA3, NCAM1), and IBM with T cell response associated proteins (CD6, XCL1). Patients with interstitial lung disease and skin rashes showed higher levels of circulating lung and skin associated proteins respectively. Patients with IMNM showed the highest tissue score for skeletal muscles, and ASyS for lung associated proteins. In terms of autoantibody groups, the MDA5 group showed the highest liver and lung tissue scores. Skeletal muscle scores were strongly correlated with muscle visual analog scale (VAS) scores, CK levels and MMT8. Lung scores were correlated with pulmonary VAS scores, and skin scores were higher in patients with heliotrope rash than those without, indicating potential involvement or damage of these organs.

Conclusions. Our results suggest that the blood proteome not only represents a complex repertoire showing systemic changes, but also, through careful dissection, could reveal distinct tissue-specific responses. Moreover, these tissue responses on molecular level are associated with disease activity and involvement of tissue damage in patients with myositis.

Key words: proteomics, olink, biomarker, myositis

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CIRCULATING AND MUSCLE FSTL3 IN IDIOPATHIC INFLAMMATORY MYOPATHIES: ASSOCIATIONS WITH DISEASE ACTIVITY, INFLAMMATION, AND FUNCTIONAL STATUS

Lucia Vernerova[1], Lucie Lážnovská[1,2], Jiří Baloun[1,3], Veronika Balounová[1], Martina Vokurková[1], Martin Klein[1,3], Heřman Mann[1,3], Sabína Oreská[1,3], Michal Tomčík[1,3], Tereza Kropáčková[1], Tomáš Kičura[1], Jozef Ukropec[4], Barbara Ukropcová[4,5], Jiří Vencovský[1,3]

[1]Institute of Rheumatology, Prague, Czech Republic, [2]Department of Physiology, Faculty of Science, Charles University, Prague, Czech Republic, [3]Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [4]Institute of Experimental Endocrinology, Biomedical Research Center, Slovak Academy of Sciences, Bratislava, Slovakia, [5]Institute of Pathophysiology, Faculty of Medicine, Comenius University, Bratislava, Slovakia

Background. Follistatin-like 3 protein (FSTL3) is a secreted glycoprotein that binds and neutralizes members of the TGF-β superfamily, particularly myostatin and activin A. By antagonizing these ligands, FSTL3 is functionally involved in the regulation of muscle mass, immune responses, and fibrotic processes. Therefore, an imbalance in FSTL3 may contribute to both the inflammatory and degenerative components of idiopathic inflammatory myopathies (IIM). This study aimed to investigate systemic FSTL3 levels and muscle tissue gene expression in newly diagnosed IIM patients in relation to clinical manifestations, and to compare these findings with those in chronic IIM patients and healthy controls (HC).

Methods. A total of 65 newly diagnosed, untreated or minimally treated IIM patients (ND), 74 chronic patients, and 134 HC were enrolled. Among these, muscle biopsy samples were obtained from 62 ND patients at baseline, 19 ND patients after six months of standard therapy, 20 chronic patients, and 21 HC. Serum samples and clinical data were collected (at baseline and after six months in ND). Circulating FSTL3 concentrations were measured by ELISA, and muscle gene expression was quantified by qPCR using the TaqMan® system. Associations between circulating FSTL3 and clinical or functional parameters were analyzed using linear mixed-effects models (LMMs).

Results. Serum FSTL3 levels were significantly higher in newly diagnosed IIM patients compared with chronic patients (p=0.0201) and healthy controls (p<0.0001). However, FSTL3 mRNA expression in muscle tissue did not differ between groups. Neither serum FSTL3 nor muscle mRNA levels changed after six months of therapy in ND patients. In subtype analyses, the highest serum FSTL3 concentrations were found in antisynthetase syndrome (ASyS) compared with dermatomyositis and immune-mediated necrotizing myopathy (IMNM), whereas muscle FSTL3 mRNA was lowest in ASyS. LMM analyses performed in newly diagnosed IIM patients over the six-month period revealed significant associations between circulating FSTL3 and several outcomes, including CRP (p<0.001), MYOACT (p=0.014), SF-36 physical component score (p=0.002), and SF-36 mental component score (p=0.026). These associations remained largely stable after adjustment for covariates.

Conclusions. FSTL3 levels differ across disease stages and subtypes of IIM and are associated with greater systemic inflammation and reduced physical and mental health. These findings suggest that FSTL3 may be linked to muscle dysfunction and disease activity in IIM.

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Key words: myositis, muscle dysfunction, disease activity

Cancer Myositis

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IMPLICATIONS OF CANCER AND POTENTIAL THERAPY WITH IL-17A NEUTRALIZING ANTIBODIES IN DERMATOMYOSITIS USING A MURINE MODEL OF TIF1-γ INDUCED MYOSITIS

Karin Endo[1], Yuki Ichimura[1,2], Risa Konishi[1,3], Taku Namatame[1], Tadatsune IIda[1], Naoko Okiyama[1]
[1]Department of Dermatology, Graduated School of Medical and Dental Science, Institute of Science Tokyo, Japan, [2]Division of Rheumatology, Department of Internal Medicine, Tokyo Women's Medical University, Japan, [3]Department Dermatology, Faculty of Medicine, University of Tsukuba, Japan

Background. Dermatomyositis (DM) is an idiopathic inflammatory myopathy characterized by muscle and multi-organ inflammation with distinctive skin eruptions. Myositis-specific autoantibodies against transcriptional intermediary factor1-γ (TIF1γ) are frequently detected in cancer-associated DM, and clinical improvement of myositis is often observed following cancer treatment. This study aimed to elucidate the relationship between TIF1γ autoimmunity, cancer coexistence, and myositis using a murine model of TIF1γ-induced myositis (TIM).
Methods. C57BL/6 mice were immunized with recombinant human full-length TIF1γ protein to induce experimental myositis (TIM) (1). Expression levels of TIF1γ in various cancer cell lines were assessed by western blotting. A TIF1γ-high cell line (F9 embryonal carcinoma) and a TIF1γ-low cell line (MC38 colon adenocarcinoma) were subcutaneously implanted on the backs of TIM and control mice. The Gene expression of inflammatory cytokines in muscle tissue was evaluated using quantitative PCR. TIM and control mice implanted with F9 cells were treated with anti-interleukin-17A (IL-17A) antibodies. Femoral muscle and tumor tissues were analyzed histologically and immunohistochemically.
Results. Growth of implanted F9 tumors was significantly inhibited in TIM mice compared with controls, whereas no difference in tumor growth was observed between TIM and control mice implanted with MC38 cells. T-cell infiltration into F9 tumors was markedly higher in TIM mice (median [IQR] = 35.7 [20.8-36.3]) than in controls (15.3 [13.8-26.2], p=0.02 by Mann-Whitney U test). F9-implanted TIM mice developed more severe myositis than those implanted with MC38. IL17A mRNA expression in muscle tissue was significantly upregulated in TIM mice compared to controls (mean relative expression ± SEM, 4.35 ± 1.38 *vs*. 1.00±0.22, p=0.006 by Mann-Whitney U-test). Treatment with anti-IL-17A antibodies ameliorated myositis in F9-implanted TIM mice without promoting tumor progression.
Conclusions. In the TIM model, TIF1γ autoimmunity not only induced experimental myositis but also contributed to the suppression of tumor growth in cancers expressing TIF1γ. Conversely, the presence of cancer exacerbated the severity of myositis. IL-17A blockade alleviated muscle inflammation without promoting tumor growth, suggesting that IL-17A neutralization could be a promising therapeutic strategy for cancer-associated DM.
Key words: cancer, dermatomyositis

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Classification of Inflammatory Myopathies

O-206

2025 EULAR/ACR CLASSIFICATION CRITERIA FOR ANTI-SYNTHETASE SYNDROME

Lorenzo Cavagna[1,2], Rohit Aggarwal[3], Akira Yoshida[4], Eduardo Dourado[5,6,7], Iazsmin Bauer Ventura[8], Daphne Rivero Gallegos[9], Francisca Bozan[10], Gianluca Sambataro[11], Sangmee Shron Bae[12], Aravinthan Loganathan[13,14,15], Davide Rozza[16], Angela Ceribelli[17,18], Carlo Selmi[17,18], Albert Selva-O'Callaghan[19,20], Andrew Mammen[21,22], Carlo Albero Scirè[23,24], Carlomaurizio Montecucco[1,2], Chester Oddis[3], David Fiorentino[25], Francesco Bonella[26], Frederick Miller[27], Ingrid E. Lundberg[28], Jens Schmidt[29,30], Jorge Rojas-Serrano[9], Marie Hudson[31], Masataka Kuwana[4], Miguel Angel González-Gay[32,33], Neil McHugh[14], Tamera J Corte[34], Tracy Jennifer Doyle[35], Victoria Werth[36], Latika Gupta[37,38], Veronica Codullo[2], Siamak Moghadam-Kia[3], Florenzo Iannone[39], Ilaria Cavazzana[40], Veronica Wolff[41], Johannes Knitza[42,43], Matteo Piga[44], Elena Bravi[45], Corrado Campochiaro[46,47], Javier Bachiller-Corral[48], Diana Isabel Perez Roman[9], Deverasetti Phani Kumar[38], Samuel Katsuyuki Shinjo[49], Fabrizio Luppi[23], Elizabeth Volkmann[12], Adam Schiffenbauer[50], Lisa Rider[50], Raquel Campanilho-Marques[51], Marco Sebastiani[52,53], Prateek Gandiga[54], Harsha Gunawardena[55], Sara Faghihi-Kashani[3,56], Giovanni Zanframundo[1,2]
[1]Università Di Pavia, Pavia, Italy, [2]Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [3]University of Pittsburgh School of Medicine, Pittsburgh, USA, [4]Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [5]Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal, [6]Aveiro Rheumatology Research Centre, Egas Moniz Health Alliance, Aveiro, Portugal, [7]Rheumatology Research Unit, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal, [8]University of Chicago, Chicago, USA, [9]Instituto Nacional de Enfermedades Respiratorias, Ismael Cosío Villegas, Mexico City, Mexico, [10]Hospital Clínico Universidad de Chile, Chile, [11]University of Enna "Kore", Enna, Italy, [12]University of California Los Angeles, Los Angeles, USA, [13]Royal National Hospital for Rheumatic Diseases, Bath, UK, [14]University of Bath, Bath, UK, [15]Arthritis Australia, Glebe , Australia, [16]Italian Society of Rheumatology, Milan, Italy, [17]Humanitas University, Pieve Emanuele, Italy, [18]IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy, [19]Vall d'Hebron University Hospital, Barcelona, Spain, [20]Universitat Autònoma de Barcelona, Barcelona, Spain, [21]Johns Hopkins University School of Medicine, Baltimore, USA, [22]National Institutes of Health, Bethesda, USA, [23]University of Milano Bicocca, Milan, Italy, [24]IRCCS San Gerardo dei Tintori Foundation, Italy, [25]Stanford University School of Medicine, Redwood City, USA, [26]University of Duisburg-Essen, Essen, Germany, [27]National Institutes of Health, Durham, USA, [28]Karolinska Institutet, Stockholm, Sweden, [29]University Medical Center Göttingen, Göttingen, Germany, [30]University Hospital of the Brandenburg Medical School, Brandenburg, Germany, [31]McGill University, Montréal, Canada, [32]IIS-Fundacion Jimenez Díaz, Madrid, Spain, [33]University of Cantabria, Spain, [34]Royal Prince Alfred Hospital and University of Sydney, Sydney, Australia, [35]Brigham and Women's Hospital, Boston, USA, [36]Perelman School of Medicine & Corporal Michael J. Crescenz , Philadelphia, USA, [37]Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, UK, [38]University of Manchester, Manchester, UK, [39]University of Bari, Bari, Italy, [40]ASST Spedali Civili, Brescia, Università di Brescia, Brescia, Italy, [41]Instituto Nacional del Torax, Santiago, Chile, [42]University Hospital of Giessen and Marburg, Philipps-University Marburg, Marburg, Germany, [43]Friedrich-Alexander-Universität Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany, [44]University of Cagliari and AOU Cagliari University Clinic , Cagliari, Italy, [45]Ospedale Guglielmo da Saliceto, Piacenza, Italy, [46]Vita-Salute San Raffaele University, Milan, Italy, [47]IRCCS San Raffaele Hospital, Milan, Italy, [48]Hospital Universitario Ramon y Cajal, Madrid, Spain, [49]Universidade de Sao Paulo, Brazil, [50]National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, USA, [51]Universidade de Lisboa and Centro Hospitalar Universitario Lisboa Norte, Lisbon, Portugal, [52]AULS Piacenza, Piacenza, Italy, [53]University of Parma, Parma, Italy, [54]Emory University, School of Medicine, Atlanta, USA, [55]North Bristol NHS Trust, Bristol, UK, [56]University of California San Francisco, San Francisco, USA

Background. Standardized classification criteria for anti-synthetase syndrome (ASyS) are currently unavailable. Our objective was to establish validated and widely applicable criteria.
Methods. Through the CLASS project, an international multicenter collaboration, we created evidence-based and expert-consensus classification criteria for ASyS. Our approach combined systematic literature review, clinical expert agreement, real-world patient data, and multi-criteria decision analysis (MCDA). Variable selection involved both linear regression modeling and expert panel input. Three distinct cohorts were utilized for validation purposes: derivation, performance evaluation, and independent validation. Additional assessment occurred in a gold-standard cohort featuring centralized autoantibody analysis through immunoprecipitation. Criteria finalization incorporated expert consensus alongside patient perspectives.
Results. Participating centers (n=103) from 20 nations contributed data on 1953 ASyS patients and 2093 control subjects. The resulting classification criteria, derived from statistical and consensus methodologies, incorporated

interstitial lung disease, myositis, arthritis, mechanic's hands (or hiker's feet), inflammatory cutaneous manifestations, unexplained fever, Raynaud's phenomenon, anti-aminoacyl-tRNA synthetase antibodies (anti-ARS), cytoplasmic ANA staining patterns, and anti-Ro52 positivity. A three-tier system – "definite", "probable", and "possible" – was created using weighted score thresholds. Definite ASyS achieved sensitivity/specificity of 86.8%/99.2% (independent validation) and 94.3%/99.7% (gold-standard). Probable ASyS yielded 92.7%/87.3% and 97.5%/87.5%, while possible ASyS demonstrated 96.5%/75.4% and 98.7%/80.1%, respectively.

Conclusions. These novel ASyS classification criteria emerged from rigorous international data-driven and consensus-building methodology. The weighted scoring approach exhibited robust diagnostic performance across validation populations, offering a uniform framework for advancing research and therapeutic trials.

Acknowledgements. CLASS project participating investigators.
Key words: anti-synthetase syndrome

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Clinical Trials

O-4

SAFETY AND EARLY EFFICACY OF RAPCABTAGENE AUTOLEUCEL, AN AUTOLOGOUS CD19-DIRECTED CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY, IN SEVERE REFRACTORY IDIOPATHIC INFLAMMATORY MYOPATHIES

Alexander Pfeil[1], Masataka Kuwana[2], Ingrid E. Lundberg[3], Olivier Benveniste[4], Elena Schiopu[5], Matthew Matasar[6], Merav Lidar[7], Takashi Matsushita[8], Ran Nakashima[9], Yves Allenbach[4], Steve Draikiwicz[10], Muhsen Alani[10,11], Anna Grinienko[10], Nigel Yateman[12], Bibha Das[12], Angelika Jahreis[12], Susanne Diehl[12], Brian Porter[11], Rohit Aggarwal[13]

[1]Center of Rheumatology with Section Rheumatology and Osteology, Department of Internal Medicine III, Jena University Hospital – Friedrich Schiller University Jena, Jena, Germany, [2]Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [3]Division of Rheumatology, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden, [4]Pitié-Salpêtrière University Hospital, Paris, France, [5]Medical College of Georgia at Augusta University, Augusta, USA, [6]Rutgers Cancer Institute, New Brunswick, USA, [7]Chaim Sheba Medical Center, Ramat Gan, Israel, [8]Kanazawa University Hospital, Kanazawa Ishikawa, Japan, [9]Kyoto University Hospital, Kyoto, Japan, [10]Novartis Pharmaceuticals, East Hanover, USA, [11]University of Washington, Seattle, USA, [12]Novartis Pharma AG, Basel, Switzerland, [13]University of Pittsburgh School of Medicine, Pittsburgh, USA

Background. Idiopathic inflammatory myopathies (IIM) are rare, systemic autoimmune disorders characterized by chronic muscle inflammation, progressive weakness, and frequent extramuscular manifestations. Despite advances in immunosuppressive therapies, many patients remain refractory to treatment, and durable drug-free remission is rarely achieved. CD19-targeted chimeric antigen receptor (CAR)-T cell therapy has demonstrated potential in inducing deep and sustained B cell depletion, offering a possible "immune system reset" and a path toward remission in challenging autoimmune conditions. This study evaluates rapcabtagene autoleucel, a rapidly manufactured autologous CD19-directed CAR-T cell therapy, in patients with severe, active, refractory IIM.

Methods. This Phase 2, open-label, controlled study (NCT06665256) includes two cohorts. Cohort 1 is a single-arm safety cohort assessing the safety and tolerability of rapcabtagene autoleucel, followed by Cohort 2, a randomized cohort. Here we report data from Cohort 1, including six eligible IIM participants who received protocol-defined lymphodepleting chemotherapy (fludarabine and cyclophosphamide), followed by a single intravenous infusion of rapcabtagene autoleucel. The first three participants were dosed sequentially with a 28-day observation period between each; subsequent participants were dosed in parallel following safety review. All participants were hospitalized for at least 14 days post-infusion and monitored closely for adverse events.

Results. As of this data cutoff, patients treated in Cohort 1 demonstrated rapid and profound B cell depletion and CAR-T cell expansion. All three patients with ≥12 weeks of post-infusion follow-up showed moderate-to-major improvement in Total Improvement Score, including a major response reported in an immune-mediated necrotizing myopathy patient. Circulating CD19+ B cells reappeared in all three patients by Day 87 post-infusion. All six patients were able to discontinue immunosuppressive agents. Among the three patients with ≥12 weeks of follow-up, prednisone was tapered to ≤5 mg per day by the data cutoff. Cytokine release syndrome (CRS) occurred in five of six patients (Grade 1: n=3; Grade 2: n=1; Grade 3: n=1). Tocilizumab was administered in four patients and all CRS cases resolved without sequelae. Transient Grade 3/4 neutropenia was observed in two patients (both resolved without sequelae). No cases of immune effector cell-associated neurotoxicity syndrome or immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome were reported.

Conclusions. Preliminary data from Cohort 1 suggest a favorable safety profile, robust CAR-T cell expansion, effective B cell depletion and early signs of efficacy of rapcabtagene autoleucel without concomitant immunosuppressive agents in patients with severe, refractory IIM. These findings support continued evaluation of this novel therapeutic approach in autoimmune myopathies.

Key words: CAR-T cell therapy, emerging therapies, clinical trial

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TOFACITINIB FOR CALCINOSIS CUTIS ASSOCIATED WITH JUVENILE DERMATOMYOSITIS: AN OPEN-LABEL SINGLE-ARM STUDY

Pragati Jain[1], Supraja Laguduva Mohan[2], Shivani Kaushik[3], Rakesh Deepak[3], Dibyanshu Mishra[4], MA Khan[4], Vishal Gupta[5], Priyanka Naranje[2], A.V. Ramanan[6], Rakesh Lodha[1], Manisha Jana[2], Narendra Kumar Bagri[1*]

[1]Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), New Delhi, India, [2]Department of Radiodiagnosis and Interventional Radiology, All India Institute of Medical Sciences, New Delhi, [3]Department of Transplant Immunology and Immunogenetics, All India Institute of Medical Sciences, New Delhi, [4]Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India, [5]Department of Dermatology, All India Institute of Medical Sciences, New Delhi, India, [6]Department of Pediatric Rheumatology, Bristol Royal Hospital for Children, Upper Maudlin Street, Bristol, UK

**Presenting and corresponding author: drnarendrabagri@gmail.com*

Background. Calcinosis cutis (CC) is dystrophic calcification affecting 20-40% of patients with juvenile dermatomyositis (JDM). Management of CC is challenging as there is no effective therapy. Type I interferon-mediated immune dysregulation plays a pathogenic role in CC, thus altering JAK-STAT signalling through JAK inhibitors might offer a therapeutic benefit.

Methods. We conducted an open-label, single-arm study at AIIMS, New Delhi, evaluating tofacitinib as adjunct therapy in children (2–18 years) with JDM/JDM-SSc overlap and CC. Children with JDM and clinical/radiological evidence of CC were enrolled for this study. Exclusion criteria were concomitant cyclophosphamide, rituximab, topical tacrolimus, active tuberculosis, or hematological abnormalities. The study drug tofacitinib was administered orally as per weight bands. The concomitant treatment with stable doses of steroids (<1mg/kg/day), methotrexate and/or MMF and/or HCQ was allowed. The primary objective was to study the effect of tofacitinib on the burden of CC at 24 ± 2 weeks, assessed by Agatston score using low-dose whole body CT scan (WBCT). Secondary objectives were to evaluate the effect on CDASI, CMAS Scales, steroid doses, IFN-α and β levels and adverse events. Data were analysed using STATA version 16.

Results. Data of twenty children (11 boys; 90% JDM, 10% JDM–SSc overlap with a mean (SD)age of 10.4 (3.6) years), who completed the study, were analysed using per-protocol analysis. The median durations for disease and calcinosis were 57 and 31 months, respectively. The mean (SD) duration of follow-up for the study participants was 29.9 ± 1.4 weeks. There was a significant reduction in the Agatston score, median (IQR) at follow-up compared to baseline 6349(3765-65255) *vs*. 4007(1616-55515) p=0.012, with a moderate effect size (d-robust -0.52). The follow-up CMAS, and CDASI scores did not show any difference from baseline (44.94 ± 8.4 *vs*. 46.5 ± 6.8, p=0.145 and 2 (1–6) *vs*. 1 (0–4), p=0.08, respectively). At baseline, five participants were receiving concomitant oral prednisone, among whom only 2 continued steroids at the last follow-up. There was a significant reduction in steroid dosage [mean (SD)]; 0.536 (0.4) at baseline to 0.19 (0.16) mg/kg/day at follow-up in these 2 participants (p=0.03). Median (IQR) IFN-α levels decreased from 17.03 (11.37–22.21) pg/mL to 12.02 (5.82–19.21) pg/mL, and IFN-β from 17.09 (15.42–20.10) to 10.39 (9.95–11.87) (p<0.001 for both). Tofacitinib was temporarily withheld in two patients due to acute febrile illness; none experienced any significant adverse events.

Conclusions. Tofacitinib, along with standard therapy, demonstrated a significant reduction in the Agatston score in children with JDM and CC. No major safety signals were observed during the study period.
Acknowledgements. We acknowledge the University of Pennsylvania for permission to use the CDASI score. We also acknowledge the data safety and monitoring board for their valuable contribution
Trial registration. The Study was registered under the Clinical Trial Registry of India CTRI (REF/2023/12/076915)
Funding. AIIMS, New Delhi, India; a research grant was provided for the biomarker study.
Declaration of interests. The study drug (tofacitinib) was provided by MSN Pharmaceuticals (MSN House, plot No. C 24, Sanath Nagar, Hyderabad, Telangana, India), which had no role in the study design, conduct, analysis, or interpretation of results.
Key words: calcinosis cutis, juvenile dermatomyositis, Agatston score, tofacitinib, JAK-i

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EFFICACY AND SAFETY OF EGARTIGIMOD PH20 SC IN ADULT PARTICIPANTS WITH ACTIVE IDIOPATHIC INFLAMMATORY MYOPATHY: PHASE 2 RESULTS FROM THE ALKIVIA STUDY

Rohit Aggarwal[1], Sebastian C. Rodriguez-Garcia[2], Agna Neto[2], Despoina Papadopoulou[2], Ben Van Baelen[2], Paul Duncombe[2], Todd Siluk[2], Leentje De Ceuninck[2], Bas Van Der Woning[2], Hector Chinoy[3,4]
[1]University of Pittsburgh Medical Center, Pittsburgh, USA, [2]argenx, Ghent, Belgium, [3]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Center, Salford, UK, [4]Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK

Background. Idiopathic inflammatory myopathy (IIM) is a rare, systemic, autoimmune, rheumatic disease with different subtypes, characterized by muscle weakness and extramuscular involvement. To date, no therapies treating different IIM subtypes are approved. Efgartigimod is a human immunoglobulin G1 (IgG1) antibody Fc fragment engineered for increased affinity to the neonatal Fc receptor (FcRn), and uniquely only contains that part of the IgG antibody that normally binds FcRn. The efficacy and safety of subcutaneous (SC) efgartigimod PH20 (co-formulation of efgartigimod and recombinant human hyaluronidase PH20) was assessed versus placebo in patients with IIM in the ALKIVIA study (NCT05523167).
Methods. ALKIVIA is an operationally seamless phase 2/3, randomized, double-blinded, placebo-controlled, parallel-group, multicenter study in adults with IIM. Randomized patients (1:1) received weekly efgartigimod PH20 SC or placebo in addition to background standard of care treatment for IIM. The primary endpoint was the 2016 ACR/EULAR Total Improvement Score (TIS) at Week 24. This composite endpoint is based on improvement in Physician's Global Disease Activity, Patient Global Disease Activity, manual muscle testing-8, Health Assessment Questionnaire Disability Index, muscle enzymes, and Extramuscular Global Disease Activity.
Results. The 24-week phase 2 study randomized 89 participants. Least-squares mean (LSM) TIS at Week 24 was statistically significantly higher in the efgartigimod PH20 SC arm than the placebo arm (LSM 50.45 *vs*. 35.65, 2-sided p=0.0004). Individual components comprising the TIS also favored efgartigimod. Safety was comparable between treatment arms.
Conclusions. ALKIVIA, the first study of an FcRn inhibitor in IIM, established proof of concept. The results demonstrate the mechanistic relevance of FcRn inhibition in IIM, indicating the potential pathogenicity of autoantibodies in IIM and supporting further evaluation of efgartigimod PH20 SC in the ongoing phase 3 part of the study.
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Key words: efgartigimod, idiopathic inflammatory myopathy, myositis, randomized clinical trial

O-211

PROMISING EARLY OUTCOMES WITH BMS-986353, A CD19-DIRECTED CHIMERIC ANTIGEN RECEPTOR (CAR) T CELL THERAPY IN SEVERE REFRACTORY IDIOPATHIC INFLAMMATORY MYOPATHIES (IIMS): SAFETY AND EFFICACY FINDINGS FROM THE ONGOING PHASE 1 BREAKFREE-1 TRIAL

Rohit Aggarwal[1], David S. Korman[2], Margrit Wiesendanger[3], Vikas Majithia[4], Ellen De Langhe[5], Marc Schmalzing[6], Melissa Griffith[7], Philipp Köhler[8,9], Joanna Schiller[8,9], Dimitrios Mougiakakos[10], Mohamad Cherry[11], Richard Nash[12,13], Jacques Azzi[3], Ernesto Ayala[4], Peter Vandenberghe[5], Max Topp[6], Jonathan Gutman[7], Eugen Feist[14], Brandon Law[15], Alisha Desai[15], Alexis Melton[15], Alice Wozniak[15], San-San Ou[15], Melissa Harnois[15], Jerill Thorpe[15], Praneeth Jarugula[15], Takafumi Ide[15], Ashley Koegel[15], Neil Kramer[11,16]
[1]University of Pittsburgh, Pittsburgh, USA, [2]Mountain Rheumatology, HCA HealthONE, Denver, USA, [3]Icahn School of Medicine at Mount Sinai, New York, USA, [4]Mayo Clinic Hospital, Jacksonville, USA, [5]University Hospitals Leuven, Leuven, Belgium, [6]University Hospital Würzburg, Würzburg, Germany, [7]University of Colorado Anschutz Medical Campus, Aurora, USA, [8]University of Cologne, Faculty of Medicine and University Hospital Cologne, Department I of Internal Medicine, Cologne, Germany, [9]Division of Clinical Immunology and Center for Integrated Oncology (CIO) Aachen Bonn Cologne Duesseldorf, Cologne, Germany, [10]University Hospital Magdeburg, Magdeburg, Germany, [11]Atlantic Health System, Morristown, USA, [12]HealthOne Cares, Denver, USA, [13]Colorado Blood Cancer Institute, Denver, USA, [14]Helios Vogelsang-Gommern Specialist Clinic, Gommern, Germany, [15]Bristol Myers Squibb, Princeton, USA, [16]Overlook Medical Center, Summit, USA

Background. IIMs are systemic autoimmune diseases affecting muscles, skin, lungs, joints, and several other organs; many patients are refractory to available therapy, highlighting the need for novel treatments. BMS-986353 is a CD19-directed autologous CAR T cell therapy being studied in autoimmune diseases. We present data on the tolerability and efficacy of BMS-986353 in patients with severe refractory IIMs from Breakfree-1 (NCT05869955).
Methods. Patients with IIMs with severe muscle involvement (manual muscle test [MMT]-8 <130) despite treatment with glucocorticoids and ≥2 immunosuppressants (ISTs) were treated with a single BMS-986353 infusion of 10×10^6 CAR T cells following lymphodepletion. Patients discontinued IIM-specific therapies and steroids (≥5 mg prednisone equivalent, except when directed for adrenal insufficiency) before lymphodepletion. Primary endpoint: safety.
Results. Thirteen patients were evaluable for safety. Patients received a median 6 (range, 3–9) prior ISTs. Eleven patients were evaluable for efficacy (antisynthetase syndrome, n=3; dermatomyositis, n=3; polymyositis, n=2; immune-mediated necrotizing myopathy [IMNM], n=3), with median baseline MMT-8 score of 121 (range, 72–133). Median follow-up: 87 days (range, 4–375).
Six of 13 (46.2%) patients developed low-grade cytokine release syndrome (grade 1, n=5; grade 2, n=1). One patient had immune effector cell-associated neurotoxicity syndrome (grade 3) with decreased level of consciousness and aphasia, which resolved in 3 days with dexamethasone. Grade ≥3 hematologic treatment-emergent adverse events were brief and reversible without clinical sequelae. There were no prolonged (>28 days) cytopenias or treatment-emergent serious infections.
Among 11 efficacy-evaluable patients, 7 (63.6%) achieved a major response and 3 (27.3%) a moderate response based on Myositis Response Criteria–Total Improvement Score (MRC-TIS). All 11 patients experienced rapid and significant improvement in muscle strength; median increase in MMT-8 score from baseline was 22.0 points at day 85 (n=6) and 27 points at day 169 (n=3). One patient with IMNM with a >10-year disease duration and minimally elevated baseline creatine kinase had improved MMT-8 without achieving at least moderate MRC-TIS response. Ten of 11 efficacy-evaluable patients remained off IIM-directed therapy at last follow-up; 1 patient empirically restarted intravenous immunoglobulin for elevated creatine kinase despite improvement in MMT-8 score.
All patients had robust CAR T cell expansion and achieved complete peripheral blood B-cell depletion. Median time to B-cell repopulation was 85 days.
Conclusions. Findings from Breakfree-1 demonstrate a manageable safety profile, robust CAR T cell expansion, complete B-cell depletion, and promising efficacy of BMS-986353 without IIM-directed therapies in >90% of patients with severe refractory IIMs.
Acknowledgements. Results previously presented at ACR 2025, abstract LB14.
Key words: idiopathic inflammatory myopathies, CAR T cell therapy, safety

O-321

RESET-MYOSITIS: CLINICAL TRIAL EVALUATING RESE-CEL (RESECABTAGENE AUTOLEUCEL), A FULLY HUMAN, AUTOLOGOUS 4-1BB CD19-CAR T CELL THERAPY IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Erin Marie Wilfong[1], Tahseen Mozaffar[2], Elie Naddaf[3], Nizar Chahin[4], Huifang Lu[5], Iazsmin Bauer-Ventura[6], Cuoghi Edens[6], Jason Sluzevich[7], Courtney Little[8], Claire Miller[8], Jennifer Gresh[8], Gaurav Choudhary[8], Jenell Volkov[8], Daniel Nunez[8], Thomas Furmanak[8], Jason Stadanlick[8], Larissa Ishikawa[8], Zachary Vorndran[8], Alexandra Ellis[8], Quynh Lam[8], Fatemeh Hadi-Nezhad[8], Rohit Aggarwal[9], Raj Tummala[8], Samik Basu[8], David Chang[8]
[1]Vanderbilt University, Nashville, USA, [2]University of California, Irvine, USA, [3]Mayo Clinic Rochester, Rochester, USA, [4]Oregon Health & Science University, Portland, USA, [5]MD Anderson Cancer Center, Houston, USA, [6]University of Chicago, Chicago, USA, [7]Mayo Clinic, Jacksonville, USA, [8]Cabaletta Bio, Philadelphia, USA, [9]University of Pittsburgh, Pittsburgh, USA

Background. Treatments for idiopathic inflammatory myopathy (IIM) aim to reduce morbidity and improve inflammation, muscle performance, and quality of life. Therapies providing clinical responses and durability are lacking. Rese-cel, is a fully human, autologous 4-1BB CD19-CAR T cell therapy, designed to deeply and transiently deplete CD19 positive cells following a single, weight-based infusion with the potential to enable an "immune reset," resulting in durable responses without the need for chronic immunomodulatory (IM) therapy. RESET-MyositisTM (NCT06154252) is an ongoing Phase 1/2 trial evaluating rese-cel in patients with IIM [dermatomyositis (DM), antisynthetase syndrome (ASyS), immune mediated necrotizing myopathy (IMNM) and juvenile IIM].
Methods. Patients aged 6–75 years with active, refractory IIM received rese-cel (1×10^6 CAR T cells/kg) after fludarabine/cyclophosphamide preconditioning. All non-glucocorticoid (GC) IM agents were discontinued by Day –5. Adverse events, IM use and Total improvement score [TIS] were assessed. CAR T cells and B cells were profiled in peripheral blood pre- and post-infusion by digital PCR and flow cytometry, respectively.
Results. As of 11 September 2025, 13 patients (6 IMNM, 4 DM, 2 ASyS and 1 juvenile IIM) have received rese-cel with ≥ 1 month of follow-up. Rese-cel was generally well tolerated with Grade 1 cytokine release syndrome (CRS) in 4 patients. No dose-limiting toxicity or immune effector cell-associated neurotoxicity syndrome (ICANS) was observed. Of patients with ≥16 weeks follow-up, 3 of 3 DM and 1 of 2 ASyS achieved TIS ≥40. Two of 4 IMNM patients with follow-up of ≥ 24 weeks achieved TIS ≥20; antibodies persisted in 3 IMNM patients who did not achieve or maintain response. All responses were achieved off IM medications and on no more than low dose GCs. Rese-cel expanded and peaked within 2 weeks post-infusion and contracted to undetectable levels within 8 weeks in most patients. B cells (CD19+/CD20+) were depleted by 2 weeks post infusion. Peripheral B cells repopulated between 1 and 4 months post infusion in patients with sufficient follow-up and were predominantly transitional naïve (CD19+CD20+CD38++CD24++).
Conclusions. Acceptable safety, early IM-free clinical responses, and deep B-cell depletion were observed with Rese-cel in IIM. DM and ASyS patients showed greater improvement than IMNM. These findings support rese-cel's potential to achieve an immune reset and achieve meaningful, drug-free responses in most refractory myositis patients.
Key words: idiopathic inflammatory myopathies, cell therapy, CD19, immune reset, B-cell depletion, total improvement score

Extra-Muscular Organ Involvement

O-186

SPATIALLY DISTINCT INFLAMMATORY FIBROBLASTS RECRUIT IFN-β-PRODUCING MMP9$^+$ MYELOID CELLS THAT DRIVE UVB-MEDIATED INTERFACE DERMATITIS IN SKIN DERMATOMYOSITIS

Yuqing Wang[1], Khashayar Afshari[1], Nazgol-Sadat Haddadi[1], Carolina Salomão Lopes[1], Chee-Huat Linus Eng[2], Nuria Martinez[1], Leah Whiteman[1], Ksenia Anufrieva[3], Kevin Wei[3], Kirsten Frieda[2], Stefania Gallucci[1], Misha Rosenbach[4], Ruth Ann Vleugels[3], John Harris[3], Manuel Garber[1], Mehdi Rashighi[1]
[1]UMass Chan Medical School, Worcester, USA, [2]Spatial Genomics, Pasadena, USA, [3]Harvard Medical School, Boston, USA, [4]University of Pennsylvania Philadelphia, USA

Background. Using a comparative multiomic approach across two photosensitive skin diseases (cutaneous lupus erythematosus and dermatomyositis) and two photoresponsive diseases (psoriasis and vitiligo), as well as healthy controls, we sought to define the UVB-driven immunological events that lead to keratinocyte injury in skin dermatomyositis (DM).
Methods. We integrated single-cell RNA sequencing, spatial transcriptomics, and high-throughput proteomics from lesional and non-lesional skin of four skin diseases with in vitro functional assays and in vivo photoprovocation studies.
Results. High-throughput proteomics using Olink's Proximity Extension Assay revealed a selective and marked elevation of IFN-β protein in interstitial skin fluid from lesional DM, but not from other diseases or healthy individuals. Single-cell RNA sequencing identified CD14$^+$ myeloid cells as the most expanded myeloid subset in DM skin, virtually absent in photoresponsive diseases and healthy skin. Using spatial transcriptomics, we further identified a spatially distinct subset of CD14$^+$ myeloid cells characterized by high MMP9 and low LYVE1 expression, uniquely enriched in the superficial dermis of lesional DM. These cells represented the principal source of IFN-β and colocalized with cytotoxic CD4$^+$ T cells near the dermal–epidermal junction.
In vivo, UVB irradiation of sun-protected skin from DM patients, but not healthy controls, induced a rapid influx of CD14$^+$ myeloid cells, implicating UVB-mediated keratinocyte damage in their recruitment. In vitro, IFN-β enhanced CD4$^+$ T-cell cytotoxicity, while IFN-β-primed keratinocytes exhibited increased UVB-induced cell death and released TNF-α and IL-1β. Cytokines released from UVB-damaged keratinocytes activated CD14$^+$dendritic cells but lacked the chemokines required for their recruitment. Spatial transcriptomics revealed that CD14$^+$ cells highly expressed CCR1, CCR2, CCR5, CCR7, and CXCR4, spatially correlating with upregulation of CCL2, CCL8, CCL13, and CCL19 in superficial inflammatory fibroblasts, particularly those adjacent to MMP9$^+$ CD14$^+$ cells. Notably, stimulation of fibroblasts with TNF-α and IL-1β induced strong expression of CCL2, CCL7, and CCL13, confirming a cytokine-driven relay in which UVB-injured keratinocytes activate fibroblasts to produce chemokines that recruit IFN-β-producing MMP9$^+$ CD14$^+$ cells. These myeloid cells, in turn, amplify CD4$^+$ T-cell cytotoxicity, reinforcing epithelial injury.
Conclusions. Our findings delineate a multicellular inflammatory circuit in photosensitive DM skin in which IFN-I–primed keratinocytes secrete cytokines that activate MMP9$^+$ CD14$^+$ myeloid cells, enhancing CD4$^+$ T-cell cytotoxicity through IFN-β. A spatially distinct subset of inflammatory fibroblasts orchestrates this process by producing chemokines that selectively recruit CD14$^+$ myeloid cells to the dermal-epidermal junction, thereby driving interface dermatitis in dermatomyositis.
Key words: dermatomyositis, photosensitivity, fibroblasts, myeloid cells, spatial transcriptomics, single-cell RNA sequencing

O-204

RISK STRATIFICATION AND IMMUNOSUPPRESSANT USE IN REDUCING RESPIRATORY PROGRESSION AMONG ANTI-MDA5 PATIENTS: A JAPANESE-TAIWANESE STUDY

Ting-yuan Lan[1], Tsuneo Sasai[2], Pai-Hsinq Lai[3], Ran Nakashima[2], Ko-Jen Li[1]
[1]Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, [2]Kyoto University Graduate School of Medicine, Kyoto, Japan, [3]Division of Allergy, Immunology and Rheumatology, Department of Internal Medicine, Taipei City Hospital, Zhongxiao Branch, Taipei, Taiwan

Background. Management for anti-MDA5 interstitial lung disease (ILD) is challenging. While the 2023 ACR CTD-ILD guideline recommends dual immunosuppressive (IS) therapy for anti-MDA5-positive ILD, the necessity of universal intensive combination therapy remains controversial, given variable disease trajectories, high infection risks, and inconsistent treatment responses. Risk-prediction models are therefore developed, yet few focused on respiratory progression in patients without severe symptoms. Moreover, few were validated in different populations. We explored to stratify RP-ILD risk among those without established respiratory failure, and correlated IS regimens with outcomes.
Methods. We reviewed 97 patients with anti-MDA5 disease from National Taiwan University Hospital and hospitals around Kyoto area from 2008 to 2025. Patients without established respiratory failure were included. The primary outcome was RP-ILD, defined as new-onset respiratory failure requiring >10 L/min oxygen. ROC and LASSO regression were used to develop the RPILD prediction model. The IS regimens utilized were also compared. In addition, the Hong Kong FLAW model for RPILD prediction – fever, LDH >300 U/L, age >50, and neutrophil-to-lymphocyte (N/L) ratio >7 – were also validated in this international collaborative registry (1).
Results. The mean age of 79 included patients was 52 years. Seventy-one percent had CADM, 25% DM and 4% isolated ILD. RP-ILD developed in 28% (22/79), with 72% (16/22) mortality.
The AAC model (Age >50, Acute onset <3 months, CRP >1 mg/dL) was developed and effectively predicted RP-ILD (0%, 3%, 38%, 55% for scores 0–3). With the 0–1 *vs*. 2–3 cutoff, RP-ILD occurred in 3% (1/37) and 47% (17/36). JAKi-containing regimens (n=6) had lower RP-ILD rate (17%) than calcineurin inhibitor (CNI)-based without JAKi (50%) or other IS combinations (60%).
The FLAW model effectively stratified RP-ILD risk in our cohort, with RP-ILD incidence of 0%, 11%, 36%, 44%, and 75% for scores 0–4, respectively. Grouped as low-risk (0–1) *vs*. high-risk (2–4), RP-ILD occurred in 6% (2/32) and 43% (18/43). Among high-risk patients, RP-ILD incidence did not differ significantly by the number of IS agents (40%, 39%, 56% for one, two, or three agents). However, JAKi-combination (n=5) yielded 0% RP-ILD, versus 42% (11/26) CNI-based regimen without JAKi and 64% (7/11) with other regimens.
Conclusions. Low-risk patients, with less than 5% developing RP-ILD, shared non-progressive features across models, highlighting the importance of risk stratification. JAKi-containing IS combination were associated with reduced RP-ILD in high-risk patients. Prospective studies incorporating risk-based treatment strategies are warranted to confirm these findings.
Key words: anti-MDA5, interstitial lung disease, rapid progressing interstitial lung disease

Reference
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Inclusion Body Myositis

O-91

BARICITINIB AMELIORATES INFLAMMATORY AND PROTEINOPATHIC PATHOLOGY IN A GENETIC IFN-γ-DRIVEN MODEL OF INCLUSION BODY MYOSITIS

Jessica Day[1,2,3], Pranavie Vijayakumar[1,3], Kael Schoffer[1,3], Fanfei Ji[1,3], Jacinta Hansen[1,3], Maria Tanzer[1,3], Ian Wicks[1,2,3]
[1]Walter And Eliza Hall Institute, Parkville, Melbourne, Australia, [2]Rheumatology Department, Royal Melbourne Hospital, Parkville, Melbourne, Australia, [3]University of Melbourne, Parkville, Melbourne, Australia

Background. Inclusion body myositis (IBM) is characterised by endomysial cytotoxic T cells, an IFN-γ signature, protein aggregation, metabolic abnormalities and resistance to immunomodulation. A reproducible and predictable animal model which recapitulates both the inflammatory and degenerative features of the disease is needed to enable mechanistic studies and therapeutic testing.
Suppressor of cytokine signalling 1 (SOCS1) is a critical negative regulator of IFN-γ signalling. SOCS1 deficiency causes fatal perinatal autoinflammatory disease, which can be rescued by IFN-γ deletion (1). Notably, SOCS1-/-IFN-γ+/- mice survive beyond the perinatal period but spontaneously develop myositis (2). This study further characterised the myopathic features of SOCS1-/-IFN-γ+/- mice and assessed the therapeutic efficacy of baricitinib.
Methods. SOCS1-/-IFN-γ+/- mice and relevant controls were evaluated at ethical endpoints. Muscles were dissected tendon-to-tendon and assessed for inflammation, atrophy, fibrosis, MHC-I expression and p62 aggregation using histopathology, immunostaining, and flow cytometry. Laser microdissection and proteomics were performed on p62+ and p62- myofibres. Lymphoid organs were profiled by flow cytometry. Primary myotubes were used to model IFN-γ-induced stress. Baricitinib or vehicle was administered to mice thrice weekly; outcomes included survival and muscle inflammation, fibrosis and proteinopathy.
Results. 100% of SOCS1-/-IFN-γ+/- mice exhibited severe myositis by 5 weeks of age, with an expansion of myeloid and T cells and an increased CD8:CD4 ratio. Within affected muscle, substantial proportions of CD8+ T cells expressed KLRG1 (45.1%), PD-1 (38.1%) and CD38 (55.2%; all $p<0.0001$ *vs*. controls). Lymphoid analyses showed differentiated T cell effector phenotypes were specifically enriched in muscle, consistent with local maturation. Expansion of fibroadipocyte progenitor cells and muscle atrophy with increased fibrosis were also observed.
p62+ myofibres were markedly increased in SOCS1-/-IFN-γ+/- mice and displayed proteomic signatures of mitochondrial dysfunction, cytoskeletal stress, reduced antioxidant capacity, and activation of protein-aggregation defence pathways. In vitro, exposure of myotubes to IFN-γ induced MHC-I/II upregulation and $p62^+$ aggregates. Baricitinib treatment ameliorated all disease features in SOCS1-/-IFN-γ+/- mice, reducing muscle inflammation, p62+ aggregates and fibrosis, and extending survival.
Conclusions. The SOCS1-/-IFN-γ+/- model reproduces key histological and molecular hallmarks of IBM, including highly differentiated $CD8^+$ T-cell infiltration, MHC-I upregulation, myofibre atrophy, fibrosis, metabolic dysfunction and $p62^+$ aggregates. This reproducible, scalable system links chronic IFN-γ-driven inflammation with downstream proteinopathy and provides a powerful preclinical research platform. Baricitinib ameliorated inflammatory and proteinopathic disease features, highlighting the pathogenic role of chronic IFN-γ signalling in IBM.
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Key words: inclusion body myositis, animal models, baricitinib, interferon gamma

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O-92

A SERUM-DERIVED 14-PROTEIN SIGNATURE DISTINGUISHES IBM FROM HISTOLOGICAL POLYMYOSITIS AND ALIGNS WITH TISSUE TRANSCRIPTOMIC PATTERNS ACROSS MYOSITIS SUBTYPES

Jessica Day[1,2,3], Allan Motyer[1,3], Jinjin Chen[1,3], Sam Olechnowicz[1,3], Katrina Reardon[4], Penny McKelvie[4], Tony Papenfuss[1,3], Rory Bowden[1,3], Vidya Limaye[5], Ian Wicks[1,2,3]

[1]Walter And Eliza Hall Institute, Parkville, Melbourne, Australia, [2]Rheumatology Department, Royal Melbourne Hospital, Parkville, Melbourne, Australia, [3]University of Melbourne, Parkville, Melbourne, Australia, [4]St Vincent's Hospital Melbourne, Fitzroy, Melbourne, Australia, [5]Royal Adelaide Hospital, Adelaide, Australia

Background. Inclusion body myositis (IBM) is a debilitating inflammatory myopathy characterised by progressive muscle weakness and limited therapeutic options. Diagnosis is often delayed by years, with many patients initially misclassified. To improve diagnostic precision and better understand IBM pathogenesis, we integrated serum proteomics with spatial transcriptomic analyses to identify circulating biomarkers reflective of muscle pathology.

Methods. Serum samples from 39 IBM, 36 polymyositis, and 13 healthy controls were analysed using Olink proximity extension assays (Inflammation Panels I & II, Reveal, and Cardiometabolic) to quantify 1,782 proteins. Statistical modelling adjusted for age and sex identified differentially expressed proteins and pathway enrichment was performed using GSEA. Predictive models were developed using lasso logistic regression.

Subcellular spatial transcriptomics was performed on 13 muscle biopsies (4 IBM, 6 non-IBM myositis, 3 controls) using the Xenium 5K panel. Spatial expression patterns were analysed using FICTURE, a segmentation-free method suited for complex tissue architecture.

Results. Differential expression analyses identified 992 serum proteins differing across groups and 459 differing between IBM and polymyositis. Enrichment analysis highlighted adaptive immunity, leucocyte proliferation, lymphocyte activation, immune effector regulation and cell adhesion as dominant IBM pathways.

Lasso regression identified a 14-protein signature (KLRK1, LY9, CRTAM, ADAM22, NME3, ENG, PAM, AGER, FCRL2, EVL, IL31RA, DDC, CLEC6A, AK1) that optimally discriminated IBM from polymyositis (AUC = 0.795). These proteins collectively reflect cytotoxic and adaptive immune activation, innate and stromal signalling, and mitochondrial-metabolic processes as characteristic of IBM.

Spatial transcriptomics demonstrated transcriptional upregulation of KLRK1 and CLEC6A within floridly diseased IBM muscle. KLRK1 localised to cytotoxic T cells expressing IFNG and granzyme transcripts, while CLEC6A co-localised with macrophage markers CD68/CD163 and chemokines CCL13/CCL18, consistent with M2-like macrophages driving tissue remodelling. FICTURE identified a KLRK1 ligand (ULBP2) expressed within stressed myofibres in IBM and anti-synthetase muscle. Xenium data also revealed KLRK1 ligands MICA and MICB within diseased muscle. ENG was broadly expressed within muscle samples, but co-localised with vascular stress/remodelling in inflamed samples.

Conclusions. Serum proteomic analyses identified a novel 14-protein signature distinguishing IBM from polymyositis, offering a potential diagnostic biomarker and providing mechanistic insight into disease pathogenesis. Spatial transcriptomic validation confirmed upregulation of KLRK1 and CLEC6A within diseased IBM muscle. Detection of ULBP2, MICA and MICB transcripts in affected muscle suggests KLRK1-mediated immune recognition of stressed myofibres in IBM. CLEC6A expression within macrophage-enriched regions underscores chronic tissue remodelling and immune recruitment as integral features of IBM muscle pathology.

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Key words: inclusion body myositis, polymyositis, proteomics, Olink, biomarkers, spatial transcriptomics, Xenium, multiomics

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PHASE 2/3 STUDY OF ULVIPRUBART IN INCLUSION BODY MYOSITIS: STUDY DESIGN, PATIENT CHARACTERISTICS, AND TOPLINE RESULTS

Namita A. Goyal[1], Pedro M. Machado[2,3], Dana P. Ascherman[4], Olivier Benveniste[5], Said R. Beydoun[6], Thomas H. Brannagan III[7], James Caress[8], Lisa Christopher-Stine[9], Michael P. Collins[10], Jan L. De Bleecker[11], Mazen Dimachkie[12], Stacy Dixon[13], Alex Dmitrienko[14], David R. Fernandez[15], Miriam Freimer[16], Christopher Geiger[17], Paloma Gonzalez-Perez[18], Neelam Goyal[19], Kelly Gwathmey[20], Daragh Heitzman[21], Robert Henderson[22,23], Lisa D. Hodson-Webb[24], Yessar Hussain[25], Lawrence Korngut[26], Christina Liang[27,28,29], James B. Lilleker[30,31], Thomas Lloyd[32,33,34], Payam Mohassel[35], Elie Naddaf[36], Merrilee Needham[37,38,39], Ezequiel Piccione[40], Colin C. Quinn[41], Laura Rosow[42], Bhaskar Roy[43], Tobias Ruck[44,45], Jens Schmidt[46,47], Arjun Seth[48], Jaimin Shah[49], Aziz Shaibani[50], Perry B. Shieh[51], Zachary Simmons[52], Kumaraswamy Sivakumar[53], Leo H. Wang[54], Conrad C. Weihl[55], H. Jeffrey Wilkins[56], Anthony A. Amato[57]

[1]Department of Neurology, University of California Irvine, Orange, USA, [2]Department of Neuromuscular Diseases, UCL Queen Square Institute of Neurology, University College London, London, UK, [3]NIHR University College London Hospitals Biomedical Research Centre, University College London Hospitals NHS Foundation Trust, London, UK, [4]Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, USA, [5]Department of Internal Medicine and Clinical Immunology, Pitié-Salpêtrière University Hospital, Sorbonne Université, AP-HP, Paris, France, [6]University of Southern California, Los Angeles, USA, [7]Neurological Institute, Columbia University Medical Center, New York, USA, [8]Wake Forest University School of Medicine, Winston-Salem, USA, [9]Johns Hopkins University School of Medicine, Baltimore, USA, [10]Medical College of Wisconsin, Milwaukee, USA, [11]Department of Neurology and Neuromuscular Reference Center, Ghent University Hospital, Ghent, Belgium, [12]Department of Neurology, The University of Kansas Medical Center, Kansas City, USA, [13]University of Colorado, Aurora, USA, [14]Department of Biostatistics, Mediana, San Juan, USA, [15]Department of Rheumatology, Hospital for Special Surgery, New York, USA, [16]Department of Neurology, The Ohio State Wexner Medical Center, Columbus, USA, [17]University Hospitals-Cleveland Medical Center, Case Western Reserve University, Cleveland, USA, [18]Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, USA, [19]Stanford Neuroscience Health Center, Palo Alto, USA, [20]Department of Neurology, Virginia Commonwealth University, Richmond, USA, [21]Texas Neurology, Dallas, USA, [22]Department of Neurology, Royal Brisbane and Women's Hospital, Brisbane, Australia, [23]Centre for Clinical Research, University of Queensland, Brisbane, Australia, [24]Neuromuscular Division/Department of Neurology, Duke University, Durham, USA, [25]Austin Neuromuscular Center, Austin, USA, [26]Hotchkiss Brain Institute, Department of Clinical Neurosciences, Cumming School of Medicine, University of Calgary, Alberta, Canada, [27]Faculty of Medicine and Health, University of Sydney, Camperdown, New South Wales, Australia, [28]Department of Neurology, Royal North Shore Hospital, Northern Sydney Local Health District, Sydney, New South Wales, Australia, [29]Neuroscience Research Australia, Sydney, New South Wales, Australia, [30]Manchester Centre for Clinical Neurosciences, Northern Care Alliance NHS Foundation Trust, Salford, UK, [31]The University of Manchester, Manchester, UK, [32]Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, USA, [33]Department of Neurology, Baylor College of Medicine, Houston, USA, [34]Department of Clinical Research, Imricor Medical Systems, Burnsville, USA, [35]Department of Neurology, Mayo Clinic, Rochester, USA, [36]Perron Institute, QEII Medical Centre, Nedlands, Western Australia, Australia, [37]University of Notre Dame, Perth, Western Australia, Australia, [38]Fiona Stanley Hospital, Perth, Western Australia, Australia, [39]Murdoch University, Perth, Western Australia, Australia, [40]Department of Neurology, University of Nebraska Medical Center, Omaha, USA, [41]Neuromuscular Division, Neurology Department, University of Pennsylvania, Philadelphia, USA, [42]University of California San Francisco, San Francisco, USA, [43]Department of Neurology, Yale School of Medicine, New Haven, USA, [44]Ruhr University Bochum, BG-University Hospital Bergmannsheil Department of Neurology, Bochum, Germany, [45]Heimer Institute for Muscle Research, BG-University Hospital Bergmannsheil Department of Neurology, Bochum, Germany, [46]Department of Neurology, Neuromuscular Center, University Medical Center Göttingen, Göttingen, Germany, [47]Department of Neurology and Pain Treatment, Neuromuscular Center, Center for Translational Medicine, Immanuel University, Hospital, Brandenburg Medical School, Rüdersdorf bei Berlin, Germany, [48]Department of Neurology, Northwestern Memorial Hospital, Chicago, USA, [49]Department of Neurology, Mayo Clinic, Jacksonville, USA, [50]Nerve and Muscle Center of Texas, Houston, USA, [51]Department of Pediatrics, University of California Los Angeles, Los Angeles, USA, [52]Department of Neurology, Penn State University College of Medicine, Hershey, USA, [53]The Neuromuscular Research Centre and Neuromuscular Clinic of Arizona, Phoenix, USA, [54]Department of Neurology, University of Washington, Seattle, USA, [55]Department of Neurology, Washington University in St Louis, St. Louis, USA, [56]Abcuro, Inc., Newton, USA, [57]Brigham and Women's Hospital, Harvard Medical School, Boston, USA

Objective. Describe the study design and results of a phase 2/3 study of ulviprubart for treatment of inclusion body myositis (IBM).

Background. IBM is a rare, progressive disorder characterized by invasion of muscle by highly differentiated cytotoxic CD8+ T cells. IBM can cause difficulty walking, loss of grip strength, and dysphagia. There are no pharmacological treatments approved for IBM. Ulviprubart, a humanized mono-

clonal antibody, selectively depletes cytotoxic CD8+ KLRG1+ T cells by targeting KLRG1 expressed on most IBM-muscle–infiltrating T cells.
Design/Methods. This randomized, double-blind, placebo-controlled trial (NCT05721573) included patients aged ≥40 years with an IBM diagnosis otherwise fulfilling 2011 European Neuromuscular Center criteria. Ulviprubart (0.5 or 2.0 mg/kg) or placebo (1:1:1) was administered subcutaneously every 8 weeks for 76 weeks, with the option to receive treatment at 2.0 mg/kg in an open-label extension study. Efficacy endpoints included mean changes from baseline to week 76 in Inclusion Body Myositis Functional Rating Scale (IBMFRS; primary), manual muscle testing (MMT) of 23 muscle groups converted to a Kendall score, hand grip and quadriceps strength by dynamometry, and modified Timed Up and Go (mTUG). Safety monitoring included assessment of treatment-emergent adverse events.
Results. Overall, 272 patients were enrolled. Mean (SD) patient age at baseline was 68.1 (7.8) years, and 186 patients were male (68%). Mean (SD) age at diagnosis was 65.1 (8.1) years. Mean (SD) baseline IBMFRS score was 27.3 (5.0); 14 patients had baseline IBMFRS scores of <20, 63 had scores of 20–24, and 195 had scores of ≥25. Mean (SD) baseline values for MMT, grip strength (dominant), quadriceps strength (dominant), and mTUG score were 7.8 (1.2), 11.7 (7.0) kg, 11.0 (7.6) kg, and 0.32 meters/second, respectively.
Conclusions. This is the largest prospective interventional study of patients with IBM with a range of clinically significant disease burden. Topline efficacy and safety results will be presented.
Key words: interventional study, clinical trial

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IMMUNE-MYOFIBER SIGNALING NETWORKS DRIVE INFLAMMATION AND TISSUE REMODELING IN INCLUSION BODY MYOSITIS

Thorge Dobbertin[1,2], Sven Wischnewski[1], Hannah Kempf[1], Joelle Olivia Vogelmann[1], Hans-Werner Rausch[1], Lucas Schirmer[1,3,4]
[1]Division of Neuroimmunology, Department of Neurology, Medical Faculty Mannheim at Heidelberg University, Mannheim, Germany, [2]Faculty of Biosciences, Heidelberg University, Heidelberg, Germany, [3]Interdisciplinary Center for Neurosciences (IZN), Heidelberg University, Heidelberg, Germany, [4]Mannheim Center for Translational Neuroscience (MCTN) and Institute for Innate Immunoscience (MI3), Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany

Background. IBM presents a complex inflammatory environment characterized by sustained chronic damage and infiltration of immune cells. While traditional analyses have started to reveal the cellular composition and transcriptional states of the affected muscle, they often overlook the intercellular signalling processes within the muscle microenvironment that coordinate and perpetuate this pathology. To identify molecular drivers, it is crucial to capture immune-myofiber interactions and how signals propagate into downstream transcriptional responses.
Methods. We integrated previously published (Wischnewski *et al*., 2024) single-nucleus RNA sequencing and spatial transcriptomic data from IBM muscle biopsies. Cell-cell communication was inferred using LIANA to identify ligand-receptor pairs, focusing on immune and myofiber populations. NicheNet was used to predict downstream target genes in receiver cells, such as myofibers, while RIDDEN-derived receptor activity scores were applied to validate and refine ligand-target predictions. Comparative analyses were performed across IBM, healthy controls, and IMNM to identify disease-specific signaling changes.
Results. We observed a shift in macrophage populations from dormant resident states toward activated, pro-inflammatory phenotypes. Our computational framework jointly highlighted the activation of gene programs related to antigen processing and presentation, leukocyte recruitment, and integrin-mediated adhesion in myofibers. These pathways were most prominent in damaged myofiber subsets, suggesting focal immune-muscle crosstalk. Spatial transcriptomic mapping confirmed colocalization of involved immune cells with more active myofibers as well as molecular gradients, indicating localized niches within inflammation zones.
Conclusions. We uncovered a coordinated network of immune-myofiber interactions correlated with inflammation and tissue remodeling in IBM. Integrating complementary computational tools for ligand–receptor inference and downstream target prediction provides a robust framework to dissect immune dysregulation. This displays how infiltrating immune cells are recruited, activated, and sustained through cross-talk with activated myofibers.
Key words: cell-cell communication, single-nucleus RNA sequencing, computational biology

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O-296

INCREASED SENSITIVITY OF IBM-ASSOCIATED ANTI-CN1A/ANTI-NT5C1A AUTOANTIBODY DETECTION BY IMMUNOFLUORESCENCE

Ger Pruijn[1], Fleur Brinkman[1], Isa Verlangen[1], Filine Swets[1]
[1]Radboud University, Nijmegen, Netherlands

Background. Anti-cN1A (anti-NT5C1A) autoantibodies are frequently found in the sera of inclusion body myositis (IBM) patients. Various methods have been developed for the detection of anti-cN1A autoantibodies (1). These assays have a wide range of sensitivity and specificity. Here, we report the development of an assay that takes advantage of the perinuclear accumulation of the GFP-cN1A fusion protein in HEp-2 cells to detect anti-cN1A autoantibodies.
Methods. Transiently transfected HEp-2 cells expressing a GFP-cN1A fusion protein were fixed and incubated with patient sera, followed by fluorescent secondary antibodies. Strong antibody signals co-localizing with the filamentous GFP-cN1A accumulations are indicative of anti-cN1A reactivity in the sera. Anti-cN1A reactivity in the same samples was also assessed by full-length recombinant protein and cN1A-derived synthetic peptide ELISAs (2).
Results. We analyzed anti-cN1A reactivity in the sera from IBM (n=82), dermatomyositis (DM, n=34), polymyositis (PM, n=60), systemic lupus erythematosus (SLE, n=28), and Sjögren's syndrome (SjS, n=19) patients and from healthy individuals (n=35) using the GFP-cN1A-based immunofluorescence assay. In 59% of the IBM sera anti-cN1A autoantibodies were detected using this assay, whereas only 7% of the non-IBM samples were anti-cN1A positive. Using the same sera, the full-length protein and synthetic peptides ELISAs resulted in a significantly lower fraction of reactive samples, 38% anti-cN1A-positive in both assays, even though the specificity of the immunofluorescence assay (93%) was higher than that of the ELISA assays (91% and 87%, respectively).
Conclusions. A highly sensitive and specific immunofluorescence assay was developed for the detection of anti-cN1A autoantibodies in patient sera. The higher sensitivity compared to protein/peptide ELISA assays (59% *vs*. 38%) suggests that the detection of anti-cN1A autoantibodies by cN1A presented in a cellular context is superior to assays based on antigenic molecules immobilized on a solid surface.

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O-302

GENOME-WIDE ASSOCIATION STUDY IDENTIFIES NOVEL RISK LOCI FOR INCLUSION BODY MYOSITIS

Nathan Routledge[1], Alaa Khan[1], Iwona Skorupinska[1], Conceição Bettencourt[2], Jana Vandrovcova[1], Matteo Zanovello[1], Ashirwad Merve[3], Qiang Gang[4], Sara Nagy[5], Michael Sinnreich[5], Christina Liang[6], Jerome Coudert[7], Merrilee Needham[7], Mridul Johari[8], Jan L. De Bleecker[9], Boel De Paepe[9], Willem De Ridder[10], Jonathan Baets[10], Edmar Zanoteli[11], Damien Amelin[12], Chrysa Chrysovitsanou[13], Miren Zulai[14], Dario Dattilo[1], Francesca Paron[15], Paola Tonin[16], Giulia Marchetto[16], Gaetano Vattemi[16], Maurizio Romano[17], Emanuele Buratti[15], Gianni Soraru[18], Marina Mora[19], Corrado Angelini[20], Michela Ripolone[21], Diego Lopergolo[22], Anders Oldfors[23], Ambreen Tariq[24], Aleksandar Radunovic[24], Kathryn Walker[25], Stefen Brady[26], Hector Chinoy[27], James B. Lilleker[27], Dawn Caraballo[28], Anthony Amato[29], Tom Loyd[30], Perry Shieh[31], Brianna Blume[32], Matthew P. Wicklund[33], Richard J. Barohn[34], Jeffrey Guptil[35], Linda Carter[36], Elie Naddaf[37], Aziz Shaibani[38], Heidi Runk[39],

Mazen M. Dimachkie[40], Amy Bartlett[41], John Kissel[41], Marinos Dalakas[42], Tahseen Mozaffar[43], Namita A. Goyal[43], Olimpia M. Carbunar[44], Conrad C. Weihl[45], Andrew B. Singleton[46], Pietro Fratta[1], Janine A. Lamb[47], Michael G. Hanna[1], Henry Houlden[1], Pedro M. Machado[1]

[1]Department of Neuromuscular Diseases, UCL Queen Square Institute of Neurology, University College London, London, UK, [2]Department of Neurodegenerative Disease, UCL Queen Square Institute of Neurology, University College London, London, UK, [3]Department of Neuropathology, UCL Queen Square Institute of Neurology, University College London, London, UK, [4]Department of Neurology, Peking University First Hospital, Beijing, China, [5]Department of Neurology, University Hospital Basel, University of Basel, Basel, Switzerland, [6]Department of Neurology, Royal North Shore Hospital, New South Wales, Australia, [7]Western Australian Neurosciences Research Institute (WANRI), University of Western Australia & Murdoch University; Fiona Stanley Hospital, Perth, Australia, [8]Harry Perkins Institute of Medical Research, Centre for Medical Research, University of Western Australia, Perth, Australia, [9]Department of Neurology and Neuromuscular Reference Centre, Ghent University Hospital, Ghent, Belgium, [10]Department of Neurology, Neuromuscular Reference Centre, University Hospital of Antwerp, Antwerp, Belgium, [11]Department of Neurology, Medical School of the University of São Paulo (FMUSP), São Paulo, Brazil, [12]Sorbonne University, Paris, France, [13]National University of Athens Medical School, Athens, Greece, [14]Department of Neurology and Neurosciences, Donostia University Hospital & Biogipuzkoa Health Research Institute, Donostia-San Sebastián, Spain, [15]International Centre for Genetic Engineering and Biotechnology, Italy, [16]Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy, [17]Department of Life Sciences, University of Trieste, Trieste, Italy, [18]Department of Neurology, University of Padua, Padua, Italy, [19]Neuromuscular Diseases and Neuroimmunology Unit, Fondazione IRCCS Istituto Neurologico C. Besta, Milan, Italy, [20]Neuromuscular Unit, BioBank of Skeletal Muscle, Nerve Tissue, DNA & cell lines, Italy, [21]Neuromuscular Unit, IRCCS Foundation Ca' Granda Ospedale Maggiore Policlinico; Dino Ferrari Centre, University of Milan, Milan, Italy, [22]Department of Medicine, Surgery and Neurosciences, University of Siena, Siena, Italy, [23]Sahlgrenska University Hospital, Gothenburg, Sweden, [24]Department of Clinical Neurosciences, Barts Health NHS Trust, London, UK, [25]Clinical Ageing Research Unit, The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle , UK, [26]Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, Oxford, UK, [27]Manchester Centre for Clinical Neuroscience, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [28]Cleveland Clinic, Cleveland, USA, [29]Department of Neurology, Brigham and Women's Hospital, Boston, USA, [30]Department of Neurology, Baylor College of Medicine, Houston, USA, [31]Department of Neurology, University of California, Los Angeles, Los Angeles, USA, [32]Department of Neurology, University of Colorado School of Medicine, Aurora, USA, [33]Department of Neurology, University of Texas at San Antonio, San Antonio, USA, [34]Department of Neurology, University of Missouri, Columbia, USA, [35]Duke University Medical Center, Durham, USA, [36]KUMC Nerve and Muscle Centre of Texas, USA, [37]Department of Neurology, Mayo Clinic, Rochester, USA, [38]Nerve and Muscle Center of Texas , Houston, USA, [39]Penn State Hershey Medical Center, Hershey, USA, [40]University of Kansas Medical Center, Kansas City, USA, [41]The Ohio State University Wexner Medical Center, Columbus, USA, [42]Thomas Jefferson University, Philadelphia, USA, [43]University of California Irvine Neuromuscular & ALS Center, Orange, USA, [44]University of Miami Miller School of Medicine, Miami, USA, [45]Washington University School of Medicine, St. Louis, USA, [46]Global Parkinson's Genetics Program, Chevy Chase, USA, [47]Epidemiology & Public Health Group, School of Health Sciences, University of Manchester, Manchester, UK

Background. Inclusion Body Myositis (IBM) is a distinct subtype of idiopathic inflammatory myopathies (IIM), characterised by both inflammatory and degenerative muscle pathology. Despite its clinical relevance, IBM has historically been underrepresented in genetic studies, often included only as a minor subset within broader IIM analyses. This study presents the first genome-wide association study (GWAS) dedicated specifically to IBM, aiming to identify novel genetic risk loci and provide insights into disease mechanisms.

Methods. A total of 1,184 IBM patient samples were genotyped and 5,614 controls were analysed. Following rigorous quality control and sex-ratio matching (male:female = 6:4), 1,036 IBM cases of European ancestry were retained, and matched with 4,240 controls. IBM samples were collected through the International IBM Genetics Consortium, under the Neuromuscular Study Group (NMSG). Controls were sourced from the Wellcome Trust Case Control Consortium (WTCCC) and the National Blood Survey cohort. Genotype imputation was followed by single-variant association testing using the Scalable and Accurate Implementation of Generalised Mixed Model (SAIGE). Downstream analyses included gene-set enrichment, pathway analysis, co-localisation (comparison with MYOGEN dataset), and functional prediction. Finally, GWAS hits were cross-referenced with published IBM muscle tissue RNA-seq data (GSE151758) to assess overlap with differentially expressed genes.

Results. The strongest association was observed at the HLA-DRB1 locus. Four novel non-HLA loci reached genome-wide significance: AHRR, CD200, RMI2, and ORMDL3, as well as previous IIM associated loci PTPN22 and SH2B3/ATXN2 confirmed via co-localisation analysis. Multimarker Analysis of GenoMic Annotation (MAGMA) analysis identified additional significant associations with the genes SCHIP1, GSDMB and PDCD6. Functional annotation revealed enrichment of lead SNPs within regulatory regions for skeletal muscle and immune cells. RNA-seq analysis highlighted IKZF3 (within the ORMDL3 locus) as the only gene within genome-wide significant loci that was also among the most differentially expressed in IBM muscle tissue.

Conclusions. This GWAS identifies novel genetic risk loci for IBM and highlights IKZF3 as a potential key contributor to disease pathogenesis, bridging genetic susceptibility with transcriptional dysregulation in affected muscle tissue. These findings provide new insights into IBM pathogenesis and highlight potential molecular targets for future therapeutic development.

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Key words: inclusion body myositis, GWAS, genetics, pathogenesis, juvenile myositis

O-100

VALIDATION OF GALECTIN-9 AND CXCL10 AS PREDICTIVE BIOMARKERS FOR DISEASE FLARES IN JUVENILE DERMATOMYOSITIS

Saskia Veldkamp[1,2], Julia Drylewicz[2], Yeo Joo Guan[3,4], Thomas Moreau[5], Diego Bletry[5], Kai Liang Teh[4], Judith Wienke[2], Sebastiaan Vastert[1], Joost Swart[1], Erika Van Nieuwenhove[1], Wineke Armbrust[6], Merlijn Van Den Berg[7], Petra Hissink Muller[8], Esther Hoppenreijs[9], Sylvia Kamphuis[10], Ellen Schatorjé[9], Isabelle Melki[11], Mathieu Rodero[12], Thaschawee Arkachaisri[4], Brigitte Bader-Meunier[11], Brian Feldman[13], Annet Van Royen-Kerkhof[1], Femke Van Wijk[2], Marc Jansen[1]

[1]Department of Paediatric Rheumatology and Immunology, University Medical Center Utrecht, Wilhelmina Children's Hospital, Utrecht, The Netherlands, [2]Center for Translational Immunology, University Medical Center Utrecht, Utrecht, The Netherlands, [3]Translational Immunology Institute, SingHealth Duke-NUS Academic Medical Centre, Singapore, Singapore, [4]KK Women's and Children's Hospital, Singapore, Singapore, [5]Laboratoire de Chimie et de Biochimie Pharmacologiques et Toxicologiques UMR8601, CNRS , Paris, France, [6]Department of Paediatric Rheumatology and Immunology, University Medical Center Groningen, Groningen, The Netherlands, [7]Department of Paediatric Immunology, Rheumatology and Infectious Diseases, Amsterdam University Medical Centres, location AMC, Emma Children's Hospital, Amsterdam, Amsterdam, The Netherlands, [8]Department of Paediatric Rheumatology, Leiden University Medical Centre, Willem Alexander Children's Hospital, Leiden, The Netherlands, [9]Department of Paediatric Rheumatology, Radboud University Medical Centre, Amalia Children's Hospital, Nijmegen, The Netherlands, [10]Department of Paediatric Rheumatology, Erasmus University Medical Centre, Sophia Children's Hospital, Rotterdam, The Netherlands, [11]Paediatric Haematology-Immunology and Rheumatology Department, Necker-Enfants Malades Hospital, AP-HP, Paris, France, [12]Laboratoire de Chimie et de Biochimie Pharmacologiques et Toxicologiques UMR8601, CNRS, Paris, France, [13]Division of Rheumatology & Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, Canada

Background. Juvenile dermatomyositis (JDM) is a rare, heterogeneous autoimmune disease with an unpredictable disease course; approximately half of affected children experience recurrent or persistent disease activity. Reliable biomarkers to predict impending flares are urgently needed to guide individualized treatment and prevent long-term damage. Interferon-induced biomarkers Galectin-9 and CXCL10 have previously been identified as robust markers of disease activity in JDM and may serve as potential prognostic indicators. Our aim is to validate Galectin-9 and CXCL10 as biomarkers predictive of disease flare in an international JDM cohort.

Methods. Galectin-9 and CXCL10 concentrations were measured in over 1,100 longitudinal serum or plasma samples collected from 158 patients across four countries. Biomarker trajectories during the two years preceding a flare were compared with trajectories in patients who remained clinically stable. A flare was defined as a treatment intensification prompted by worsening disease activity. Joint latent class mixed models (jointLCMM) were used to jointly analyze biomarker trajectories and time to flare. Models with one to five latent classes were fitted, and the optimal structure was selected using the Bayesian Information Criterion (BIC). Mean posterior probabilities assessed class assignment accuracy. Additionally, Cox proportional hazards models quantified flare risk per $\log_2$ increase in biomarker levels and for combined biomarker elevations.

Results. Both Galectin-9 and CXCL10 began to increase approximately one year prior to flare, while remaining low in patients without flares. In contrast, creatine kinase (CK) rose only during the final four months before flare. For

both biomarkers, three latent classes were identified. For Galectin-9, two classes showed elevated trajectories (representing 4% and 16% of patients, respectively) and were associated with a high flare risk (100% and 89%). For CXCL10, we found very similar results. In the Cox proportional hazards models, each $\log_2$ increase (*i.e.* a doubling) in Galectin-9 and CXCL10 conferred hazard ratios for flare of 2.9 (95% CI 2.3–3.7) and 2.4 (2.0–2.9), respectively (p<0.001). Galectin-9 was not associated with an increased risk of skin-only flares. Combined elevations of Galectin-9 and CXCL10 above the 75th percentile yielded a hazard ratio of 10.1 (4.8–21.1, p<0.001), with a 30% flare rate within 6 months.

Conclusions. In this large international prospective JDM cohort, rising Galectin-9 and CXCL10 levels strongly predicted disease flares within one year, preceding conventional markers. Combining both biomarkers substantially improved risk stratification. These findings support the use of Galectin-9 and CXCL10 to guide treatment tapering and pre-emptive intervention in children with JDM.

Key words: juvenile dermatomyositis, biomarkers, prediction models, interferon

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LONGITUDINAL SINGLE CELL TRANSCRIPTOMIC ANALYSIS OF TYPE I AND II INTERFERON (IFN) RESPONSE GENES (IRG) IN REFRACTORY JUVENILE DERMATOMYOSITIS (JDM) PATIENTS WITH BARICITINIB TREATMENT

Jessica Simpson[1], Vicky Chen[2], Adeline Chin[1], Ujana Zajmi[1], Amy Kaneshiro[1], Megan Darrell[1], Stephen Brooks[3], Faiza Naz[4], Robert A. Colbert[5], Lisa Rider[6], Stefania Dell'Orso[4], Hanna Kim[1]

[1]Juvenile Myositis Pathogenesis and Therapeutics Unit (JMPTU), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, USA (USA), [2]Integrated Data Sciences Section, Research Technologies Branch, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, USA, [3]Biodata Mining and Discovery Section, NIAMS, NIH, Bethesda, USA, [4]Genomic Technology Section, NIAMS, NIH, Bethesda, USA, [5]Pediatric Translational Research Branch, NIAMS, NIH, Bethesda, USA,[6]Environmental Autoimmunity Group, National Institute of Environmental Health Sciences (NIEHS), NIH, Bethesda, USA

Background. JDM pathogenesis is incompletely understood, though dysregulated type I/II IFN signaling is well-documented. Refractory JDM patients had clinical improvement on janus kinase inhibition (baricitinib) (Kim, 2021), which inhibits IFN-signaling. This study aimed to assess cell-specific changes in IFN-signaling with treatment.

Methods. Peripheral blood mononuclear cells from 4 refractory JDM patients before and after baricitinib treatment (week 0, 4, 24, 72) were analyzed by single-cell RNA-seq (10X Genomics). Data was processed with Seurat (R), with Azimuth (R) cell type annotation. Cell types with <30 cells were excluded from analysis. Three "IFN-scores" (hallmark IFN-alpha response (IRG-alpha), hallmark IFN-gamma response (IRG-gamma) (both from https://www.gsea-msigdb.org), validated interferonopathy 28 IFN-regulated genes (IRG-28) (Kim, 2018)) were analyzed by Seurat module score (R), comparing individual baseline to follow-up timepoints by Wilcoxon rank sum test with Bonferroni correction.

Results. Samples were collected from JDM patients (n=4) 5.8–20.7 years old, 75% female, 50% Caucasian, 2 each with anti-TIF-1 and anti-NXP2 autoantibodies.

By cell type across patients and timepoints, the most frequent significant decreases in IFN-score were in CD4 central memory T (TCM) cells (97% overall, 12/12 IRG-alpha, 11/12 IRG-gamma, 12/12 IRG-28) and CD8 naïve cells (94% overall, 11/12 IRG-alpha, 12/12 IRG-gamma, 11/12 IRG-28). Mucosal-Associated Invariant T (MAIT) cells (64% overall, 8/11 IRG-alpha, 9/11 IRG-gamma, 4/11 IRG-28) and CD14 monocytes (78% overall, 8/9 IRG-alpha, 8/9 IRG-gamma, 5/9 IRG-28) had the least frequent significant decreases. By patient, significant IFN-score decreases across cell types and timepoints ranged from 40/54 (74%) to 39/42 (93%). By timepoint, significant decreases in IFN-score ranged from 83% (19/22 IRG-alpha, 18/22 IRG-gamma, 18/22 IRG-28) at timepoint 4 (T4, 72 weeks) to 86% (18/22 IRG-alpha, 22/22 IRG-gamma, 17/22 IRG-28) at T3 (24 weeks). IRG-gamma score had the most frequent significant decreases (58/65, 89%), while IRG-28 had the least (52/65, 80%). One patient had significant increases in score at T4 CD14 monocytes (IRG-alpha, IRG-gamma) and B-cells (IRG-gamma).

Conclusions. Refractory JDM patients had decreases in 3 IRG scores (alpha, gamma, 28) in most peripheral cell types at most timepoints (4-72 weeks) on baricitinib. CD4 TCM cells were the most sensitive to baricitinib (most frequent significant decreases in IFN-scores), while MAIT cells were the least sensitive (least frequent significant decreases in IFN-scores). IRG-gamma score was the most sensitive to baricitinib while IRG-28 score was the least. Type I and II IFN-regulated gene scores decreased in multiple cell types on baricitinib, correlating with clinical response.

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Key words: baricitinib, single cell RNA-sequencing, type I/II interferons

Other

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UNDERSTANDING RELAPSE IN IDIOPATHIC INFLAMMATORY MYOPATHIES: INSIGHTS FROM A MULTICENTRIC INTERNATIONAL COHORT

Maria Rosa Pellico[1,2], Cristina Bochicchio[1,2], Claudia Iannone[1,2], Silvia Cavalli[1,2], Lekshmi Minikumari Rahulan[3], Marco Fornaro[11], Ilaria Cavazzana[9], Edoardo Conticini[10], Masataka Kuwana[4], Akira Yoshida[4], Silvia Grazzini[10], Florenzo Iannone[11], Vikas Agarwal[3], Roberto Caporali[1,2], Nicoletta Del Papa[1,2], Latika Gupta[5,6,7,8]

[1]ASST-Gaetano Pini CTO, Milan, Italy, [2]University of Milan, Milan, Italy, [3]Department of Clinical Immunology and Rheumatology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, [4]Department of Allergy and Rheumatology, Nippon Medical School, Tokyo, Japan, [5]Department of Rheumatology, The Royal Wolverhampton NHS Trust, Wolverhampton, UK, [6]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham, Birmingham, UK, [7]Division of Musculoskeletal and Dermatological Sciences, Centre for Musculoskeletal Research, School of Biological Sciences, The University of Manchester, Manchester, UK, [8]Francis Crick Institute, London, UK, [9]Rheumatology and Clinical Immunology, ASST Spedali Civili di Brescia, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy, [10]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University of Siena, Siena, Italy, [1]Interdisciplinary Department of Medicine, Rheumatology Unit, Policlinico di Bari, Bari, Italy

Background. Relapse remains a major challenge in idiopathic inflammatory myopathies (IIMs), yet its definition and predictors are poorly characterized across studies. This study aimed (1) to identify baseline clinical, serological, and laboratory predictors of relapse, and (2) to assess the influence of treatment strategies – steroid induction dose, immunosuppressants, and intravenous immunoglobulins (IVIG) – on relapse risk and timing.

Methods. This retrospective, multicentre study included 239 adults with IIM – dermatomyositis (DM), polymyositis (PM), antisynthetase syndrome (ASyS), immune-mediated necrotizing myopathy (IMNM), and overlap myositis (CTD-IIM) – from seven centres in Italy, the UK, India, and Japan, each with ≥2 years of follow-up. All patients met the 2017 EULAR/ACR classification criteria. Cancer-associated IIM and inclusion body myositis were excluded.

Relapse was defined as physician-documented clinical deterioration requiring escalation of immunosuppressive and/or glucocorticoid therapy. Clinical and laboratory characteristics were compared using chi-square, Mann-Whitney U, or Student's t-test. Predictors of relapse were identified through multivariable logistic regression. To explore relapse heterogeneity, an unsupervised hierarchical cluster analysis integrated clinical, serological, and therapeutic variables. Statistical analyses were performed in Python 3.12.10.

Results. Relapses occurred in 137 of 239 patients (57.3%). Relapsers exhibited higher baseline aldolase (37.6 *vs*. 12.1 U/L, p<0.001), CPK (3436 *vs*. 2174 U/L, p=0.029), PhGA (4.38 *vs*. 3.34, p=0.007), and PtGA (5.02 *vs*. 3.59, p=0.04). Gastrointestinal (19.7% *vs*. 9.8%, p=0.036) and systemic involvement (19.0% *vs*. 9.8%, p=0.031) were also more frequent among relapsers.

Independent predictors of relapse included elevated baseline CPK (OR 1.89, p=0.013), non-classic cutaneous involvement (OR 3.69, p=0.042), extramuscular manifestations (OR 3.11, p=0.016), and IVIG use (OR 4.40, p=0.022). Induction with corticosteroids >1 mg/kg/day reduced relapse risk (OR 0.24, p=0.001). Cluster analysis identified two major endotypes among relapsers and non-relapsers: (1) ASyS-dominant extramuscular phenotypes with high ILD and Ro52 prevalence, and (2) DM-dominant, muscle-predominant phenotypes (Mi-2/TIF1γ). Treatment tendencies mirrored these phenotypes: IVIG was concentrated in relapsers (q=0.036)—whereas high-dose steroid induction was most common in non-relapsers (Δ=+22.1 pp, q=0.045); the timing of steroid initiation was similar across groups.

Conclusions. In this international, multicentre cohort, relapses occurred in nearly two-thirds of patients within two years of diagnosis. High baseline

enzyme activity, extramuscular burden, and non-classic cutaneous involvement were associated with increased relapse risk, whereas high-dose steroid induction (>1 mg/kg/day) appeared protective. These findings highlight the need for phenotype-guided, autoantibody-informed relapse prevention strategies in IIM.

Key words: myositis, relapse, predictors

Pathogenesis of Inflammatory Myopathy

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INFLAMMATORY PREDICTORS OF RITUXIMAB RESISTANCE IN REFRACTORY MYOSITIS: RESULTS FROM THE MYOPROSP STUDY

Xia Lyu[1,2,3], Shraddha Rane[1,20], Patrick Gordon[4], Harsha Gunawardena[5], Neil McHugh[6], Athiveeraramapandian Prabu[7], Peter Lanyon[8], James Miller[9], Voon Ong[10], Anthony Isaacs[11], Chee-Seng Yee[12], Caroline Cotton[13], Patrick Kiely[14], Eleni Stathopoulou[15], James Taylor[16], Rachel Jeffery[16], Anurag Bharadwaj[17], Paul New[1], James Lilleker[1,18], Janine Lamb[3], Hector Chinoy[1,19,20]

[1]Division of Musculoskeletal and Dermatological Sciences, University of Manchester, Manchester, UK, [2]Department of Rheumatology, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China, [3]Epidemiology and Public Health Group, School of Health Sciences, University of Manchester, Manchester, UK, [4]Department of Rheumatology, King's College Hospital NHS Foundation Trust, London, UK, [5]Department of Rheumatology, North Bristol NHS Trust, and Academic Rheumatology, University of Bristol, Bristol, UK, [6]Department of Life Sciences, University of Bath, Bath, UK, [7]Department of Rheumatology, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, UK, [8]Department of Rheumatology, Nottingham University Hospitals NHS Trust, and Lifespan and Population Health, School of Medicine, University of Nottingham, Nottingham, UK, [9]Department of Neurology, Royal Victoria Infirmary, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK, [10]Department of Rheumatology, Royal Free Hospital, Royal Free London NHS FT, London, UK, [11]Department of Rheumatology, London North West University Healthcare NHS Trust, London, UK, [12]Department of Rheumatology, Doncaster and Bassetlaw Teaching Hospitals NHS Foundation Trust, Doncaster, UK, [13]Department of Rheumatology, Aintree University Hospital NHS Foundation Trust, Liverpool, UK, [14]Department of Rheumatology, St George's University Hospitals NHS Foundation Trust, London, UK, [15]Department of Rheumatology, Solihull Hospital, University Hospitals of Birmingham NHS FT, Birmingham, UK, [16]Department of Rheumatology, Northampton General Hospital, Northampton General Hospital NHS Trust, Northampton, UK, [17]Department of Rheumatology, Basildon Hospital, Basildon and Thurrock University Hospitals Foundation Trust, Basildon, UK, [18]Manchester Centre for Clinical Neurosciences, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [19]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Salford, UK, [20]National Institute for Health Research Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, University of Manchester, Manchester, UK

Background. The MYOPROSP (NCT02468895) study is a prospective, multicentre observational cohort that recruited adult patients with idiopathic inflammatory myopathies (IIM) from 23 UK centres between 2016 and 2020. We previously have reported that, despite longer disease duration and more prior treatment failures, refractory adult IIM patients treated with rituximab in this cohort achieved a higher Total Improvement Score response rate than those on conventional immunosuppressants. However, 29.6% of refractory cases still responded poorly to rituximab, and clinically validated biomarkers that can predict response to rituximab remain lacking.

Methods. We conducted a translational extension of the above cohort study, leveraging prospectively collected paired pre- and post-rituximab whole-blood, PAXgene RNA, and serum samples from the rituximab-treated cases, with healthy controls from the National Repository of Healthy Volunteers. 25-colour Cytek PBMC immunophenotyping, 32-gene NanoString inflammation panel and NULISAseq™ 250-plex serum proteomics were performed; differential proteins ($p<0.05$) underwent network/GO analysis.

Results. Differential gene transcription revealed that MX1, IFI6, IFI44L, ISG15, SOCS1 and PD-L1 were significantly elevated in refractory IIM patients at baseline compared with healthy controls. Immunophenotyping showed that the non-responder group had fewer baseline B-lineage cells, including plasma blasts, whereas the proportion of $CD11c^+IgD^-CD27^-$ double-negative B cells remained higher both before and after rituximab. Non-classical monocytes were lower at baseline in non-responders but increased post-rituximab. $CD1c^+CD141^+$ DCs were consistently higher in non-responders, who also exhibited fewer Tregs, fewer NK cells, higher $CD45RA^+CCR7^-$ $CD4^+$ T cells, and a higher ratio of memory and effector subsets within $CD8^+$ T cells; all these differences persisted despite rituximab treatment. Among inflammatory proteins, IL-6, TNFRSF13 and IL-36 were differentially regulated after rituximab treatment. Comparing rituximab responders with non-responders, a distinct set of proteins including IL6ST, IFNW1, IL-17A, TNFRSF1, IL-36B and TNSF8 showed differential regulation. GO analysis demonstrated association of these markers with immune response, adaptive immune response, T-cell activation, cytokine stimulus and cytokine-mediated signalling pathways.

Conclusions. Refractory IIM patients exhibited up-regulation of the type I interferon pathway. Non-responders to rituximab showed an inflammation-dominant, immune-exhausted subtype. Proteome analysis identified differentially expressed markers that show promise for predicting rituximab treatment outcome; larger studies are warranted.

Acknowledgements. X. Lyu and S.S. Rane contributed equally to this work.

Key words: rituximab resistance, type I interferon pathway, immune exhaustion

Reference

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INTERFERON SIGNALLING DISRUPTS TISSUE REMODELLING AND ACCELERATES AGING IN DERMATOMYOSITIS MUSCLE CELLS: INSIGHTS FROM SPATIAL TRANSCRIPTOMICS AND EX VIVO STUDIES

Linda Chenane[1], Wilhelm Bouchereau[2], Julian Dal-Cin[1], Damien Amelin[1], Bérénice Tendrel[1], Céline Anquetil[1], Angéline Madelaine[3], Sarah Leonard-Louis[1,4], Claus M. Azzalin[5,6], Patricia A Lona Abreu[5], Bénédicte Chazaud[2], Armelle Corpet[2], Patrick Lomonte[2], Yves Allenbach[1,3], Olivier Benveniste[1,3]

[1]Sorbonne University-INSERM-Center of Research in Myology-UMRS 974, Paris, France , [2]Institut NeuroMyoGène, Université Claude Bernard Lyon 1, CNRS UMR 5261, INSERM U 1315, Lyon, France, [3]Department of Internal Medicine and Clinical Immunology-Sorbonne Université-Pitié-Salpêtrière, Paris, France, [4]AP-HP-Pitié-Salpêtrière Hospital-Neuropathologie Laboratory-Reference Center for Muscle Diseases Paris-Est-Myology Institute, Paris, France, [5]GIMM - Gulbenkian Institute for Molecular Medicine, Lisbon, Portugal, [6]Faculty of Medicine, University of Lisbon, Lisbon, Portugal

Background. Dermatomyositis (DM) is an inflammatory myopathy leading to non-infectious inflammatory skin and muscles damages. Myopathological analysis as well as transcriptomic data show muscle type I interferon (IFN-I) pathways activation, regenerative and atrophic features. Whether IFN-I could induce muscle tissue remodelling and damaged at the fiber-type level has not been investigated yet

Methods. In this study, we take advantages from spatial transcriptomics from controls (CTRL, n=4) and DM (n=5) donors to investigate the muscle fiber typing, including the oxidative slow-twitch type expressing the Myosin Heavy Chain (MYH) 7 and the glycolytic/oxidative fast-twitch type expressing either MYH1 or MYH2 and in their inflammatory microenvironment. We then did validation at the protein level. Using muscle stem cells derived from DM muscles (DM-MuSC) and control muscles (CTRL-MuSC), we also conducted in vitro modelling to functionally assess the impact of the IFN-I microenvironment on muscle fiber remodelling

Results. Spatial transcriptomics analysis of 5103 spots (CTRL, n=4 and DM n=5) showed an enrichment of type I muscle fibers (MYH7) at the expense of type II muscle fibers (MYH1). MYH1 immunostaining validated this observation but also revealed an increase MYH7+/ MYH2+ hybrid reflecting an active remodelling process. Using Gene Ontology (GO) analysis the comparison of DM and CTRL muscle fiber domains classified by fiber subtype, according to the expression levels of MYH isoforms revealed that DM domains displayed inflammatory processes including antigen processing and presentation, type I interferon signalling and a marked reduction in energy-generation processes. In particular, oxidative phosphorylation-related pathways were severely decreased in MYH7+ domains. In vitro CTRL-MuSC exposed to IFN-I recapitulates at the transcriptomic level both the pro-inflammatory signalling and the decrease of mitochondrial respiration. In addition, it strikingly decreases MYH1 expression. Moreover, DM-MuSC nuclei characterisation shows the acquisition of senescence phenotype including enlarged nuclei and increased γH2AX foci. Finaly, these cells exhibited a pro-inflammatory phenotype and secrete inflammatory molecules including chemokines likely to sustain the chronic immune system recruitment.

Conclusions. Ex vivo and in vitro studies indicate that type I interferon promotes a shift toward slow-twitch muscle fibers in dermatomyositis and

diminishes mitochondrial gene expression. These effects appear to be long-lasting, as parts of muscle cells from DM patients maintain a senescent and pro-inflammatory phenotype even outside an inflammatory context. Overall, these findings suggest that type I interferon contributes to an aging-like phenotype in the muscle of patients with dermatomyositis.
Key words: dermatomyositis, type I interferon

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DISTINCT SPATIAL INTERFERON ARCHITECTURES IN DERMATOMYOSITIS SKIN FOLLOWING INTERFERON RECEPTOR BLOCKADE: INSIGHTS FROM SPATIAL TRANSCRIPTOMICS AND COMPARISON TO CUTANEOUS LUPUS

Ksenia S. Anufrieva[1*], Rochelle L. Castillo[1,2*], Ce Gao[1], Sean Prell[1], Jessica Liu[1], Katharina S. Shaw[3], Ruth Ann Vleugels[2#], Kevin Wei[1#]
[*]Co-first authors, [#]Co-senior authors
[1]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA, [2]Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA, [3]Department of Dermatology, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA

Background. Dermatomyositis (DM) is an interferon (IFN)-driven inflammatory disease characterized by immune infiltration, vascular injury, and epidermal dysfunction in skin. Anifrolumab, a monoclonal antibody targeting the type I IFN receptor, has demonstrated efficacy in IFN-mediated diseases such as DM and lupus, yet its tissue-level effects on cutaneous architecture and cellular niches remain incompletely defined. We used spatially resolved cellular and molecular profiling to compare immune composition and IFN-signaling programs in DM before and after treatment with the type I IFN receptor antagonist anifrolumab and compared this to cutaneous lupus erythematosus (CLE) skin.
Methods. We performed high-resolution spatial transcriptomic profiling using the Xenium Skin Panel on lesional skin biopsies from patients with DM (n=3) and CLE (n=3), as well as healthy controls (n=2), collected before and after anifrolumab therapy in patients who were clinically responsive to treatment. Spatial niche analysis, immune cell characterization, and compartment-specific gene expression were assessed, with a focus on IFN-response signatures and proliferative states.
Results. Pre-treatment DM lesions exhibited robust IFN response signatures across keratinocytes, fibroblasts, and endothelial cells, and expansion of immune populations. These molecular changes were accompanied by disrupted spatial organization and reduced capillary density in the dermis adjacent to the basal keratinocyte layer. Comparative analyses revealed disease-specific spatial IFN architectures between DM and CLE. DM lesions demonstrated high keratinocyte IFN scores with relatively modest proliferative activity, whereas lupus lesions showed concurrent IFN activation and increased keratinocyte proliferation. Vascular cells demonstrated uniformly high IFN scores in both diseases, consistent with a widespread endothelial IFN imprint. In contrast, fibroblast IFN activation was disease-specific, with DM lesions displaying a pronounced IFN-high fibroblast population that was less evident in CLE.
Following anifrolumab treatment, lupus skin exhibited marked immune remodeling, including a pronounced reduction in immune cell ratios, normalization of keratinocyte IFN signaling, and resolution of hyperproliferative signatures. In contrast, DM skin showed less prominent immune normalization, with a less marked reduction immune ratios and residual keratinocyte IFN activation despite minimal changes in proliferation. Vascular IFN signatures remained only partially normalized in both diseases, with more pronounced persistence in DM. Although fibroblast IFN scores in DM improved after treatment, they did not return to levels observed in healthy skin, in contrast to CLE, which converged toward the healthy baseline. These suggest that endothelial cells and fibroblasts may act as durable IFN reservoirs in DM. Notably, despite clinical improvement, anifrolumab treatment did not restore lesional skin transcriptomes to a healthy phenotype, suggesting that clinical resolution may not immediately equate to full transcriptomic or structural recovery.
Conclusions. Using spatially resolved transcriptomic profiling, we identify dermatomyositis skin as harboring distinct, cell type-specific interferon niches that are only partially reversible with type I IFN receptor blockade. While anifrolumab effectively normalized immune composition and keratinocyte and fibroblast IFN signaling in lupus skin, DM lesions retained elevated immune ratios, residual epidermal IFN activity, and a durable vascular and fibroblast IFN imprint despite clinical improvement, highlighting endothelial cells and fibroblasts as potential modulators of therapeutic remodeling. Together, these findings suggest that IFN-driven pathology in DM may be spatially organized and compartmentally resistant to IFN-directed monotherapy, providing a mechanistic framework for incomplete tissue normalization and supporting the need for combination or cell-targeted therapeutic strategies in dermatomyositis.
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Key words: dermatomyositis, anifrolumab, interferon

Therapeutic Advances

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ADVANCING CARE IN NECROTIZING MYOPATHIES: RETHINKING HIGH-DOSE GLUCOCORTICOIDS FOR IMPROVED OUTCOMES IN ANTI-HMGCR+ PATIENTS

Angeles Galindo-Feria[1,2,3], Belen Miguel-Ibañez[4], Silvia Grazzini[5], Rui Da Silva-Rodrigues[6], Ingrid E Lundberg[1,2,3], Maryam Dastmalchi[1,2,3]
[1]Division of Rheumatology, Department of Medicine, Solna, Sweden, [2]Center for Molecular Medicine, Karolinska Institutet, Solna, Sweden, [3]Department of Gastro, Dermatology and Rheumatology, Theme Inflammation and Aging. Karolinska University Hospital, Solna, Sweden, [4]Rheumatology service of the Salamanca University Hospital Complex, Spain, [5]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University of Siena, Italy, [6]Department of Clinical Immunology and Transfusion Medicine, Karolinska University Hospital, Solna, Sweden

Background. Anti-HMGCR immune-mediated necrotizing myopathy (IMNM) is a rare, debilitating autoimmune disorder marked by progressive muscle weakness and sustained creatine kinase (CK) elevation. Without prompt therapy, it results in irreversible myofiber necrosis and fatty replacement, causing significant morbidity. Current management involves glucocorticoids (GC), immunosuppressants (IS), intravenous immunoglobulin (IVIG), and biologics, but no approved treatments exist, and evidence remains observational. Despite widespread use of high-dose GC as first-line therapy, its impact on recovery remains unexamined, presenting a critical gap in clinical management. This study challenges conventional practice by evaluating whether intensive GC regimens improve outcomes in anti-HMGCR IMNM.
Methods. This retrospective cohort included 42 patients with anti-HMGCR IMNM categorized by initial GC regimen. Group 1 (n=12, 2017–2019) received intravenous (IV)-GC pulses (500–1000 mg per dose) plus oral-GC ± IS. Group 2 (n=30, after 2019) received oral-GC ± IS without IV-GC. Clinical and serological parameters, including muscle strength (MMT8), physician and patient global assessments disease activity, CK normalization, and relapse, were recorded longitudinally. Cumulative GC doses and concomitant treatments (methotrexate, MTX, and IVIG) were compared. Kaplan-Meier analysis estimated time to CK normalization, with group differences tested using the Breslow method. Cox regression models, adjusted for age, sex, and baseline disease activity, evaluated the associations between cumulative GC exposure and outcomes.
Results. Only 28% of the No GC-IV group received oral glucocorticoids (range 0–109 g) versus 100% in the IV group (range 0.65–275.7 g; p=0.001). Methotrexate and IVIG use were similar between groups (92% *vs*. 93% and 92% *vs*. 87%, respectively). Despite comparable baseline disease activity and statin exposure (p=0.5), the No GC-IV group demonstrated significantly faster CK normalization (27.2 *vs*. 39 months; p=0.038) and accelerated moderate clinical response (34 *vs*. 52 months; p=0.02). Most strikingly, high cumulative GC dose (>7 g) was associated with 94% slower CK normalization (HR=0.06; p<0.001) and a 97% reduced likelihood of complete clinical response at 6 months compared with no GC use, suggesting a dose-dependent detrimental effect. Relapse rates were comparable between groups.
Conclusions. High-cumulative GC dose or IV-glucocorticoid exposure in anti-HMGCR IMNM is associated with delayed CK normalization and slower clinical recovery without reducing relapse risk. These findings challenge the widespread use of high-dose GC as first-line therapy and provide quantitative evidence supporting glucocorticoid-sparing strategies. Our findings suggest that early initiation of immunosuppressants and IVIG, with minimal or no glucocorticoids, may optimize outcomes in anti-HMGCR IMNM while reducing treatment-related toxicity, warranting prospective validation.
Key words: glucocorticoids, prognostic factors, autoantibodies, outcome measures

Biomarkers & Imaging

PT-20

DEVELOPMENT AND VALIDATION OF THE MDA-FI SCORE: A SIMPLE PROGNOSTIC TOOL AT DIAGNOSIS IN ANTI-MDA5 DERMATOMYOSITIS

Quentin Astouati[1], Valentine Pagis[2], Lucas Pacoureau[3], Yann Nguyen[4], Pierre Bay[5], Antoine Roux[6], Hubert De Boysson[7], Laure Gallay[8], Vincent Cottin[9], Benjamin Terrier[10], Alain Meyer[11], Charles Cerf[12], Mathilde Neuville[13], Baptiste Hervier[14], Arthur Renaud[15], Benoit Suzon[16], Nicolas Schleinitz[17], Benjamin Thoreau[18], Thomas Papo[19], Pascaline Priou[20], Arsène Mekinian[21], Audrey Ullmer[22], Erwan Oehler[23], Noémie Gensous[24], Alice Berezne[25], Luc De Saint Martin[26], Mickael Martin[27], Amélie Servettaz[28], Maxime Samson[29], Eric Hachulla[1], David Launay[1], Hilario Nunes[30], Yurdagul Uzunhan[30], Olivier Benveniste[2], Yves Allenbach[2]

[1]Univ. Lille, Inserm, CHU Lille, U1286 - INFINITE - Institute for Translational Research in Inflammation, CHU Lille, Department of Internal Medicine, Centre de Référence des Maladies Auto-Immunes et Auto-Inflammatoires Rares du Nord, Nord-Ouest, Méditerranée et Guadeloupe (CeRAINOM), Lille, France, [2]Department of Internal Medicine, Pitié-Salpêtrière Hospital, AP-HP, Paris, France, [3]Department of Internal Medicine, Bicêtre Hospital, AP-HP, Paris, France, [4]Department of Internal Medicine, Beaujon Hospital, AP-HP, Paris, France, [5]Department of Medical Intensive Care, Henri-Mondor Hospital, AP-HP, Créteil, France, [6]Department of Respiratory Medicine, Foch Hospital, Suresnes, France, [7]Department of Internal Medicine, CHU Caen Normandie, Caen, France, [8]Department of Internal Medicine, Edouard-Herriot Hospital, HCL, Lyon, France, [9]Department of Respiratory Medicine, Louis-Pradel Hospital, HCL, Lyon, France, [10]Department of Internal Medicine, Cochin Hospital, AP-HP, Paris, France, [11]Department of Rheumatology, Hautepierre Hospital, CHU Strasbourg, Strasbourg, France, [12]Intensive Care Unit, Foch Hospital, Suresnes, France, [13]Department of Medical Intensive Care, Bichat-Claude-Bernard Hospital, AP-HP, Paris, France, [14]Department of Internal Medicine, Saint-Louis Hospital, AP-HP, Paris, France, [15]Department of Internal Medicine, CHU Nantes, Nantes, France, [16]Department of Internal Medicine, CHU Martinique, Martinique, France, [17]Department of Internal Medicine, La Timone Hospital, AP-HM, Marseille, France, [18]Department of Internal Medicine, CHU Tours, Tours, France, [19]Department of Internal Medicine, Bichat-Claude-Bernard Hospital, AP-HP, Paris, France, [20]Department of Respiratory Medicine, CHU Angers, Angers, France, [21]Department of Internal Medicine, Saint-Antoine Hospital, AP-HP, Paris, France, [22]Department of Internal Medicine, Pontoise Hospital, Pontoise, France, [23]Department of Internal Medicine, CH de Polynésie Française, Pirae, France, [24]Department of Internal Medicine, CHU Bordeaux, Bordeaux, France, [25]Departments of Internal Medicine and Infectious Diseases, CH Annecy Genevois, Annecy, France, [26]Departments of Vascular Medicine, Internal Medicine, and Respiratory Medicine, CHU Brest, Brest, France, [27]Department of Internal Medicine, CHU Poitiers, Poitiers, France, [28]Departments of Internal Medicine and Infectious Diseases, CHU Reims, Reims, France, [29]Department of Internal Medicine, CHU Dijon, Dijon, France, [30]Department of Respiratory Medicine, Avicenne Hospital, AP-HP, Bobigny, France

Background. Anti-MDA5 dermatomyositis (MDA5-DM) carries a high mortality risk, mainly driven by interstitial lung disease (ILD), which can be rapidly progressive (RP-ILD). However, the disease course remains unpredictable, and while early intensive immunosuppressive therapy can improve outcomes, it also significantly increases the risk of severe infections. Some patients face a high risk of death requiring aggressive care, whereas others have a more favorable profile in whom intensified immunosuppression can be avoided.

To date, neither individual prognostic factors nor risk scores have demonstrated robust external validation, especially in European cohorts. Most available models have been derived in Asian populations. We aimed to develop and validate a simple, clinically applicable prognostic score to predict 1-year death and/or intensive care unit (ICU) admission at MDA5-DM diagnosis.

Methods. We conducted a retrospective, multicenter French cohort study including 240 patients with MDA5-DM. Patients were randomly allocated by center into derivation and validation cohorts. Candidate variables were selected based on their associations with the primary outcome (1-year death and/or ICU admission) in univariable analyses, clinical relevance, and routine availability. A multivariable Cox model with iterative combination testing was fit in the derivation cohort, and β-coefficients were converted into weighted integer points. Performance was assessed in the validation cohort.

Results. In the overall cohort, several prognostic factors were associated with the primary outcome: older age, male sex, poor performance status, fever, dyspnea, ILD or RP-ILD, anti-Ro52 positivity, elevated ferritin, high C-reactive protein (CRP), and lymphopenia.

In the derivation cohort, the 'MDA-FI' score was developed and includes five variables: male sex, dyspnea NYHA ≥III, age, fever, and inflammation (CRP ≥10 mg/L).

In the validation cohort, the 'MDA-FI' score showed strong discrimination for the primary outcome (AUC (1-year binary outcome) 0.91; sensitivity 0.92; specificity 0.83). Three risk groups were defined: low, moderate and high. At 1 year, death and/or ICU admission occurred in 0%, 19% and 63% of patients, respectively.

Conclusions. The 'MDA-FI' score is a simple, clinically applicable prognostic tool based on readily available variables. At diagnosis, it enables early risk stratification in MDA5-DM and may guide therapeutic decisions and future trial design. An external validation across independent European and Asian cohorts is ongoing.

Key words: MDA5, myositis, prognostic

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AN APPLICATION OF GROUP-BASED TRAJECTORY MODELLING TO IDENTIFY DISTINCT INITIAL 3-MONTH TRAJECTORIES OF ANTI-MDA5 AUTOANTIBODY LEVELS IN PATIENTS WITH DERMATOMYOSITIS: A PILOT STUDY IN A MYOSITIS REFERRAL CENTRE

Akira Yoshida[1], Yuka Okazaki[1], Takahisa Gono[1,2], Masataka Kuwana[1,2]

[1]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [2]Scleroderma and Myositis Centre of Excellence, Nippon Medical School Hospital, Tokyo, Japan

Background. The presence of anti-MDA5 autoantibody is useful for predicting disease course and outcomes in patients with dermatomyositis (DM), but the utility of anti-MDA5 autoantibody level changes measured by quantitative enzyme-linked immunosorbent assays (ELISA) in monitoring disease activity remains controversial. This study aimed to investigate whether the initial 3-month trajectories of anti-MDA5 autoantibody levels could predict long-term outcomes of patients with anti-MDA5-positive DM.

Methods. This was a single-centre retrospective study conducted at a myositis referral centre in Japan. The inclusion criteria were consecutive patients with DM who were identified as positive for anti-MDA5 autoantibodies at diagnosis and received at least two anti-MDA5 level measurements by ELISA (MESACUP™ , Medical and Biological Laboratories, Tokyo, Japan) within the first three months following diagnosis. We subjected anti-MDA5 levels at 0, 1, 2, and 3 months after treatment introduction to group-based trajectory modelling (GBTM) and identified subgroups with distinct anti-MDA5 level trajectories. Clinical features and initial treatment regimens were compared between the subgroups. Multivariable logistic regression was employed to identify baseline clinical characteristics associated with the trajectory assignment. Relapse-free survival of patients in each trajectory group was assessed using the Kaplan-Meier curves and was compared using the log-rank test.

Results. We assessed 30 patients with anti-MDA5-positive DM, with a median age of 52 years [interquartile range 46–64] and 76.7% being female. GBTM identified two subgroups with distinct initial 3-month anti-MDA5 level trajectories: Trajectory 1 (low; n=13) and Trajectory 2 (high; n=17). The median anti-MDA5 levels at 0, 1, 2, and 3 months after treatment introduction in the two groups (Trajectory 1 *vs.* 2) were 1020 [630–1224] *vs*. 3000 [2030–4025], 535 [350–700] *vs*. 1910 [1670–2959], 87 [80–322] *vs*. 1150 [1025–1335], and 72 [59–81] *vs*. 818 [695–896] (index). There was no statistical difference in clinical features and initial treatment regimens between the two trajectory groups. None of the baseline characteristics but the baseline anti-MDA5 autoantibody levels were associated with the trajectory assignment (p=0.024). Relapse-free survival tended to be poor in Trajectory 2 (log-rank p=0.096).

Conclusions. Two distinct initial 3-month trajectories of anti-MDA5 autoantibody levels were identified by GBTM. Baseline anti-MDA5 autoantibody levels were associated with the trajectory assignment. Our results warrant large-scale studies to elucidate whether serial measurement of anti-MDA5 autoantibody levels is useful in monitoring disease activity in patients with anti-MDA5-positive DM.

Key words: dermatomyositis, MDA5, autoantibodies

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SEMI-QUANTITATIVE MEASUREMENT OF MYOSITIS-SPECIFIC AUTOANTIBODIES IN PATIENT SERA USING MULTIPLEX IMMUNOASSAYS: WITHIN LOT AND LOT-TO-LOT VARIABILITY OF TESTING

Georgina Harvey[1], Kimberly Loh[1,2], Charmaine Donald[3], Hui Lu[1], Adrian Heaps[3], Saša Čučnik[4], Sarah Tansley[1,2]
[1]University Of Bath, Bath, UK, [2]Royal United Hospitals Bath NHS Foundation Trust, Bath, UK, [3]Severn Pathology North Bristol NHS Trust, Westbury-on-Trym, UK, [4]Ljubljana University Medical Centre, Ljubljana, Slovenia

Background. We recently assessed interlaboratory variability of myositis-specific autoantibody (MSA) testing; Of concern was that particular MSA results often varied between laboratories using the same sample and immunoassay. Others have shown batch-to-batch variation in single-centre results using the EuroImmun line immunoassay (LIA). Inter- and intra-laboratory discrepancies may affect clinical interpretation. Quantifying interlaboratory and lot-to-lot variability is crucial to understanding diagnostic platform reliability and guiding standardisation.
Objective. To determine within-lot and lot-to-lot variability of multiplex testing strips.
Methods. Six sera, previously characterised in Bath, UK, by radioimmunoprecipitation (Radio-IP) were selected: anti-Tif1γ (2), anti-MDA5 (1), anti-Zo (1) and none detected (ND) (2). Two high-turnover serological laboratories used automated testing platforms to measure MSA (Bristol, UK: Euroimmun 16-antigen LIA*; Ljubljana, Slovenia: D-Tek 12-antigen dot immunoassay† (DIA)).
Within-lot variability: Sera were assayed 3 times by single-lot LIA strips at intervals maximising possible impacts from analyser cleaning schedules. For within-assay, lot-to-lot variability, testing-strip lots were varied (LIA, n=3; DIA, n=7). Output data consisted of semi-quantitative arbitrary units corresponding to MSA titres.
Results. Within-lot and lot-to-lot variability of LIA:
No significant differences§ were found between titres measured using three strips from the same lot; similarly, titres from three separate strip lots were not significantly different§. However, for one ND sample, anti-Jo1 titres were variably classified as + (in-house negative) or ++, and two positive sera (anti-MDA5; anti-Tif1γ) spanned ++ and +++ classifications.
Lot-to-lot variability of DIA:
Titres measured using seven different strip lots were not significantly different#. One anti-Tif1γ sample was equivocal once. The same ND sample as previously was positive for anti-Jo1 on two strips, and equivocal on two others.
Inter-assay variability:
After excluding the anti-Zo serum‡, 15/25 (60.0%) LIA, and 20/35 (57.1%) DIA strips agreed with Radio-IP. (cf on-board camera cut-off: 9/25 (36.0%) LIA strip/Radio-IP agreement). For one anti-Tif1γ-positive serum, tests generally agreed with Radio-IP (LIA: 5/5; DIA: 6/7), while all tests disagreed for the other (LIA: 0/5; DIA: 0/7).
Conclusions. We found no significant within-lot, or lot-to-lot, variation in results using LIA or DIA. However, variation was seen between strips for individual specificities, regarding both 'level' of positivity and, crucially, determination of positivity/negativity, which could influence clinical decision making. Nevertheless, the same locally optimised in-house thresholds were shown to improve overall LIA/Radio-IP agreement, underscoring the need for laboratory-specific validation of cut-off values.
*Euroline Myositis Profile 4G; †BlueDiverDot MYOS12DIV-24; ‡Zo not included in LIA/DIA; §Wilcoxon signed-rank test; #Friedman rank sum test; p<0.05 significance levels
Key words. myositis, autoantibodies, immunoassay

PT-298

REAL-TIME MRI AND QUANTITATIVE MUSCLE ULTRASOUND FOR CHARACTERIZATION OF DYSPHAGIA IN IBM AND OPMD

Rachel Zeng[1], Anke Rietveld[2], Omar Al-Bourini[3], Rosemarie H.M.J.M. Kroon[2], Arno Olthoff[4], Matthias Weidenmüller[4], Per-Ole Carstens[1], Isabel Kommerell[1], Saskia Schütz[1], Corinne G.C. Horlings[2], Johanna G. Kalf[2], Bert J.M. de Swart[2], Baziel G.M. van Engelen[2], Tim Friede[5], Sabine Hofer[1], Jens Frahm[6], Ali Seif Amir Hosseini[3], Jens Schmidt[1,7,8], Christiaan G.J. Saris[2]
[1]Department of Neurology, University Medical Center Goettingen, Goettingen, Germany, [2]Department of Neurology, Radboudumc Research Institute for Medical Innovation, Nijmegen, The Netherlands, [3]Department of Clinical and Interventional Radiology, University Medical Center Goettingen, Goettingen, Germany, [4]Department of Otorhinolaryngology, Phoniatrics and Pedaudiology, University Medical Center Goettingen, Goettingen, Germany, [5]Department of Medical Statistics, University Medical Center Goettingen, Goettingen, Germany, [6]Biomedical NMR, Max Planck Institute for Multidisciplinary Sciences, Goettingen, Germany, [7]Department of Neurology and Pain Treatment, Immanuel Klinik Rüdersdorf, University Hospital of the Brandenburg Medical School Theodor Fontane, Ruedersdorf bei Berlin, Germany, [8]Faculty of Health Sciences Brandenburg, Brandenburg Medical School Theodor Fontane, Ruedersdorf bei Berlin, Germany

Background. Dysphagia is a frequent and severe symptom in many muscle diseases. Identifying the underlying pathophysiology is critical for accurate diagnosis and targeted treatment. However, standard assessments have limitations. In the present study, we investigated the utility of novel real-time MRI and quantitative muscle ultrasound for characterizing dysphagia in inclusion body myositis (IBM) and oculopharyngeal muscular dystrophy (OPMD).
Methods. This prospective cohort study included patients with IBM and with OPMD from two European Neuromuscular research centers (Nijmegen, NL; Göttingen, DE). Swallowing function was studied using real-time MRI (RT-MRI), FEES (flexible endoscopic evaluations of swallowing) and clinical assessments. T1-mapping and quantitative muscle ultrasound (QMUS) were used to analyze tissue properties in swallowing muscles. Outcomes were compared between the two disease groups and to healthy subjects and non-myopathic patients.
Results. 18 patients with IBM (33% female, age 68.9 ± 7.7 years) and 13 OPMD (62% female, age 55.9 ± 7.0 years) were enrolled in this study. RT-MRI revealed significantly prolonged pharyngeal transit time in IBM *vs.* controls (difference between means = 1132.8 ms, 95% CI 482.2-1783, p=0.009). Oral transit time was significantly prolonged in OPMD *vs.* controls (difference between means = 581.2 ms, 95% CI 225.9-936.4, p=0.02). A cricopharyngeal bar was identified in 80% patients with IBM compared to 53% in OPMD. Fatty degeneration of the tongue in OPMD significantly correlated between MRI-T1 values and ultrasound echogenicity (Spearman`s ϱ= -0.52, p=0.005). ROC revealed excellent discrimination between diseases by combining RT-MRI, T1-mapping and QMUS (AUC= 0.95, 95% CI 0.86-1.00), while FEES and clinical assessments failed to differentiate specific patterns of dysphagia.
Conclusions. This study demonstrates the diagnostic value of real-time MRI and quantitative muscle ultrasound as novel imaging techniques for characterizing different phenotypes of dysphagia in muscle diseases. While IBM patients exhibited a pharyngeal obstruction associated with a cricopharyngeal bar, OPMD patients showed a characteristic tongue atrophy and an impaired oral phase of swallowing. These imaging techniques may facilitate symptomatic treatment of dysphagia and provide useful biomarkers.
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Key words: imaging, breathing, diaphragm

PT-332

COMPARISON OF CT AND MRI FOR DETECTING SOFT TISSUE CALCIFICATIONS IN THE THIGHS OF PATIENTS WITH LONG-TERM JUVENILE DERMATOMYOSITIS

Eva Kirkhus[1], Else Merckoll[1,2], Kristin Schjander Berntsen[3,4], Tomas Sakinis[1,5], Trond Mogens Aaløkken[1], Helga Sanner[1]
[1]Department of Radiology, Oslo University Hospital, Oslo, Norway, [2]Unilabs Norway, Oslo, Norway, [3]Department of Rheumatology, Oslo University Hospital, Oslo, Norway, [4]Department of Rheumatology, Martina Hansens Hospital, Sandvika, Norway, [5]Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway

Background. Juvenile dermatomyositis (JDM) is a rare inflammatory disease characterized by muscle weakness and distinctive skin rash, often complicated by dystrophic calcifications that may lead to functional impairment and pain. Accurate imaging is essential for assessing the extent and distribution of soft tissue calcifications. This study aimed to evaluate the volume and distribution of thigh soft tissue calcifications in patients with long-term JDM using computed tomography (CT), and to assess the sensitivity of magnetic resonance imaging (MRI) in detecting these calcifications, using CT as the gold standard.
Methods. Patients from the nationwide Norwegian JDM (NorJDM) cohort who underwent both CT and MRI of the thighs as part of a cross-sectional study were included. Two experienced musculoskeletal radiologists independently assessed the presence of calcifications on MRI and CT (0 = no, 1 = yes), with consensus reached by discussion. One radiologist quantified the calcification volume on CT and recorded their distribution across tissue layers (subcutis/cutis, fascia, or muscle). We analyzed the frequency, size, and location of calcifications and compared MRI and CT findings, focusing on volumetric data and potential correlations with clinical parameters. Continuous variables are presented as median (IQR).
Results. Forty-nine patients were included (59% female; median age 26 years [18.1–40.0]). Calcifications were detected by CT in 17 of 49 patients (34.7%) and by MRI in 11 of 49 (21.2%) ($p < 0.01$). Patients with CT-detected calcifications had a younger age at diagnosis (5.8 years [3.7–8.5] *vs*. 8.8 years [5.8–12.0]), longer time from symptom onset to diagnosis (6.0 months [3.0–14.5] *vs*. 3.0 months [1.9–6.0]), longer disease duration (24.3 years [17.1–30.4] *vs*. 13.6 years [7.9–28.3]) and higher disease activity scores (DAS) for JDM (5.0 [4.5–6.3] *vs*. 4.0 [2.0–5.0]; (all $p<0.05$). All MRI-detected calcifications were also identified by CT, resulting in a positive predictive value for MRI of 0.64. CT-derived calcification volumes ranged from 9 mm^3 to 105079 mm^3. Small, superficial calcifications measured 9–141 mm^3 were not visualized on MRI, while all lesions larger than 1900 mm^3 were detected, except for one superficial calcification (4486 mm^3).
Conclusions. CT demonstrated significantly higher sensitivity than MRI in detecting soft tissue calcifications in long-term JDM, particularly for small and superficial lesions. MRI effectively identified larger, deeper calcifications located within fascial and muscular compartments. These findings highlight CT as the preferred imaging modality for comprehensive assessment of calcinosis in JDM. Volumetric quantification of calcifications may represent a useful approach for more precise assessment of disease burden in JDM and warrants further investigation.
Key words: juvenile dermatomyositis, dystrophic calcifications, computed tomography, magnetic resonance imaging

Cancer Myositis

PT-13

SPATIAL DYNAMICS BETWEEN RESIDENT IMMUNE CELLS INVOLVE AN IFNγ AND IL15 AXIS IN IMMUNE CHECKPOINT BLOCKADE-INDUCED MUSCLE TOXICITY

Celine Anquetil[1], Julian Dal Cin[1], Sarah Léonard-Louis[2], Joe-Elie Salem[3], Damien Amelin[1], Berenice Tendrel[1], Aude Rigolet[1], Nicolas Champtiaux[1], Pascale Daniel[1], Nadege Wesner[5], Michelle Rosenzwajg[4], Fathia Mami-Chouaib[6], Olivier Benveniste[1], Stephanie Corgnac[6], Yves Allenbach[6]
[1]Department of Internal Medicine and Clinical Immunology, Pitie Salpetriere Hospital, AP-HP, Paris, FRANCE, [2]Neuropathologie Laboratory, Reference Center for Muscle Diseases Paris-Est, Myology Institute, Paris, FRANCE, [3]Department of Pharmacology, UNICO-GRECO Cardio-Oncology Program, Sorbonne University, INSERM CIC-1901, AP.HP.Sorbonne, Pitié-Salpêtrière Hospital, Paris, FRANCE, [4]INSERM UMRS_959; APHP. Sorbonne, Pitié-Salpêtrière Hospital, Clinical Investigation Center in Biotherapy (CIC-BTi) and Immunology-Inflammation-Infectiology and Dermatology Department (3iD), Sorbonne Université, France, [5]Department of Internal Medicine, Louis Pasteur Hospital, Colmar, FRANCE, [6]INSERM UMR 1186, Integrative Tumour Immunology and Immunotherapy, Gustave Roussy, Fac. de Médecine - Univ. Paris-Sud, Université Paris-Saclay, Villejuif, France

Background. deciphering the mechanisms of immune escape in cancer has led to the development and approval of immune checkpoint blockade (ICB) therapy in numerous cancers (1). Though improving the overall survival of cancer patients, these treatments induce frequent immune toxicities such as ICB-induced myositis, a rare and severe toxicity with only partially known physiopathology (2).
Methods. integrative spatial and single-cell transcriptomic analyses were performed on human muscle tissue samples. Protein validation included multiplex immunohistochemistry stainings, flow cytometry profiling of inflammatory cells, and functional cytotoxic assay.
Results. we uncovered pro-inflammatory dynamics between muscle-resident immune cells in ICB-induced myositis. Known for their contribution to tissue immune surveillance, we showed that CD8+ resident memory T (TRM) cells from patient muscle are poised to produce IFNγ and cytotoxic molecules. They display an activated profile, with expression of immune checkpoints and JAK/STAT signaling gene signature. They also co-localize with IFNγ-primed macrophages, producing IL-15 in a proinflammatory loop. Functionally, these TRM cells display a highly specific cytotoxic activity against autologous muscle cells. By contrast, CD8+ TRM cells from normal muscle tissue harbor a precursor-like phenotype, suggesting a role in the initiation of ICB-induced myositis.
Conclusions. This work highlights the impact of resident immune cells within muscle tissue on the pathophysiology of ICB-induced myositis.
The presence of precursor-like TRM cells in healthy muscle opens new perspectives on the muscle regeneration and homeostasis processes. Targeting the JAK/STAT signaling pathway in muscle-resident immune cells might be a therapeutic target in ICB-induced myositis to improve patient management while preserving the anti-tumor response to ICB.
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Key words: immune-checkpoint inhibitor, cancer, resident memory T cell, JAK/STAT

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PT-87

RISK AND SURVIVAL OF SECOND PRIMARY CANCERS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Weng Ian Che[1], Fredrik Baecklund[2,3], Ralf Kuja-Halkola[4], Ingrid E. Lundberg[5,6], Karin Hellgren[7,8], Marie Holmqvist[7,6]
[1]Department of Public Health and Medicinal Administration, Faculty of Health Sciences, University of Macau, Macau SAR, China, [2]Pediatric Oncology Unit, Karolinska University Hospital, Stockholm, Sweden, [3]Rare diseases group, Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden, [4]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden, [5]Division of rheumatology, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden, [6]ME Gastro, Derm and Rheuma, Theme Inflammation and Aging, Karolinska University Hospital, Stockholm, Sweden, [7]Clinical Epidemiology Division, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden, [8]Academic Specialist Center, Stockholm Health Services, Stockholm, Sweden

Background. Patients with idiopathic inflammatory myopathies (IIM) have an increased risk of cancer. As survival of IIM improves with modern care, characterizing burden of subsequent cancers in IIM cancer survivors becomes essential for optimizing long-term care. We aimed to assess the long-term risk of second primary cancers and death in patients diagnosed with cancer following idiopathic inflammatory myopathies (IIMs).
Methods. Using nationwide Swedish healthcare and population registers, we identified 1,826 patients diagnosed with IIM at the age of ≥18 years between 1998 and 2020. Patients were followed for up to 23 years for first and second post-IIM primary cancers of any types and death. In addition to cumulative incidence function and incidence rate, a flexible parametric multistate model was used to estimate transition probabilities to cancer and death events. In this model, risk and prognostic factors for second primary cancers were also evaluated.
Results. Of 306 patients diagnosed with cancer at or after IIM diagnosis, 50 developed a second primary cancer during a median follow-up of 2.4 years (IQR 0.8-4.8 years, maximum 18 years). Non-melanoma skin cancer (NMSC) was the most common second primary cancer, observed in 27 patients, 20 of whom had NMSC as their first post-IIM NMSC. The transition probability to a second primary cancer peaked between 5 and 10 years after a first post-IIM cancer, with 9% (95% CI 7-13%) at year 5 and 8% (95% CI 5-12%) at year 10. Male patients had a significantly higher second cancer risk than females (hazard ratio, HR=1.88, 95% CI 1.06-3.34). The five-year all-cause mortality risk after a second primary cancer was 57% (95% CI 44-70%). Patients with dermatomyositis had a markedly elevated mortality risk compared to non-dermatomyositis subtypes (HR=3.77, 95% CI 1.46-9.75).
Conclusions. These novel findings underscore the long-term cancer burden in IIM and the need for continued cancer surveillance and close clinical monitoring, particularly among male patients and those with DM.
Acknowledgements. We are grateful to Dr Hannah Bower for her invaluable guidance on the analytical approach.
Key words: idiopathic inflammatory myopathies, dermatomyositis, polymyositis, second cancer risk, survival

PT-290

THE MYOSCREEN STUDY – INVESTIGATING THE UTILITY OF BLOOD-BASED LIQUID BIOPSY AS A METHOD OF CANCER SCREENING IN PEOPLE WITH IDIOPATHIC INFLAMMATORY MYOPATHY

Chhavi Mahajan[1,2], Annabel Peachey[3], Aram Safrastyan[3], Dominic Rothwell[3], Pedro Machado[4,5,6,7], Hector Chinoy[1,2,8], Caroline Dive[3], Florent Mouliere[3], Alexandra Clipson[3], Alexander Oldroyd[1,2,8]
[1]National Institute for Health Research Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, University of Manchester, Manchester, UK, [2]Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK, [3]Cancer Research UK (CRUK) National Biomarker Centre, Manchester, Manchester, UK, [4]Centre for Rheumatology, Division of Medicine, University College London, London, London, UK, [5]Department of Neuromuscular Diseases, Division of Medicine, University College London, London, UK, [6]National Institute for Health Research, University College London Hospitals Biomedical Research Centre, University College London Hospitals National Health Service Trust, London, UK, [7]Department of Rheumatology, Northwick Park Hospital, London North-West University Healthcare NHS Trust, London, UK, [8]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK

Background. Adults with idiopathic inflammatory myopathy (IIM) face a markedly increased risk of malignancy within three years of disease onset, peaking in the 12 months before and after presentation. Cancer is the leading cause of death in this population, and associated malignancies are often diagnosed late. Blood-based "liquid biopsy" offers a novel opportunity for cancer early detection in people with new-onset IIM. This study aims to generate pilot data on its potential clinical utility.
Methods. Thirty adults aged ≥50 years with new-onset IIM (<3 years since onset) and at least one cancer risk factor (anti-TIF1γ positivity, anti-NXP2 positivity, dysphagia, or cutaneous necrosis) were recruited from 10 NHS hospital sites across England. Patients with a prior cancer diagnosis were excluded. All participants underwent baseline blood sampling alongside conventional cancer screening, in line with the 2023 IIM Cancer Screening Guideline. Liquid biopsy processing and analysis were performed at the CRUK National Biomarker Centre. Circulating free DNA (cfDNA) was isolated from plasma and underwent whole-genome sequencing (WGS) for fragmentomic analysis. Fragment size profiles were assessed, and the proportion of short fragments (100–150 bp), indicative of tumour-derived cfDNA, was calculated. Concordance between liquid biopsy and conventional cancer screening was evaluated.
Results. Baseline analysis included nineteen participants (68% female; mean age 69 years, SD 12). Sixteen participants tested negative for malignancy via liquid biopsy and conventional screening. Of those testing positive for cancer, one had lung cancer diagnosed at the time of IIM-onset and study recruitment; one participant had breast cancer diagnosed at the time of IIM-onset, and a further participant demonstrated features indicative of ovarian cancer (sequentially rising CA-125, anti-TIF1γ-positive). cfDNA yield was higher in 2/3 cancer-positive participants (mean 69 ng/mL, SD 0.6) compared with cancer-negative participants (mean 6 ng/mL, SD 4). Fragmentomic analysis of 11 samples (3 cancer-positive, 8 cancer-negative) showed a 1.4-fold higher median proportion of short cfDNA fragments in 2/3 cancer-positive samples.
Conclusions. The MyoScreen Study is the first to explore the clinical feasibility of using a blood-based liquid biopsy for early cancer detection in IIM. Preliminary results showed promising differentiation between cancer-positive and cancer-negative participants, suggesting this approach may facilitate cancer detection in IIM. Further work is ongoing to complete WGS analyses for the remaining samples. A larger cohort is needed to determine diagnostic accuracy and refine a detection method suited to IIM, where malignancy is often occult. This approach may help support more rationalised and earlier cancer detection in clinical practice.
Key words: idiopathic inflammatory myopathy, cancer-associated myositis, cancer screening, liquid biopsy, circulating-free DNA, early cancer detection, whole-genome sequencing, fragmentomics

Clinical Trials

PT-299

A TRIAL OF FIRST-LINE ADD-ON INTRAVENOUS IMMUNE GLOBULIN IN IDIOPATHIC INFLAMMATORY MYOPATHIES: TIME IS MUSCLE

Pinar Özkaynar[1], Sanne Evers[1], Renske Kamperman[1], Frank Smithuis[2], Floor Groepenhoff[2], Filip Eftimov[1], Dutch Myositis Network[5], Johannes Bogaards[3], Ivo van Schaik[1,4], Anneke van der Kooi[1], Joost Raaphorst[1]
[1]Department of Neurology and Clinical Neurophysiology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands, [2]Department of Radiology and Nuclear Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands, [3]Department of Epidemiology and Data Science, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands, [4]Sanquin Blood Supply Foundation, Amsterdam, The Netherlands, [5]Time is Muscle Study Group of the Dutch Myositis Network: Eleonora Aronica, Umesh Badrising, Marc Besseling, Irene Bronner, Ester Brusse, Corianne de Borgie, Jantine Coolen, Robert Hemke, Jessica Hoogendijk, Mario Maas, Christiaan Saris, Camiel Verhamme, Marianne de Visser, Nicol Voermans, Hannah Walter

Background. The optimal medical treatment strategy in newly diagnosed Idiopathic Inflammatory Myopathies (IIM, excluding inclusion body myositis) is unknown. Standard first-line immunosuppressive treatment consists of high dosed glucocorticoids, often with a steroid-sparing agent. Upfront more intensive treatment may lead to faster and larger improvement of disease activity, which includes muscle strength and physical functioning. Evidence for efficacy and safety of intravenous immunoglobulin (IVIG) was shown in refractory dermatomyositis (add-on) and has been suggested in newly diagnosed IIM (monotherapy). Our hypothesis is that first-line IVIG in addition to prednisone results in a superior clinical response in treatment-naïve IIM patients, as compared to monotherapy prednisone.
Methods. We conducted a double-blind randomized clinical trial in newly diagnosed, treatment-naïve IIM patients with substantial muscle weakness. All patients started on oral prednisone 1mg/kg/day. Patients in the treatment arm received IVIG 2g/kg at baseline, 4 and 8 weeks; in the control arm intravenous placebo was administered. The primary outcome was the Total Improvement Score (TIS) at 12 weeks. Key secondary outcomes were time to improvement (time to reach TIS of ≥40), individual core set measures (CSM), muscle MRI and Patient Reported Outcome Measures (PROMs). Safety data were collected. Forty-two patients were required based on sample size calculations. Patients who dropped-out due to reasons unrelated to IIM or study medication were replaced. Patients with insufficient treatment response or clinical deterioration necessitating rescue medication within 12 weeks reached a premature endpoint; these data were included in the analyses of the primary outcome with last observation carried forward.
Results. Between 2021 and 2025 44 patients (50% female) with a mean age of 59 years (SD 14.9) were included. IIM subtypes were immune mediated necrotizing myopathy (n=16), dermatomyositis (n=14), overlap- or non-specific myositis (n=10) and anti-synthetase syndrome (n=4). There were two drop-outs and five patients reached a premature endpoint. One asymptomatic deep venous thrombosis was detected on muscle MRI in the IVIG group. Nine other serious adverse events were considered to be unrelated to study medication.
Conclusions. The Time Is Muscle trial provides data on efficacy and safety of first-line add-on IVIG in newly diagnosed IIM patients. The primary outcome, safety and a selection of secondary outcomes have been analyzed and will be presented at the conference.
Acknowledgements. This study was investigator initiated, with financial support from the Prinses Beatrix Spierfonds (W.OR21-05) and Prothya Biosolutions.
Key words: IVIG, first-line treatment, total improvement score

Extra-Muscular Organ Involvement

PT-132

DEFINING CDASI THRESHOLDS OF DISEASE SEVERITY: INTEGRATING PHYSICIAN ASSESSMENTS OF DISEASE ACTIVITY WITH PATIENT PERSPECTIVES ON QUALITY OF LIFE

Sarah Jun[1,2], Hammad Ali[1,2], Touraj Khosravi-Hafshejani[1,2], Sarini Saksena[1,2], Elena Wei[1,2], Ahmed Eldaboush[1,2], Rafael Ozan Homer[1,2], Lais Lopes Almeida Gomes[1,2], Victoria P. Werth[1,2]
[1]Department of Dermatology-School of Medicine, University of Pennsylvania, Philadelphia, USA, [2]Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, USA

Background. The Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) is a validated assessment correlating with disease severity and treatment response, but thresholds for mild, moderate, and severe disease remain undefined. We sought to identify CDASI-Activity (CDASI-A; 0-100 points) cut-offs corresponding to the Physician Global Assessment (PGA) 5-point Likert Scale (None, Mild, Moderate, Severe, Extremely Severe) and Visual Analog Scale (VAS; 0-10cm). We further assessed whether these CDASI-A ranges reflected meaningful differences in patient-reported QOL using the Skindex-29.
Methods. We conducted a retrospective review of adult patients enrolled in the University of Pennsylvania Dermatomyositis (DM) database from January 2007 to June 2025, selecting for those with Visit 1 CDASI-A and corresponding PGA-Likert (n=553) or PGA-VAS scores (n=570). Patients with Visit 1 Skindex-29 scores (n=443) were included in QOL analyses. Receiver operating characteristic (ROC) curves identified optimal CDASI-A thresholds using the Youden index for PGA-Likert categories (Mild *vs*. Moderate; Moderate *vs*. Severe/Extremely Severe) and PGA-VAS cutoffs (>2.5cm, >5cm, >7.5cm). Skindex-29 scores were compared across CDASI-A ranges using Kruskal-Wallis and *post-hoc* Dunn's tests with Bonferroni adjustment.
Results. ROC analysis of PGA-Likert data identified CDASI-A cutoffs of 14 distinguishing Mild from Moderate disease (AUC 0.93, Sensitivity 84%, Specificity 89%, Accuracy 86%), and 21 distinguishing Moderate from Severe disease (AUC 0.93, Sensitivity 83%, Specificity 92%, Accuracy 84%). Resulting Likert-derived CDASI-A ranges were <14 (Mild), 14 to <21 (Moderate), and ≥21 (Severe/Extremely Severe). For PGA-VAS data, CDASI-A cutoffs were 13 (AUC 0.88, Sensitivity 81%, Specificity 78%, Accuracy 80%), 16 (AUC 0.91, Sensitivity 97%, Specificity 77%, Accuracy 82%), and 23 (AUC 0.95, Sensitivity 100%, Specificity 80%, Accuracy 81%) for PGA-VAS scores of 2.5cm, 5cm, and 7.5cm, respectively. Resulting VAS-derived CDASI-A ranges were <13 (Mild), 13 to <23 (Moderate), and ≥23 (Severe/Extremely Severe). For Likert-derived ranges, all Skindex-29 domains (Emotions, Functioning, Symptoms) differed between Mild and Severe/Extremely Severe groups ($p<0.001$). Emotions and Functioning differed between Mild and Moderate groups ($p<0.01$); Symptoms trended towards significance ($p=0.0507$). Moderate and Severe/Extremely Severe scores differed in Symptoms ($p<0.05$). For VAS-derived ranges, all domains differed between Mild and Moderate ($p<0.001$), as well as between Mild and Severe/Extremely Severe groups ($p<0.001$).
Conclusions. We propose CDASI-A thresholds aligned with physician assessments and patient-reported QOL. Given potential variability in PGA-VAS scoring, we favor the Likert-derived thresholds (Mild:<14, Moderate:14 to <21, Severe/Extremely Severe: ≥21). These results may be used to monitor DM in patients and clinical trials for skin-predominant disease, an area of increasingly growing need.
Key words: dermatomyositis, cutaneous dermatomyositis disease area and severity index, quality of life

PT-141

PREDICTORS OF FATIGUE IN A SWEDISH COHORT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Karin Lodin[1,2], Thanh Hien Bui[1], Fabricio Espinosa-Ortega[1,2], Malin Regardt[3,4], Maryam Dastmalchi[2,5], Ingrid E. Lundberg[5], Marie Holmqvist[1,2], Helene Alexanderson[3,5]

[1]Division of Clinical Epidemiology, Department of Medicine, Karolinska Institutet, Solna, Sweden, [2]Department of Gastroenterology, Dermatology and Rheumatology, Karolinska University Hospital, Stockholm, Sweden, [3]Women's Health and Health Professional Theme, Medical Unit Allied Health Professionals, Karolinska University Hospital, Stockholm, Sweden, [4]Department of Neurobiology, Care Sciences and Society, Division of Occupational Therapy, Karolinska Institutet, Stockholm, Sweden, [5]Division of Rheumatology, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden, Stockholm, Sweden

Background. Idiopathic inflammatory myopathies (IIM) are rare autoimmune diseases characterized by muscle weakness and extra-muscular symptoms. Fatigue is common and persistent, significantly impairing quality of life. This study aimed to evaluate changes in fatigue over time and identify baseline predictors of fatigue at 12-month follow-up in a Swedish IIM cohort.
Methods. Newly diagnosed patients with IIM from the Karolinska cohort were included. All patients had a12-month follow-up visit and complete fatigue data at both time points. Fatigue and pain were assessed using visual analogue scales (VAS 0–100 mm). Disease activity was assessed using the core set measures developed by the International Myositis Assessment and Clinical Studies Group (IMACS). Inflammatory markers included ESR and CRP. Changes from baseline to 12 months were evaluated using non-parametric tests. Predictors of fatigue at 12 months were assessed using bootstrapped linear regression adjusted for age and sex.
Results. The cohort included 262 patients (158 women) with a mean age of 59.3 years. Mean time from diagnose to baseline was 13.9 days (SD 27.7). Fatigue decreased significantly from baseline (median 49 [IQR 21–73]) to 12 months (28.5 [9–56], p<0.001), with greater reductions in women (60 to 36.5, p=0.002) than men (37.5 to 20, p<0.001). Improvements were observed across all patient-reported outcomes, core set measures, and inflammatory markers, except for CRP in men (p=0.67). Fatigue severity varied across diagnostic subgroups. At baseline, dermatomyositis (DM) had the highest fatigue (median 65 [36–80]), followed by overlap myositis (60 [35–78]); Inclusion body myositis had the lowest (18.5 [2–51]). At 12 months, significant reductions were observed in antisynthetase syndrome, DM and immune-mediated necrotizing myopathy in both men and women (all p<0.05).
Regression analyses identified polymyositis (β=14.71, p=0.003), overlap myositis (β=20.89, p<0.001), myositis specific autoantibody (MSA)-neg/ myositis associated autoantibody (MAA)-pos (β = 13.50, p=0.005), and seronegativity (β=11.49, p=0.020) as predictors of fatigue at 12 months. Patient global assessment (β=0.35), HAQ-DI (β=8.25), pain (β=0.25), and baseline fatigue (β=0.41) were also predictive of fatigue (all p 0.001).
Conclusions. Fatigue in IIM is persistent and more pronounced in women than in men. Patient-reported outcomes, diagnostic subgroups and autoantibody profiles were significant predictors of fatigue, while inflammatory markers and physician-assessed disease activity were not. These findings support integrating patient-reported outcomes into routine care and targeting fatigue in high-risk subgroups.
Key words: idiopathic inflammatory myopathies, fatigue, patient-reported outcomes

PT-164

OUTCOMES OF IMMUNOSUPPRESSION IN MYOSITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE BASED ON RADIOLOGICAL PHENOTYPES AMONG A LARGE INDIAN COHORT

Akshay Raju[1], Ashish J. Mathew[1], John Mathew[1], Ravikumar U.[1], Leena R.V.[2], Aparna Irodi[2], Richa Gupta[3], Barney Issac T.J.[4], John Jude Antony[5], Ruchika Goel[1]

[1]Department of Rheumatology, Christian Medical College Vellore, [2]Department of Radiology, Christian Medical College Vellore, [3]Department of Respiratory Medicine, Christian Medical College Vellore, [4]Department of Pulmonology, Christian Medical College Vellore, [5]Department of Microbiology, Christian Medical College Vellore, India

Background. Data on long-term outcomes of Myositis-Interstitial Lung Disease (ILD) across radiological phenotypes and evidence on efficacy of mycophenolate in myositis associated ILD is sparse. We aimed to identify predictors of ILD progression and assess the effect of mycophenolate therapy across radiological subtypes.
Methods. Electronic medical records of patients with Myositis-ILD (2010-2025) were screened. Those with active infection, coexisting cardiopulmonary disease, or baseline long-term oxygen therapy were excluded and patients with at least 6 months follow-up were included for analysis. Clinical, laboratory, imaging, and treatment details at index and follow-up visits were collected. Radiological phenotypes (non-specific interstitial pneumonia (NSIP), organizing pneumonia (OP), other patterns) were analyzed in relation to antibody profile and immunosuppressive therapy to determine long-term outcomes. Significant ILD progression were defined using FVC (≥10% decline), radiological, or combined. Multivariate regression analyses was performed to identify predictors of disease progression. Survival analysis was used to assess outcome over time.
Results. Our cohort included 164 patients (mean age 40.6 ± 12.1years, females 65.2%). Among them, 76 (46.3%) had anti-synthetase syndrome. The most frequent antibodies were MDA5(n=36), Jo-1(n=37), PL-12(n=19), and Ro52 co-positivity(n=43). Muscle weakness was noted in 58.5% and cutaneous involvement in 86.6% patients. 103 patients with atleast 6 months of follow-up were included for outcome anlaysis.
Radiological progression was noted in 68.4% (39/57) of NSIP and 32.5% (13/40) OP patterns. Progression occurred earlier in NSIP (59.2 ± 8.2 months) than OP (75.1 ± 9.9) and overall cohort (65.3 ± 7.4). The shortest time to progression was for fibrotic NSIP (49.2 ± 9.8) and longest for OP/NSIP overlap (77.6 ± 14.7). Ro52 co-positivity was linked to earlier progression (33.0 *vs*. 82.5 months, p<0.001). On multivariate analysis, NSIP pattern had higher progression rate compared to OP (OR 0.28, 95% CI 0.1–0.72 =0.009). Ro52 co-positivity independently predictd.003) but not after adjustment.
Among this cohort, radiological progression was noted in 55.3% (57/103) patients. However, physiological progression was noted in 10.6% (10/94) only. Majority (84/103) were on Mycophenolate and 54.8% (46/84) patients on Mycophenolate progressed at median follow-up of 24 (12–56) months. More patients receiving Index steroids ≤30 mg/day switched immunosuppressants during follow-up (47% (33/70) *vs*. 33% (20/66), p=0.044).
Conclusions. Over half of Myositis-ILD cases had follow-up radiological progression over a median duration of 24(12–56) months. NSIP pattern, Antisynthetase syndrome and Ro52-co-positivity predicted patients at higher risk and earlier progression.
Key words: myositis-associated ILD, radiological subtypes, treatment outcomes, interstitial lung disease, antisynthetase syndrome

Genetic & Environmental Risk Factors

PT-134

FAMILY HISTORY OF AUTOIMMUNITY AND HERBAL SUPPLEMENT USE IN DERMATOMYOSITIS: ASSOCIATIONS WITH DISEASE ACTIVITY

Sarah Jun[1,2], Naomi Gross[1,2], Elena Wei[1,2], Sarini Saksena[1,2], Ahmed Eldaboush[1,2], Rafael Ozan Homer[1,2], Lais Lopes Almeida Gomes[1,2], Touraj Khosravi-Hafshejani[1,2], Hammad Ali[1,2], Victoria P. Werth[1,2]
[1]Department of Dermatology-School of Medicine, University of Pennsylvania, Philadelphia, USA, [2]Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, USA

Background. Herbal supplement usage has been rising in the U.S., with 2020 heralding $11.3 billion in sales. In 2024, the prevalence of herbal usage among 673 patients with dermatomyositis (DM) or cutaneous lupus erythematosus was 32%. However, growing evidence suggests that herbal supplements, often immunostimulatory, are harmful to patients with autoimmune conditions. In vitro studies with Spirulina, a common supplement, demonstrated significantly increased activation of inflammatory pathways in the blood of DM patients compared to healthy controls, suggesting that immune cells are predisposed to disease onset or exacerbation following herbal exposure. Inheritable genetic factors, potentially associated with family history of autoimmunity (FHAI), may contribute to this heightened susceptibility.
Methods. To assess associations between positive FHAI, herbal supplement use, and DM disease activity, we conducted a retrospective review of 570 patients in the University of Pennsylvania DM database (January 2007-June 2025). Patients with documentation of both family history and herbal usage history were included in analyses. Family history, including first-, second-, and third-degree relatives, was obtained during clinic visits. Herbal usage (Spirulina, Chlorella, Alfalfa, Green Algae, Echinacea, Ashwagandha, Other) was assessed through open-ended questions and a standardized handout listing immunostimulatory supplements to aid recall. DM onset or flare were defined as the presence of new or worsening skin lesions or muscle weakness reported by patients and confirmed on physical examination. A temporal association with herbal exposure was considered when onset or flare occurred after herbal supplement use in the absence of other identifiable factors (medication discontinuation, excess sun exposure). Only cases with herbal exposure within one year prior to onset or flare were included.
Results. 427 patients met inclusion criteria. Among these, 211/427 (49.4%) patients had a positive FHAI and 133/427 (31.1%) reported prior herbal supplement usage, with 19 cases associated with DM onset and 26 with DM flare. Positive FHAI was present in 73.7% (14/19) of those who experienced DM onset and 53.8% (14/26) of those who experienced DM flare following herbal use. DM onset after herbal use was significantly associated with positive FHAI (Fisher's exact test: p=0.027, OR 3.309, 95% CI 1.038-12.537); no significant association was seen for flare (p=0.67, OR 1.232, 95% CI 0.4786-3.2150).
Conclusions. Positive FHAI may confer increased risk of DM onset associated with herbal exposures, highlighting the need to counsel patients, especially those with positive FHAI, regarding the use of immunostimulatory supplements. Future studies may investigate specific genetic factors underlying this susceptibility to herbal exposures.
Key words: dermatomyositis, herbal supplements, family history of autoimmunity

PT-170

STATIN EXPOSURE AND CLINICAL OUTCOMES IN ANTI-HMGCR IMMUNE-MEDIATED NECROTIZING MYOPATHY

Marwin Groener[1], Eugene Krustev[1,2], Peixi Ge[1], Jemima Albayda[1], Christopher Mecoli[1], Brittany Adler[1], Julie J. Paik[1], Andrew Mammen[1,3], Timothy Kaniecki[1], Lisa Christopher-Stine[1], Eleni Tiniakou[1,4]
[1]Johns Hopkins University School of Medicine - Division of Rheumatology, Baltimore, USA, [2]Department of Medicine and Microbiology, Immunology, and Infectious Diseases - McCaig Institute for Bone and Joint Health - Cumming School of Medicine - University of Calgary, Calgary, Canada, [3]Muscle Disease Unit - National Institute of Arthritis and Musculoskeletal and Skin Diseases - National Institutes of Health, Bethesda, USA, [4]University of Texas Health Sciences Houston - McGovern Medical School, Houston, USA

Background. Anti-3-hydroxy-3-methylglutaryl-CoA-reductase (anti-HMGCR) immune-mediated necrotizing myopathy (IMNM) is a rare statin-associated autoimmune myopathy. We investigated the association between statin-exposure and clinical outcomes in the largest anti-HMGCR-IMNM cohort to date.
Methods. Anti-HMGCR-positive patients evaluated at our Center from 2003 to 2024 who met the ACR/EULAR myositis criteria were included. Bilateral arm abductor and hip flexor strength was assessed by manual muscle testing (MMT; total score 0-40). Multiple linear regression analysis adjusted for sex, age of onset, statin-exposure, and creatine kinase (CK) was used to examine predictors of strength
Results. Of the 218 patients (mean follow-up 5.6 years), 168 (77%) were statin-exposed, while 50 (23%) were statin-naive. Among statin-exposed patients, 148/168 (88%) received atorvastatin (33 of whom received multiple statins). Atorvastatin-exposed patients did not differ significantly from patients exposed to other statins in demographics, number of non-steroid therapies, or disease measures (MMT or CK) at diagnosis and across follow-up (6 months to 5 years).
When compared to statin-exposed patients, statin-naïve patients were younger at disease onset (38.2 *vs*. 59.8 years, p<0.0001), predominately female (70.0% *vs*. 45.8%, p=0.004), and more frequently Black (28.0% *vs*. 14.9%, p=0.025). They had a lower median baseline MMT (22 *vs*. 30, p=0.014), but no difference in median baseline CK (4662 *vs*. 3906 IU/L, p=0.47).
At one year, significantly more statin-exposed patients normalized their strength (MMT=40) (19/30 [63%] *vs*. 1/10 [10%], p=0.008), but there was no difference in the proportion who normalized their CK (<300 U/L) (18/42 [42.9%] *vs*. 5/14 [35.7%], p=0.76). MMT scores remained lower in statin-naive patients up to 2 years; CK did not differ at any time point.
Multivariate analysis demonstrated that statin exposure was associated with higher MMT at diagnosis, though not at later time-points. In contrast, older age at disease onset predicted higher MMT during years 1–4 of follow-up (0.16–0.27 MMT-points per year). Patients reaching lower CK at 6 months had better strength at one year (2.6 MMT-points per tenfold-decrease in CK); the association did not persist at later timepoints.
Conclusions. We present the largest anti-HMGCR-IMNM cohort to date. The majority of patients were exposed to atorvastatin, yet outcomes did not differ with other statin exposures. Statin-naïve patients were younger, predominantly female, more often Black, and had worse long-term strength outcomes than statin-exposed patients. Younger age of onset predicted lower strength at follow-up, independent of statin-exposure, demonstrating that age and not statin exposure is the biggest predictor of poor outcomes.
Key words: Statin, IMNM, HMGCR

PT-277

AN INITIAL GENOME-WIDE ASSOCIATION ANALYSIS OF DERMATOMYOSITIS IN ~2.1 MILLION INDIVIDUALS FROM THE DERMATOMYOSITIS GENETICS CONSORTIUM (DMGC)

Galen Foulke[1], On behalf of Dermatomyositis Genetics Consortium[1]
[1]Penn State College of Medicine, Hershey, USA

Background. Dermatomyositis (DM) is a severe autoimmune disease featuring characteristic skin and muscle involvement, strongly associated with cancer and inflammatory lung disease. Like many other autoimmune diseases, DM carries heritable risk factors. Yet the genetic basis for DM is understudied, and little progress has been made toward improving our understanding of the genetic factors influencing DM development and disease progression. Given DM's low prevalence, international collaboration is critical for aggregating sample sizes and improving power for genetic studies.
Methods. To this end, we have established the Dermatomyositis Genetics Consortium (DMGC) and conducted an initial independent large-scale discovery genome-wide association study (GWAS) meta-analysis integrating data from 13 biobanks around the globe (Fig. 1). Rigorous established quality control measures were applied to the data to exclude low quality samples or variants. Patients with DM were identified with International Classification of Disease (ICD)-9 and ICD-10 codes of DM, dermatopolymyositis and juvenile dermatomyositis (JDM). We have thus far assembled a cohort of 3,084 cases and 2,095,955 controls, making our study magnitudes larger than existing DM GWAS.
Results. An initial analysis of DMGC data uncovered 18 loci (13 novel), harboring 2,149 SNPs with p<5 x 10-8 (Fig. 2). Within the MHC region, we also performed HLA imputation and identified top HLA alleles associated with either protection against or susceptibility to DM, including HLA-B*08:01:01 (logOR = -0.42, p=8.26 x 10-21), HLA-DRB1*12:02:01 (logOR = 0.12, p=8.72 x 10-12) and HLA-DRB3*03:01:03 (logOR = 0.13, p=3.67 x 10-14). Outside the MHC region, we identified 11 loci including PHLPP1, CUL5 and LRP5 which are known tumor suppressors. PHLPP1 and CUL5 also participate in regulating the fate and function of CD4+T cells and Treg.
Conclusions. This large-scale study presents the comprehensive translational genomics of DM, casting light on the etiology of DM, highlighting genetic links to cancer development and T-cell regulation, and offering potential targets for future disease-modifying therapies. Subsequent analyses and collaborations may further illuminate the relationship between DM, cancer, and inflammatory lung disease.
Acknowledgements. DMGC, Lujia Song
Key words: dermatomyositis, genetics, GWAS

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Inclusion Body Myositis

PT-84

EARLY INTERFERON PRIMING AND LATE METABOLIC REPROGRAMMING DEFINE LONGITUDINAL TRAJECTORIES IN INCLUSION BODY MYOSITIS

Felix Kleefeld[1,2], Alexander Mensch[3], Paula Quint[1,2], Abdulhadi Kocabas[1,2], Iago Pinal-Fernandez[4,5], Andrew L. Mammen[4,5], Menekse Öztürk[1,2], Jaqueline Kinold[2], Christina Barbara Schroeter, Anne-Katrin Güttsches[1,2], Corinna Preuße[7], Anne Schänzer[8], Benedikt Schoser[9], Werner Stenzel[7], Sven G. Meuth[6], Tobias Ruck[1,2,6], Christopher Nelke[1,2,6]
[1]Ruhr University Bochum, BG University Hospital Bergmannsheil, Department of Neurology, Bochum, Germany, [2]BG University Hospital Bergmannsheil, Heimer Institute for Muscle Research, Bochum, Germany, [3]Department of Neurology, Martin Luther University Halle-Wittenberg and University Hospital Halle, Halle, Germany, [4]Muscle Disease Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, USA, [5]Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, USA, [6]Department of Neurology, Medical Faculty, Heinrich Heine University Duesseldorf, Duesseldorf, Germany, [7]Department of Neuropathology, Charité - Universitätsmedizin Berlin, Berlin, Germany, [8]Institute of Neuropathology, Justus-Liebig-University Giessen, Giessen, Germany, [9]Friedrich Baur Institute at the Department of Neurology, LMU University Hospital, LMU Munich, Munich, Germany

Background. Inclusion body myositis (IBM) is the most frequent idiopathic inflammatory myopathy (IIM) in individuals over the age of 45 and considered resistant to current immunotherapies. Our previous work has identified early mitochondrial damage as a hallmark feature and that a subset of patients with polymyositis with mitochondrial pathology (PM-Mito) progress to IBM. However, the temporal sequence and interplay of immune activation and muscle degeneration in IBM remains unresolved, largely due to the scarcity of longitudinal molecular datasets.
Methods. To address this gap, we applied single nucleus sequencing to serial muscle biopsies from IBM patients (n=4) and controls, thereby generating a time-resolved transcriptomic map spanning early and late disease stages. Early stages were muscle biopsies before the histopathological diagnosis of IBM, while the follow-up biopsy demonstrated confirmed IBM according to the ENMC criteria. IBM Early disease stages We validated our results in an external patient cohort of muscle biopsies from IIM patients, that were profiled by bulk RNA sequencing (n=669).
Results. Our analyses revealed that interferon-γ (IFN-γ) signalling is a prominent feature in early IBM, preceding extensive immune infiltration and coinciding with the emergence of distinct myofiber states characterized by inflammatory and stressed transcriptional programs. Trajectory modelling further demonstrated a lineage-specific block in myogenic maturation, most pronounced in the type II fibre trajectory, which fails to progress to a fully differentiated phenotype. Cross-validation supported substantial enrichment for IFN-γ activity in PM-Mito in an independent cohort.
Conclusions. Together, these findings identify IFN-γ-driven reprogramming of myofiber differentiation as an early event in IBM pathogenesis and point to the IFN-γ axis as a rational target for early therapeutic intervention.
Key words: inclusion body myositis, transcriptomics, serial biopsies, interferon-γ

PT-209

APPLICATION OF A SEMI-QUANTITATIVE ULTRASOUND GRADING SCALE FOR ASSESSING THE SEVERITY OF MUSCLE INVOLVEMENT IN INCLUSION BODY MYOSITIS

Takeshi Yoshida[1], Christopher Mecoli[2], Julie Paik[2], Lisa Christopher-Stine[2], Jemima Albayda[2]
[1]Chikamori Hospital, Kochi, Japan, [2]Johns Hopkins University, Baltimore, USA

Background. To assess the severity of inclusion body myositis (IBM), clinical measures such as manual muscle testing (MMT) and the IBM Functional Rating Scale (IBM-FRS) have primarily been used. Recently, we introduced the Hopkins Myositis Grading Scale, a four-point semi-quantitative ultrasound measure for evaluating the severity of muscle involvement in myositis, which has demonstrated improved reliability and validity compared with the original Heckmatt scale. In this study, we aimed to assess disease severity in IBM using muscle ultrasound and to evaluate the correlation between imaging findings and clinical measures.
Methods. Using the Hopkins image bank, we analyzed ultrasound image data from patients with IBM collected between 2015 and 2025. Clinical data, including patient demographics, muscle strength, and IBM-FRS scores were available for correlation. Transverse ultrasound images of the biceps brachii (BB), flexor digitorum profundus (FDP), and rectus femoris (RF) acquired in a standardized fashion were utilized for this study. Semi-quantitative analysis was performed by two evaluators using the Hopkins Myositis Grading Scale (ref). Statistical analyses were conducted using SPSS. Correlations between ultrasound scores (total score of all muscles or individual muscle scores) and clinical measures, including MMT and IBM-FRS, were evaluated using Spearman's correlation analysis.
Results. Ultrasound images from a total of 54 patients with IBM were analyzed. The mean age was 66 years, and the female-to-male ratio was 21:33. The correlation coefficients between the ultrasound scores for individual muscles and IBM-FRS were -0.322 ($p=0.019$), -0.351 ($p=0.013$), and -0.548 ($p<0.001$) for the BB, FDP, and RF, respectively. The total ultrasound score also showed a significant correlation with IBM-FRS ($r= -0.502$, $p<0.001$). The ultrasound score for the RF demonstrated a strong correlation with the item 8-10 of IBM-FRS, which represent leg function ($r= -0.647$, $p<0.001$), whereas ultrasound score for the FDP showed a weaker correlation with item 2-4, representing hand function ($r= -0.343$, $p=0.017$).
Conclusions. Muscle ultrasound assessed by the Hopkins Myositis Grading Scale demonstrated significant correlations with IBM-FRS, indicating its potential as a reliable tool for evaluating disease severity and monitoring progression in IBM. Among the examined muscles, the RF demonstrated the strongest correlations with the total IBM-FRS.
Key words: inclusion body myositis, muscle ultrasound, IBM-FRS

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PT-366

COMPARATIVE EVALUATION OF CLINICAL OUTCOME MEASURES IN INCLUSION BODY MYOSITIS BASED ON NT5C1A ANTIBODY SEROLOGY STATUS

Marie Wencel[1], Isela Hernandez[1], Namita A Goyal[1], Olimpia Carbunar[2], Miriam Freimer[3], Mazen Dimachkie[4], Colin Quinn[5], Thomas Lloyd[6], Payam Mohassel[6], Conrad Weihl[7], Aziz Shabani[8], Leo Wang[9], Nizar Chahin[10], Anthony A Amato[11], Matthew Wicklund[12], Stacy Dixon[12], Perry Shieh[13], Laura Herbelin[14], Richard Barohn[14], Rabi Tawil[15], Emma Ciafaloni[15], Spencer Matthews[1], Tahseen Mozaffar[1]
[1]University Of California, Irvine, [2]University of Miami, [3]The Ohio State University, [4]Kansas University Medical Center, [5]Pennsylvania State University, [6]Johns Hopkins University, [7]Washington University in St. Louis, [8]Nerve and Muscle Center of Texas, [9]University of Washington, [10]Oregon Health & Science University, [11]Brigham and Women's Hospital, [12]University of Colorado, Denver, [13]University of California, Los Angeles, [14]University of Missouri, [15]University of Rochester, USA

Background. Inclusion Body Myositis (IBM) is the most common acquired muscle disease in individuals over age 40. Characterized by progressive, asymmetric muscle weakness, IBM leads to significant impairment in mobility and daily functioning. The underlying mechanisms and progression of IBM remain incompletely understood. One biomarker of interest is the presence of NT5c1A antibodies. Previous studies in small patient cohorts have shown that seropositivity for NT5c1A antibodies is associated with more severe clinical manifestations. However, larger-scale studies are needed to further characterize the impact of NT5c1A seropositivity. The objective of this analysis is to evaluate the association between NT5c1A antibody seropositivity and how it specifically impacts functional and physical performance in a large cohort of IBM patients over an 18-month period.
Methods. INSPIRE-IBM is an ongoing, 2-year prospective observational study with 150 patients enrolled across 13 centers. Inclusion criteria included disease onset within the last 10 years of the Baseline visit. Data have been collected at Baseline, Month 6, and Month 12, with Month 18 visits. Assessments include Manual Muscle Testing (MMT), Timed Up and Go (TUG), IBMFRS, SIFA, and NIH-PROMIS Physical Function questionnaire. The rate of change of functional assessments in seropositive *vs.* seronegative patients was assessed using a Generalized Estimating Equation (GEE) model with an AR-1 working correlation structure.
Results. At the time of this analysis, 118 participants have completed the Month 18 visit. There was no significant difference found between various functional measures and the rate of their decline based on the serological status from Baseline to Month 18.
Conclusions. Anti-NT5c1A antibodies may not influence a faster functional deterioration in IBM nor predict a more rapid progression rates in the first 10 years of disease duration. Furthermore, the similarity in progression trajectories indicates that stratification by NT5c1A status may not be necessary in a clinical trial design focused on these functional outcome measures. Additional analysis will be performed at the completion of the two-year study.
Key words: inclusion body myositis

Juvenile Myositis

PT-268

SINGLE NUCLEI MULTIOME OF JUVENILE DERMATOMYOSITIS MUSCLE BIOPSIES REVEALS NOVEL UPREGULATION OF INFLAMMATORY AND VASCULAR PATHWAYS

Shannon O'Connor[1], Casey Swoboda[1], Matthew Weirauch[1], Alexander Zygmunt[1], Douglas Millay[1], Leah Kottyan[1]
[1]Cincinnati Children's Hospital Medical Center, Cincinnati, USA

Background. Juvenile dermatomyositis (JDM) is a multisystem vasculopathy and inflammatory myopathy characterized by proximal muscle weakness, distinct rash, and risk of long-term complications such as calcinosis, skin ulceration, and chronic disease. Although Type I and Type II Interferon signatures are well established, this alone does not explain the full pattern of disease; the basic biology of JDM remains poorly defined. Heterogeneity in outcomes necessitates a more fundamental understanding of disease mechanisms.
Our objective is to understand genome-scale gene dysregulation in JDM through a multiomic study of single nuclei from treatment naïve muscle biopsies. We hypothesize that JDM etiology is mediated by molecular and cellular changes in the muscle and associated small blood vessels.
Methods. Muscle biopsies were collected from treatment naïve patients with JDM and congenital myopathy (CM). Biopsies were flash-frozen in liquid nitrogen and stored at -80°C (Cincinnati Children's Hospital Medical Center (CCHMC) Pathology Core). Single nuclei isolation was performed (10x Genomics protocol with optimization performed on murine samples), followed by Chromium Next GEM Single Cell Multiome ATAC+ Gene Expression processing (CCHMC Single Cell Genomics Core).
Sequencing data were analyzed through DNA and RNA read alignment and quantification using CellRanger. Ambient mRNA was removed, doublets identified, and low-quality nuclei removed using CellBender. Data were visualized in a two-dimensional space using dimensionality reduction and cluster identification using Seurat. Additional discovery of molecular pathway signatures was performed using CellHarmony.
Results. Single nuclei clustering revealed typical cell types consistent with previously demonstrated normal muscle tissue. Differentially expressed

genes within individual cell types highlighted the known interferon signatures in multiple cell types. We also identified molecular signals consistent with dysfunction of vascular signaling pathways, especially between muscle and endothelial cells. There was marked upregulation of several inflammatory pathways that have not previously been described in JDM but have been identified in other inflammatory conditions.
Conclusions. We conducted a multiome study of single nuclei from treatment naïve muscle biopsies in JDM patients with a comparator group of congenital myopathy patients. While typical cell types of muscle are maintained, several pathways, in addition to a known interferon signature, demonstrate dysregulation, opening doors for further studies into the molecular dysfunction driving JDM pathology.
Key words: juvenile myositis, single nuclei RNAseq, vascular signaling

PT-363

SINGLE-CELL PROFILING REVEALS INTERFERON-HIGH PROLIFERATION IN JDM VERSUS NFKB-DRIVEN INFLAMMATION IN CSLE ACROSS NAIVE B AND CD56DIM CD16+ NK CELLS

Li Chen[1], Qinmengge Li[3,4], Kirsten Grant[1], Aurora Rynda[1], Lam C. Tsoi[3,4,5], J. Michelle Michelle Kahlenberg[2], Jessica L. Turnier[1]
[1]Division of Pediatric Rheumatology, Department of Pediatrics, University of Michigan Medical School, Ann Arbor, USA, [2]Division of Rheumatology, Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, USA, [3]Department of Dermatology, University of Michigan Medical School, Ann Arbor, USA, [4]Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor, USA, [5]Department of Computational Medicine & Bioinformatics, University of Michigan Medical School, Ann Arbor, USA

Background. Juvenile dermatomyositis (JDM) and childhood-onset systemic lupus erythematosus (cSLE) are pediatric autoimmune diseases that can present with overlapping clinical features yet have unique tropism for major organ involvement. The objective of this study was to characterize differences in circulating immune cell types and transcriptional signatures in treatment naive (TN) JDM *vs*. cSLE.
Methods. Fresh peripheral blood mononuclear cells (PBMCs) were isolated from TN-JDM (n=8), TN-cSLE (n=4), and healthy controls (CTL, n=4). Single cell RNA sequencing was performed on the 10x Genomics platform. We performed batch correction using Harmony, dimensionality reduction using principal component analysis (PCA) and uniform manifold approximation and projection (UMAP), and clustering using shared nearest neighbor. Cell types were annotated via published cell type specific marker genes. Pseudo-bulk counts were generated by aggregating raw counts per sample, followed by pseudo-bulk PCA, and differential analysis using limma-voom. Gene Set Enrichment Analysis (GSEA) was used to identify pathway differences between diagnoses.
Results. Memory and naïve B cells, CD56dim CD16+ NK cells, and CD16+ monocytes showed the largest transcriptional differences between JDM and cSLE. PCA indicated that naive B cells and CD56dim CD16+ NK cells were the only cell types that clearly separated the two diseases. In naïve B cells, GSEA showed upregulated Type I and II interferon signatures in both JDM and cSLE compared to controls. Beyond this, the diseases diverged along proliferative and inflammatory axes. JDM naïve B cells showed upregulated activity in MYC-E2F-G2M cell-cycle and DNA-repair pathways, indicating increased proliferative drive and metabolic engagement. In contrast, these programs were reduced in cSLE and were lower than in JDM. Instead, cSLE naive B cells showed higher cytokine and NFκB-associated inflammation, including TNFα, IL6–STAT3, and broad inflammatory-response pathways. Enhanced complement and innate effector signaling were also observed in cSLE naïve B cells. In CD56dim CD16+ NK cells, GSEA revealed a graded rise in Type I/II interferon signatures and proliferative modules (E2F, G2M, mitotic spindle, mTORC1), strongest in JDM, intermediate in cSLE, and lowest in controls. cSLE CD56dim CD16+ NK cells exhibited higher IL6-JAK-STAT3 signaling, a broad inflammatory-response module, and apoptosis relative to controls. The clearest point of divergence in CD56dim CD16+ NK cells lay in NFκB: JDM showed suppression of TNFα–NFκB, while cSLE maintained comparatively stronger NFκB-linked inflammation.
Conclusions. These data reveal two distinct immune trajectories: JDM is marked by an interferon-high but predominantly proliferative and metabolically engaged lymphocyte program, whereas cSLE is defined by stronger NFκB-centered inflammation, heightened cytokine responsiveness, and complement activation.

Other

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INCOME-BASED GLOBAL INEQUITIES IN MYOSITIS TRIAL READINESS AND ENGAGEMENT: FINDINGS FROM THE MCTC INVESTIGATOR NETWORK

Rachid Smaili[1], Kaushik Sreerama Reddy[2,3], Tang I.Y.K[4], Akira Yoshida[5], Eduardo Dourado[6,7,8], Julián Barahona-Correa[9], Océane Landon-Cardinal[10], Jennifer Ben Shimol[11], Raisa Lomanto Silva[12], Kendrea L. (Focht) Garand[13], Kathryn Cook[14], Kristin Houghton[15], Ana Valle[16], Chester V. Oddis[2], Jiří Vencovský[17], Masataka Kuwana[5], Rohit Aggarwal[2], Gandiga P.C[18], Shiri Keret[19]
[1]Division of Rheumatology, Internal Medicine & Clinical Immunology, Regional University Hospital My Ali Cherif, Errachidia, Morocco, [2]University of Pittsburgh School of Medicine, Rheumatology and Clinical Immunolog , USA, [3]Division of Infectious Diseases and International Health, Duke University School of Medicine, Durham, NC, USA , [4]Division of Rheumatology and Clinical Immunology, The University of Hong Kong, Hong Kong, [5]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan , [6]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal, Portugal, [7]Aveiro Rheumatology Research Centre, Egas Moniz Health Alliance, Aveiro, Portugal, Portugal, [8]Rheumatology Research Unit, Instituto de Medicina Molecular, Universidade de Lisboa, Lisbon, Portugal , [9]Department of Immunology and Rheumatology, Stanford University, Stanford, CA, USA , [10]Division of Rheumatology, Centre Hospitalier de l'Université de Montréal, Montréal, Canada, [11]Division of Rheumatology, Barzilai Medical Center, Ashkelon, Israel, [12]Department of Rheumatology, Allergy & Immunology, Massachusetts General Hospital, Boston, MA, USA , [13]Department of Communication Science and Disorders, University of Pittsburgh, Pittsburgh, PA, USA, [14]Division of Pediatric Rheumatology, Akron Children's Hospital, Akron, OH, USA, [15]Department of Pediatrics, Division of Rheumatology, University of British Columbia, Vancouver, BC, Canada, [16]Department of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA, [17]Institute of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [18]Division of Rheumatology, Emory University, Atlanta, GA, USA, [19]Rheumatology Unit, Bnai Zion Medical Center & Technion - Israel Institute of Technology, Haifa, Israel

Background. The 2025 World Health Assembly (WHA78) (1) recognised rare diseases as a global public health priority and called for more equitable participation in research. We assessed differences in training, self-rated assessment expertise, and research engagement among idiopathic inflammatory myopathy (IIM) investigators across high-income countries (HICs) and low-/middle-income countries (LMICs).
Methods. We analysed 527 responses from the Myositis Clinical Trials Consortium (MCTC) investigator e-survey. Countries were classified as HICs or LMICs using World Bank criteria (2). Outcomes included self-rated proficiency (Likert 1–5; 5 = certified) in assessment instruments commonly used in IIM clinical research, including IMACS core set tools such as Manual Muscle Testing (MMT-8/9), Myositis Disease Activity Assessment Tool (MDAAT), Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI), Physician Global Assessment (PhGA), and hand-held dynamometry (HHD). Research engagement was assessed via myositis publications and interventional trial participation in the past five years. Analyses used χ^2 and Mann-Whitney U-tests, and regression models adjusted for specialty and years of IIM clinical research experience.
Results. Of 527 respondents, 396 (75%) were from HICs and 131 (25%) from LMICs. Rheumatology was the most common specialty overall (74.2%) and was more prevalent among LMIC investigators (90% *vs*. 69%; p<0.001). Myositis-focused training was less common in LMICs (15.3% vs. 24.6%; p=0.03). LMIC investigators reported fewer interventional myositis trials over the past 5 years, consistent with adjusted models showing lower participation in interventional myositis trials (IRR = 0.32; 95% CI = 0.20–0.50; p<0.001). LMIC status was associated with lower self-reported experience ratings forfor MMT-8/9 (2.53 *vs*. 2.92; p=0.003), CDASI (2.26 *vs*. 2.56; p=0.031), and PhGA (2.59 *vs*. 2.94; p=0.022). All other instruments were not significant. Certification gaps were observed for CDASI (6.1% in LMICs *vs*. 16.7% in HICs; p=0.002) and MDAAT (7.6% *vs*. 16.2%; p=0.03). Prior IIM trial participation was lower among LMIC than HIC investigators (37.5% *vs*. 62%; p<0.001) and remained significantly lower after adjustment (aOR 0.37; 95% CI 0.15–0.58; p<0.001).
Conclusions. Income-stratified analyses reveal substantial disparities in IIM disease assessment capability and research participation, raising concerns about the representativeness and external validity of myositis evidence. Aligned with WHA78 priorities, equity-focused implementation strategies are needed, including scalable, standardised certification pathways, formalised

HIC–LMIC co-investigator frameworks, and targeted support for early-career investigators. Advancing global trial readiness is essential to ensure equitable translation of IIM research to patients across diverse settings.

Key words: idiopathic inflammatory myopathies, clinical trial readiness, research equity, low- and middle-income countries

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ASSOCIATION OF PARAOXONASE 1 ACTIVITY WITH CALCINOSIS IN PATIENTS WITH SCLERODERMA AND DERMATOMYOSITIS: AN EXPLORATORY ANALYSIS

Sangmee Sharon Bae[1], Srijana Davuluri[2], Brian S. Lee[2], Sean Lim[2], Daniela Marcovic[1], Ani Shahbazian[1], Jennifer M. Wang[1], Lorinda S. Chung[2], David F. Fiorentino[2], Christina Charles-Schoeman[1]
[1]UCLA Medical Center, Los Angeles, USA, [2]Stanford University, Palo Alto, USA

Background. Calcinosis is a feature seen in systemic sclerosis (SSc) and dermatomyositis (DM) that leads to significant morbidity and poor quality of life. Inflammatory vasculopathy is hypothesized to play a role in dystrophic mineral deposition. Paraoxonase1 (PON1) is a high-density lipoprotein (HDL) associated protein that protects the vascular endothelium from oxidative injury and damage. The current study aims to assess the association of calcinosis with PON1 activity in SSc and DM patients.

Methods. Calcinosis was identified in 3 longitudinal cohorts of adult patients with DM (2 cohorts) and SSc (1 cohort) that were collected from 2 academic centers. We performed a comparative analysis of clinical characteristics and PON1 activity between patients with and without calcinosis within each disease subgroup (SSc and DM).

PON1 paraoxonase activity was quantified using the paraoxon substrate as reported in previous work (PMID 34698804). Comparative analysis was performed both including and excluding plasma samples which were not optimized for the paraoxonase assay. Logistic regression was used to analyze the association between PON1 activity and calcinosis adjusting for age, sex and disease duration.

Results. Among 258 SSc patients and 652 DM patients, we identified a total of 186(20%) patients who ever had calcinosis. Calcinosis was more common in SSc (39.6%) compared to DM (13%, p<0.0001). Calcinosis was associated with longer disease duration in both SSc and DM. DM patients with calcinosis were significantly younger, had higher sedimentation rate and had higher incidence of anti SAE and NXP2 antibodies compared to DM without calcinosis.

PON1 paraoxonase activity was significantly lower in SSc patients with calcinosis compared to SSc without calcinosis, and a similar trend was seen within each DM cohort. Association between calcinosis and low PON1 was significant when the two DM cohorts were combined. Multivariate models adjusting for age, sex and disease duration demonstrated that the association between low paraoxonase and calcinosis was significant in SSc, in DM total (DM1+DM2) and in all 3 cohorts combined (SSc+DM1+DM2). SSc patients overall had a significantly lower paraoxonase activity compared to DM (p=0.0002), and SSc patients with calcinosis had the lowest paraoxonase activity.

Conclusions. Calcinosis was observed in 40% of SSc and 13% of DM patients. Calcinosis was associated with longer disease duration and ulcerations in both SSc and DM. Impairment in the activity of the PON1 enzyme, which normally protects the vascular endothelium from oxidative injury, was associated with the presence of calcinosis in both DM and SSc patients, suggesting potential involvement in the disease pathogenesis.

Key words: dermatomyositis, calcinosis

PT-294

IMPACT OF MEDITERRANEAN DIET ON OUTCOMES IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Lekshmi Minikumari Rahulan[1], Sreoshy Saha[2], Manali Sarkar[3], Maria Rosa Pellico[4,5], Elena Philppou[6,7], Praggya Yaadav[8], Tsvetelina Velikova[9], Abraham Edgar Gracia Ramos[10], Aviya Lanis[11], Karen Cheng[12,13,14], Dzifa Dey[15], Elena Nikiphorou[16,17], Jasmine Parihar[18], Vahed Maroufy[19], Vincenzo Venerito[20], Vikas Agarwal[1], Latika Gupta[21,22,23], CoVAD Group Authors[24]
[1]Sanjay Gandhi Postgraduate Institute Of Medical Sciences, Lucknow, India, [2]Mymensingh Medical College, Mymensingh, Bangladesh, [3]Sir H. N. Reliance Foundation Hospital and Research Centre, Mumbai, India, [4]Department of Clinical Sciences and Community Health, University of Milan, Italy, [5]Division of Rheumatology, ASST Gaetani Pini-CTO, Italy, [6]Department of Life Sciences, School of Life and Health Sciences, University of Nicosia, Cyprus, [7]Department of Nutritional Sciences, School of Life Course and Population Sciences, King's College London , UK, [8]Maharashtra Institute of Medical Sciences and Research, Latur, India, [9]Pediatric Rheumatologist, Children's Hospital at Montefiore, USA, [10]Department of Internal Medicine, General Hospital, National Medical Center "La Raza", Instituto Mexicano del Seguro Social, Av. Jacaranda S/N, Col. La Raza, Del. Azcapotzalco, Mexico, [11]Seattle Children's Hospital, Seattle, USA, [12]International Myositis Society, Associate Board Member, Germany, [13]MIHRA Foundation, Patient Advisory Board Member, USA, [14]Myositis Support and Understanding, EU Patient Advocate, USA, [15]University of Ghana School of Medicine and Dentistry, College of Health Sciences, Department of Medicine and Therapeutics, Korle-Bu, Ghana, [16]Centre for Rheumatic Diseases, King's College London, UK, [17]King's College Hospital, Rheumatology Department, UK, [18]All India Institute of Medical Science, Department of Neurology, India, [19]Department of Biostatistics and Data Science, The University of Texas Health Center at Houston School of Public Health, USA, [20]Rheumatology Unit, Department of Precision and Regenerative Medicine and Ionian Area, University of Bari Aldo Moro, Italy, [21]Department of Rheumatology, Royal Wolverhampton Hospitals NHS Trust, UK, [22]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham, UK, [23]Francis Crick Institute, UK, [24]CoVAD Group Authors

Background. Mediterranean diet (MedDiet) has been associated with improved cardiometabolic and inflammatory outcomes, but its influence on idiopathic inflammatory myopathies (IIM) and other rheumatic diseases remains understudied. Given the associated chronic systemic inflammation, fatigue, and multimorbidity, understanding dietary influences on physical and psychological health is clinically relevant.

Methods. This analysis utilized data from the 3rd 'Collating the Voice of People with Autoimmune Diseases' (CoVAD) study, a global multilingual survey assessing biopsychosocial determinants of health across autoimmune disorders. Data included demographics, disease characteristics, and validated measures of quality of life spanning physical health (PROMIS-PF4a, global physical health-GPH), global mental health (GMH), and psychosocial domains, alongside the 14-item Mediterranean Diet Adherence Screener (MEDAS). MedDiet intake was categorized as low (MEDAS ≤5), moderate (6–9), and high (≥10). Multivariable logistic regression identified predictors of high adherence. Factor analysis of mixed data (FAMD) and hierarchical clustering was further applied to identify meaningful clusters that differ in psychosocial, dietary, and disease-related factors.

Results. Among 4521 respondents (859 IIM, 3013 other rheumatic/musculoskeletal diseases (oRMD), 411 non-rheumatic autoimmune diseases (nRAID), 238 healthy controls), IIM participants were older (median 61 years) and predominantly female (76%) (Tables 1 & 2). Median MEDAS was 5 (4–7), comparable to other groups. Within IIM, PROMIS-PF4a and GPH improved significantly with increasing MEDAS (p = 0.026 and 0.029, respectively), while fatigue and pain showed a declining trend. There was a trend for lower basic and complex multimorbidity as well as mental health comorbidities in the high MEDAS group (Table 3).

In the various multivariable models for demographic, disease outcomes, comorbidities and socioeconomic variables, female gender (OR 2.69, 95% CI 1.09-6.60, p=0.03), dermatomyositis subtype (OR 4.61, 95% CI 1.91–11.14, p<0.001), higher PROMIS GPH (OR 1.06, 95% CI 1.02-1.11, p=0.006) lower fatigue (OR 0.88, 95% CI 0.78-0.99, p=0.04) and fewer household members (OR 0.60, 95% CI 0.43–0.83, p=0.002) showed association with high MEdDiet adherence. FAMD identified three clusters: an older, predominantly male, IBM predominant, high-damage cluster with lowest MEDAS, a symptom-dominant cluster with females with dermatomyositis and polymyositis having high comorbidity burden, and a younger, early dermatomyositis cluster with less damage and comorbidities but highest MEDAS (Fig. 1).

Conclusions. MedDiet adherence in IIM was modest but significantly associated with better physical function and a trend towards lower comorbidity burden, highlighting the potential of MedDiet to complement immunomodulatory therapy and enhance long-term functional and

psychosocial outcomes in IIM. Specific IIM clusters may benefit from targeted education and diet coaching.
Key words: diet, myositis, IIM, Mediterranean diet
Supplementary data:
https://drive.google.com/file/d/1e_gezX8NnSzcRW44zqJzHORm0_yAJatS/view?usp=sharing

Pathogenesis of Inflammatory Myopathy

PT-85

SPATIAL TRANSCRIPTOMICS IN IMMUNE-MEDIATED NECROTIZING MYOPATHY REVEALS A SPECIFIC NECROTIC SIGNATURE RELATED TO IMMUNE-DRIVEN FIBROSIS

Julian Dal Cin[1], Alexandrine Mahoudeau[1], Mona Bensalah[1], Laura Muraine[1], Bérénice Tendrel[1], Céline Anquetil[1], Damien Amelin[1], Loïs Bolko[2], Linda Chenane[1], Franck Letourneur[3], Angéline Madelaine[4], Sarah Léonard-Louis[4], Elisa Negroni[1], Capucine Trollet[1], Olivier Benveniste[1], Yves Allenbach[1]
[1]Sorbonne Université, INSERM, APHP, Paris, France, [2]Department of Rheumatology, Reims University, Reims, France, [3]Université de Paris, Institut Cochin, INSERM, U1016, CNRS UMR8104, Plateforme Séquençage et Génomique, Paris, France, [4]Reference Center for Neuromuscular Disorders, APHP, Pitié-Salpêtrière Hospital, Paris, France

Background. Immune-mediated necrotizing myopathies (IMNM) are characterized by muscle fiber necrosis, complement deposition around non-necrotic fibers, and macrophage infiltrates. Patients experience severe muscle damage and fibro-fatty replacement, often with incomplete strength recovery. While immune mechanisms have been implicated, the cellular drivers of persistent tissue remodeling remain poorly understood.
Methods. We applied spatial transcriptomics to skeletal muscle biopsies from IMNM patients and integrated the data with published single-nuclei RNA sequencing datasets to resolve gene expression in its spatial context. This approach enabled precise mapping of inflammatory, fibrotic, regenerative, and metabolic signatures within necrotic and peri-necrotic regions. Selected findings were complemented by in vitro assays to explore muscle–fibroblast interactions shaping local pathological phenotypes.
Results. We identified a distinct population of SFRP4$^+$ fibroblasts enriched in necrotic areas of IMNM muscle. These fibroblasts exhibited an immune-driven "tumor-like" inflammatory profile with complement activation and a specific interferon response marked by metallothionein expression. Peri-necrotic regions displayed pathological muscle signatures associated with interferon signaling and FABP4$^+$ metabolically dysfunctional myofibers. Functional studies supported the hypothesis that the necrotic muscle environment contributes to the emergence of this pathogenic fibroblast phenotype.
Conclusions. Our results reveal a necrotic niche in IMNM defined by SFRP4$^+$ fibroblasts interacting with macrophages and dysfunctional myofibers. This immune-driven fibroblast population may sustain chronic inflammation and fibro-fatty replacement, offering new mechanistic insight into persistent weakness and pointing toward therapeutic strategies targeting the muscle-fibroblast axis.
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Key words: immune-mediated necrotizing myopathies, necrosis, fibro-adipogenic progenitors, fibroblasts, immune-driven fibrosis, SFRP4, spatial transcriptomics, macrophages

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PROSPECTIVE MUSCLE BIOPSY TRANSCRIPTOMICS IN ACTIVE MYOSITIS IDENTIFIES MOLECULARLY DISTINCT SUBGROUPS

Julie Paik[1], Corina Antonescu[1], Doris Leung[1], Zuzana Bologna[1], Myma Albayda[1], Chris Mecoli[1], Eleni Tiniakou[2], Lisa Christopher-Stine[1], Fatima Strand[3], Liliana Florea[1]
[1]Johns Hopkins University, Baltimore, USA, [2]University of Texas, Houston, USA, [3]EMD Serono, Boston, USA

Background. Idiopathic inflammatory myopathies (IIM), or myositis, are a heterogeneous group of autoimmune muscle disorders that cause significant morbidity and disability. While prior transcriptomic studies have provided important insights into disease biology, most have relied on archived frozen muscle. To address this gap, we performed prospective needle muscle biopsies in IIM patients with active muscle disease, enabling minimally invasive, clinically relevant sampling for transcriptomic profiling. We hypothesized that this approach would reveal distinct molecular signatures across IIM subgroups and provide a feasible platform for future biomarker development.
Methods. We conducted a prospective, cross-sectional study of patients with IIM who had active disease, defined by proximal muscle weakness and/or elevated creatine kinase. Participants were classified into dermatomyositis (DM), immune-mediated necrotizing myopathy (IMNM), overlap myositis with systemic sclerosis (OM with SSc), or anti-synthetase syndrome (ASyS). Needle muscle biopsies were obtained and preserved for bulk RNA sequencing. Differential expression analysis was performed using standard RNA-seq pipelines. Significance was defined as $\log_2$ fold-change >1 with $p<0.05$ (FDR-adjusted); genes with log fold-change (log FC) >2 was emphasized in reporting. Healthy controls underwent biopsies for comparison
Results. A total of 18 IIM patients and six healthy controls were enrolled. 66% were male, 58% White, and 33% Black. Mean MMT-8 was 140 ± 11. Mean CK was 1245 ± 1633 U/L (median 322 [IQR 175–2038]); mean aldolase was 22 ± 14.8 U/L (median 17.2 [IQR 15–24]). Subgroup distribution included DM (n=4), IMNM (n=5), OM with SSc (n=6), ASyS (n=3), and controls (n=6). DM biopsies revealed 650 differentially expressed genes (DEGs, logFC >2, $p<0.05$) with enrichment of Type I IFN signaling and immunoglobulin gene expression, with strong induction of IFI6 and MMP3. IMNM showed 548 DEGs enriched for acute-phase response and regenerative pathways, including MMP3 and SPP1. OM with SSc demonstrated 368 DEGs enriched for immunoglobulin gene expression and extracellular matrix remodeling, including IGHV/IGKV family members and DMBT1. ASyS revealed 440 DEGs with prominent upregulation of immunoglobulin heavy and light chain genes.
Conclusions. Muscle transcriptomic profiling across IIM subgroups revealed distinct molecular signatures that mirror clinical heterogeneity. DM was characterized by a Type I IFN response, IMNM by regenerative pathways, ASyS by B-cell activation. OM demonstrated a strong immunoglobulin and extracellular matrix remodeling signature, highlighting an understudied subgroup where fibrosis and immune activation intersect. Together, these findings underscore the mechanistic diversity of IIM and support the feasibility of prospective needle muscle biopsies as a platform for biomarker discovery and precision trial design.
Key words: muscle transcriptomics, myositis subgroups, overlap myositis

Patient Perspectives

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LEADING THROUGH LIVED EXPERIENCE: INTERNATIONAL LEARNINGS IN PATIENT-LED RESEARCH AND PARTNERSHIP IN MYOSITIS

Kelly Beer[1,2], Kevin Austin[2,3], Bill Hawkins[3], Althea Doverty[1,2], Merrilee Needham[1,2,4,5], Rodney Jansen[6], Marlene Jansen[6,7], Yuan-Pai Hu[7], Lynn Wilson[7], Manuel Lubinus[7]
[1]Perron Institute for Neurological and Translational Science, Nedlands, Australia, [2]Murdoch University, Murdoch, Australia, [3]Enzyme Group, Sydney, Australia, [4]University of Notre Dame Australia, Fremantle, Australia, [5]Fiona Stanley Hospital, Murdoch, Australia, [6]Myositis Canada, Calgary, Canada, [7]Myositis Support and Understanding Association (MSU), Lincoln, USA

Background. Caregiver and patient experiences remain underrepresented in inclusion body myositis (IBM) research. Two patient-led initiatives – one from the United States (Myositis Support and Understanding, MSU) and one from Australia (Myositis Discovery Programme, Perth, Western Australia) – used lived-experience frameworks to explore burden, coping, and shared priorities among caregivers and patients. Together, they offer complementary insights into how relational and emotional dimensions shape disease management.
Objectives: To integrate and compare findings from the U.S. IBM Caregiver Survey (n=124) and the Australian IBM Patient and Carer Priorities Study (n=149), identifying convergent themes in emotional coping, caregiving dynamics, and planning for the future.
Methods. Both studies were designed and led by individuals with lived experience, supported by multidisciplinary collaborators. The U.S. survey used quantitative and qualitative questions across emotional, physical, financial, and relational domains. The Australian study combined interviews and surveys to identify and rank patient and caregiver priorities. Thematic synthesis identified overlapping burdens and potential areas for translational support.
Results. Common themes included emotional distress, relationship change, financial strain, and uncertainty about the future. Emotional burden: 47% of U.S. caregivers felt isolated, and 39% reported sadness or depression. Australian participants ranked mental health among their top three concerns. Relationship dynamics: 82% of U.S. caregivers felt they were the sole person their relative depended on, echoing the Australian theme of changing roles and relationships. Financial stress: Nearly half reduced essential or recreational spending, aligning with Australian reports of strain on carers' capabilities. Future planning: 78% of U.S. caregivers constantly worry about the future, and only 6.5% have a long-term care plan, mirroring Australia's top-ranked theme of uncertain future. Both studies underscored gaps in information, communication, and emotional support, with caregivers expressing limited confidence in asking for help.
Conclusions. Patient-led and caregiver-driven research highlights shared international priorities – mental health, role strain, and care planning – as central to living with IBM. Key enablers include mentorship, institutional support, equitable partnerships, and dedicated funding mechanisms. Tools such as coping frameworks may guide clinicians and researchers toward more empathetic, integrated approaches to IBM care.
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Key words: caregiver burden, Patient-led research, copying strategies

PT-161

DETERMINANTS OF SUBJECTIVE WELL-BEING IN INDIVIDUALS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Lekshmi Minikumari Rahulan[1], Meera Shah[2], Emilia Naseva[3,4], Tsvetelina Velikova[5], Tamar B Rubinstein[6], Manali Sarkar[7], Lavanya Mangla[8], Oliver Distler[9], Ingrid de Groot[10], Lisa Christ[11], Carlo Vinicio Caballero Uribe[12], Ai Lyn Tan[13,14], Abraham Edgar Gracia Ramos[15], Vidya Limaye[16,17], Jessica Day[18,19,20], Vahed Maroufy[21], Vincenzo Venerito[22], Vikas Agarwal[1], Latika Gupta[23,24,25], CoVAD Study Group[26]

[1]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, [2]Topiwala National Medical College and B Y L Nair Charitable Hospital, Mumbai, India, [3]Faculty of Public Health, Medical University of Sofia, Bulgaria, [4]Medical Faculty, Sofia University St. Kliment Ohridski, Bulgaria, [5]Children's Hospital at Montefiore, Bronx, USA, [6]Division of Rheumatology, Albert Einstein College of Medicine, Bronx, USA, [7]Sir H. N. Reliance Foundation Hospital and Research Centre, Mumbai, India, [8]Maulana Azad Medical College, 2-Bahadurshah Zafar Marg, India, [9]Department of Rheumatology, University Hospital Zurich, Switzerland, [10]Chair Dutch Myositis Working Group, Patient Association for Neuromuscular Diseases, The Netherlands, [11]Department of Rheumatology and Immunology, Inselspital, Bern University Hospital, University of Bern, Switzerland, [12]Unidad de Reumatologìa, Hospital Universidad del Norte, Barranquilla, Columbia, [13]NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, UK, [14]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, UK, [15]Department of Internal Medicine, General Hospital, National Medical Center "La Raza", Instituto Mexicano del Seguro Social, Azcapotzalco, Mexico, [16]Royal Adelaide Hospital, Adelaide, Australia, [17]Discipline of Medicine, University of Adelaide, Adelaide, Australia, [18]Department of Rheumatology, Royal Melbourne Hospital, Parkville, Australia, [19]Walter and Eliza Hall Institute of Medical Research, Parkville, Australia, [20]Department of Medical Biology, University of Melbourne, Parkville, Australia, [21]Department of Biostatistics and Data Science, The University of Texas Health Center at Houston School of Public Health, Houston, USA, [22]Rheumatology Unit, Department of Precision and Regenerative Medicine and Ionian Area, University of Bari Aldo Moro, Italy, [23]Department of Rheumatology, Royal Wolverhampton Hospitals NHS Trust, UK, [24]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham, UK, [25]Francis Crick Institute, UK, [26]COVAD Study Group

Background. Satisfaction with life is a key dimension of well-being in chronic diseases such as idiopathic inflammatory myopathies (IIM), which substantially affect physical, psychological, and social functioning. Traditional clinical measures predominantly focus on disease activity and functional impairment, but do not capture the patient's overall well-being. Evaluating life satisfaction offers insights into the psychological burden of IIM and informs holistic, patient-centred care.
Methods. This cross-sectional study utilised data from the "Collating the Voice of People with Autoimmune Diseases" (COVAD) survey, an international, patient-reported e-survey that aimed to assess the subjective well-being on health outcomes and quality of life in patients with autoimmune rheumatic diseases. Patient-reported subjective well-being was assessed using the Satisfaction With Life Scale (SWLS) in individuals with IIM, other rheumatic/musculoskeletal diseases (oRMD), non-rheumatic autoimmune diseases (nRAID), and healthy controls (HC). Logistic regression identified independent predictors of high life satisfaction (SWLS ≥ 20) within IIM.
Results. Among 6153 respondents, 1028 had IIM (median age 60(47.8–70) years; 72.7 % female; 82.6 % from very high Human Development Index (HDI) countries). Median SWLS was lower in IIM (18 (13–24)) versus oRMD (20 (15–27)), nRAID (21 (15–26)), and HC (22 (16–27); p<0.0001). Among IIM subtypes, life satisfaction varied modestly, with the lowest median SWLS in dermatomyositis and polymyositis (17 (12–25)) and the highest in juvenile dermatomyositis (24 (18–27)). Median PROMIS physical function (PROMIS-PF4a 12 (8–16); PROMIS global physical health (GPH) 37.6 (30.5–44.7)); brief resilience scale (BRS 3.33 (2.83–4.00)) and self-efficacy to manage chronic disease score (SEMCD 5.33 (4.00–7.00)) were lower in IIM compared to other disease groups and HC.
Lower fatigue (OR 0.92 (0.85–0.98), pain (OR 0.92, 0.86–0.98), and disease damage (OR 0.90, 0.84–0.97), as well as higher family support (OR 1.09, 1.03–1.15) and job satisfaction (OR 1.02, 1.00–1.03) were associated with higher SWLS, whereas loneliness (OR 0.80, 0.73–0.86) predicted lower SWLS. Fibromyalgia trended toward lower SWLS (OR 0.68, 0.45–1.01). In the integrated multivariable logistic regression model, higher self-efficacy (aOR 1.23, 1.13–1.35), resilience (aOR 1.31,1.06–1.61), and family support (aOR 1.08, 1.02–1.15) were independent predictors of greater life satisfaction, while female gender (aOR 0.64, 0.45–0.91) and higher disease damage (aOR 0.92,0.85–1.00) were inversely associated.
Conclusions. Patients with IIM demonstrated significantly lower life satisfaction than comparators. Self-efficacy, resilience, and family support along with pain severity and disease damage are key modifiable determinants of subjective well-being, underscoring the importance of integrating psychosocial interventions alongside disease-targeted care.
Key words: myositis, subjective wellbeing, IIM, chronic disease, patient perspective
Supplementary data:
https://drive.google.com/file/d/1qc2jhufy2OqBsuScbnuxtG5mMAt-7Ez4/view?usp=share_link

Therapeutic Advances

PT-53

EFFICACY OF A NOVEL MULTITARGETED REGIMEN COMBINING BARICITINIB, RITUXIMAB, AND TACROLIMUS (BRT-TX) FOR ANTI-MDA5 ANTIBODY-POSITIVE DERMATOMYOSITIS: A COMPARATIVE TRANSCRIPTOMIC STUDY

Yoshinobu Koyama[1], Moe Tokunaga[1], Yoshiharu Sato[3], Yoshinori Nishiura[1], Takako Saeki[2], Yu Nakai[1], Takeshi Natatsue[2], Kenta Shidahara[1]
[1]Japanese Red Cross Okayama Hospital, Okayama, Japan, [2]Japanese Red Cross Nagaoka Hospital, Nagaoka, Japan, [3]DNA Chip Research Inc., Kawasaki, Japan

Background. Anti–melanoma differentiation-associated gene 5 antibody-positive dermatomyositis (MDA5-DM) is characterised by rapidly progressive interstitial lung disease (RP-ILD) and poor prognosis, often refractory to the standard regimen combining tacrolimus and cyclophosphamide (TC-Tx). To improve survival in patients with multiple adverse prognostic factors, we developed a multitargeted regimen combining baricitinib, rituximab, and tacrolimus (BRT-Tx) and analysed its molecular effects focusing on interferon (IFN) signatures.
Methods. Fourteen MDA5-DM patients with poor prognostic indicators were studied. Seven received BRT-Tx, and seven previously treated with TC-Tx served as historical controls. Twelve-month survival was compared. For six cases (BRT = 3, TC = 3), transcriptome analysis of peripheral blood before and after treatment was performed. Differentially expressed genes (DEGs) were examined using cluster analysis and gene ontology (GO) enrichment to identify treatment- and prognosis-associated pathways. Longitudinal changes in type I, II, and III IFN signature scores were also evaluated.
Results. All patients treated with BRT-Tx survived 12 months, whereas four of seven (57%) in the TC-Tx group died of RP-ILD. Only one BRT-Tx patient required plasma exchange as rescue therapy, and one developed transient limbic encephalitis. Cytomegalovirus reactivation occurred in both groups (BRT 5/7; TC 6/7).
Cluster analysis revealed that gene-expression profiles did not segregate by treatment type but did clearly separate survivors from non-survivors. In BRT-Tx recipients, genes related to B-cell proliferation and receptor signalling were markedly down-regulated, while TC-Tx suppressed broader cell-proliferation pathways. Among survivors, genes associated with immunoglobulin complexes and B-cell signalling were significantly reduced, whereas fatal cases showed increased expression of glycosaminoglycan- and heparin-binding genes implicated in coagulation and vascular injury. IFN-signature scores showed no consistent treatment-based difference but declined or remained low in survivors, in contrast to post-treatment increases in fatal cases.
Conclusions. BRT-Tx may enhance survival in severe MDA5-DM by concurrently modulating B-cell, T-cell, and macrophage-driven autoimmunity, while avoiding cyclophosphamide-related risks of infertility and malignancy. A multicentre, investigator-initiated randomised controlled trial comparing BRT-Tx and TC-Tx (AMED-supported) will commence in 2026 to confirm its efficacy and safety.
Acknowledgements. We thank collaborating physicians and research staff for their contributions. This study was partially supported by the Japan Agency for Medical Research and Development (AMED) under grant no.: JP25ek0109784.
Key words: MDA5-DM, rapidly progressive interstitial lung disease, baricitinib, rituximab, tacrolimus, transcriptome, interferon signature, B-cell receptor signalling

PT-200

IN VITRO SCREENING OF NUCLEIC ACID THERAPIES TARGETING IFN BETA AS A NOVEL THERAPEUTIC APPROACH FOR ADULT AND JUVENILE DERMATOMYOSITIS

Joanna E. Parkes[1], Andrés F. Correa-Sánchez[1], Inês Fial[1], Isaac Tam[1], Mark Cunningham[1], Nick Lench[1], Peter L. Oliver[1]
[1]MRC Nucleic Acid Therapy Accelerator, Harwell Science and Innovation Campus, Didcot, UK

Background. Myositis is generally treated with corticosteroids and other immunosuppressive drugs that are not effective for all patients and cause considerable side effects. There is growing evidence that interferon (IFN) beta contributes to disease activity in adult and juvenile dermatomyositis (DM/JDM). Therefore, we propose IFN-beta mRNA knockdown with nucleic acid therapies as a novel therapeutic approach for DM/JDM.
Methods. Libraries of small interfering RNAs(siRNAs) and antisense oligonucleotides (ASOs) targeting the human IFN beta mRNA transcript IFNB1 were designed, synthesised and quality checked using in house protocols.
In vitro experiments were performed using immortalised myoblasts, dermal fibroblasts, A549 lung cells and primary healthy control and JDM myoblasts. Cells were stimulated to produce IFN beta by transfection with Poly(I:C) before transfection with siRNAs or ASOs. Quantitative qRT-PCR was then used to assess IFNB1 transcript knockdown alongside enzyme linked immunosorbent assays for secreted IFN-beta protein. Cytotoxicity was quantified using apoptosis and necrosis assays, and specificity of the lead siRNAs from the initial screen was evaluated using bulk RNA sequencing.
Results. Initially, a library of 27 siRNAs spanning the IFNB1 sequence was screened in stimulated immortalised myoblasts and five siRNAs showed greater than 50% knockdown of IFNB1. Of these, two siRNAs showed significant knockdown of both IFNB1 transcript and secreted IFN-beta protein in differentiated myotubes and dermal fibroblasts. In addition, these two lead siRNAs showed significant knockdown of IFNB1 in healthy and JDM myotubes. Cytotoxicity assays demonstrated no significant increase in apoptosis or necrosis at working concentrations of the lead siRNAs in most cell types. Importantly, RNA sequencing showed that treatment of dermal fibroblasts and JDM myotubes with either of the lead siRNAs dampened the activation of viral, immune and autoimmune pathways induced by Poly(I:C) treatment.
To screen more deeply across the IFNB1 sequence and compare siRNA and ASO modalities, a further 47 siRNAs and 67 ASOs were screened alongside the previous lead siRNAs in lung cells; 38 ASOs and 15 siRNAs showed significant knockdown of IFNB1 expression. Four ASOs and three siRNAs with greater than 70% knockdown of IFNB1 have been taken forward for evaluation in skin and muscle cells.
Conclusions. Initial screening, cytotoxicity and specificity analyses have shown that nucleic acid therapies have the potential to be a safe and effective method of knocking down expression of IFN-beta as a therapeutic approach in DM/JDM.
Acknowledgements. Cure JM Foundation grant funding. Platform for Immortalization of Human Cells, Institut de Myologie, Paris. ‘Cells, tissues and DNA from patients with neuromuscular diseases’ biobank, Milan.
Key words: nucleic acid therapy, antisense oligonucleotide, siRNA, dermatomyositis, juvenile dermatomyositis

Biomarkers & Imaging

P-9

AI-ENHANCED NAILFOLD CAPILLAROSCOPY DEFINES A MICROANGIOPATHY SIGNATURE OF ACTIVE IDIOPATHIC INFLAMMATORY MYOPATHIES AND IMPROVES CLINICAL STRATIFICATION

Jorge Álvarez-Troncoso[1], Borja del Carmelo Gracia Tello[3], Sergio Prieto-Gonzalez[4], Elena Martínez-Robles[1], Sebastián Molina-Ríos[5], Eiman Soliman[6], Diana Cristina Varela-Tabares[7], Tânia Santiago[8], Luis Sáez Comet[9], Miguel Antonio Mesa Navas[10], Franklin Uguña[11], Begoña Marí Alfonso[12], Miguel Martín Cascón[13], Tsvetoslav Georgiev[15], Grace Jimena Santamaría-Peñaloza[16], Santiago Bernal-Macias[17], Sally Patricia Pino-Hernández[18], Eva Calvo-Beguería[19], Jacek Olas[20], Eduardo Ramos Ibáñez[14], Gema María Lledó Ibáñez[2]
[1]Hospital Universitario La Paz, Madrid, Spain, [2]Hospital Regional Universitario de Málaga, Málaga, Spain, [3]Hospital Clínico Universitario Lozano Blesa, Zaragoza, Spain, [4]Hospital Clinic, Barcelona, Spain, [5]Hospital Universitario Nacional de Colombia, Bogotá, Colombia, [6]Alexandria Faculty of Medicine, Alexandria, Egypt, [7]Hospital General de Medellín, Medellín, Colombia, [8]ULS de Coimbra, Coimbra, Portugal, [9]Hospital Universitario Miguel Servet, Zaragoza, Spain, [10]Consultorio privado/Clínica del Rosario, Medellín, Colombia, [11]Sociedad Ecuatoriana de Reumatologia, Quito, Ecuador, [12]Hospital Universitario Parc Taulí, Sabadell, Spain, [13]Hospital General Universitario Morales Meseguer, Murcia, Spain, [14]Capillary.io, Zaragoza, Spain, [15]Hospital St. Marina, Varna, Bulgaria, [16]Hospital Metropolitano, Quito, Ecuador, [17]Hospital Universitario San Ignacio, Bogotá, Colombia, [18]Asoreuma, Care for Kids, Bogotá, Colombia, [19]Hospital San Jorge, Huesca, Spain, [20]Szpital Specjalistyczny im. J. Dietla, Cracow, Poland

Background. Microvascular injury is a hallmark of idiopathic inflammatory myopathies (IIM). We assessed whether quantitative nailfold video-capillaroscopy (NVC) independently discriminates disease activity and the incremental value of routine biomarkers and serology in a large, real-world cohort (CapIAMI).
Methods. Ambispective, international, multicenter study of adults with IIM. Standardized NVC was quantified with an AI platform (Capillary.io). At imaging, clinical data, biomarkers (creatine kinase [CK], aldolase, lactate dehydrogenase [LDH], C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], ferritin, ±KL-6), and myositis autoantibodies were collected. Disease activity (active *vs*. inactive) was clinically adjudicated. Prespecified models compared NVC-only versus NVC+biomarkers (regularized logistic regression; stratified 5-fold cross-validation).
Results. Among 400 records, 206 (51.5%) were active. Extramuscular activity in active cases was frequent (74%; skin 45.5%, lung 26.0%, articular 22.0%); isolated myositis 26%. Interstitial lung disease (ILD) occurred in 21.0% and associated with activity (OR 2.64; 95% CI 1.13–6.20; p=0.034).
Biomarkers. Active *vs*. inactive means were higher: CK 1,433 *vs*. 545 U/L (+163%), LDH 373 *vs*. 228 U/L (+64%; OR per SD 4.36, 95% CI 1.49–12.76; p=0.007), aldolase 16.1 *vs*. 10.2 U/L (+57%), CRP 11.71 *vs*. 8.34 mg/L (+41%), ESR 24.97 *vs*. 15.98 mm/h (+56%; OR per SD 1.78, 95% CI 1.07–2.94; p=0.026), ferritin 263 *vs*. 149 µg/L (+77%), KL-6 756 *vs*. 336 U/mL (+125%).
Serology (distribution). Ro52 positivity was more common in active disease (OR 3.78, 95% CI 1.30–11.03; p=0.017) and frequently co-occurred with Jo-1 (63%), SRP (57%), EJ (50%), PL-12 (44%), and PM/Scl (31%).
NVC patterns and quantitative phenotype: Algorithm-assigned patterns were non-specific 36.0%, normal 25.5%, scleroderma-like early 6.8%, active 10.0%, late 21.8%; patterns correlated with activity (user/Cutolo $p=1.8\times10^{-5}$; algorithmic $p=4.9\times10^{-5}$). Quantitative injury features tracked activity: % megacapillaries (OR/SD 2.40, 95% CI 1.16–4.99; p=0.0188), megacapillary area density (OR/SD 2.20, 95% CI 1.08–4.48; p=0.0293), hemorrhage density (OR/SD 2.50, 95% CI 1.17–5.32; p=0.0178), hemorrhage average area (OR/SD 2.10, 95% CI 1.19–3.72; p=0.0104), ramification average area (OR/SD 2.25, 95% CI 1.11–4.58; p=0.0249); protective signals included higher overall density (OR/SD 0.68, 95% CI 0.49–0.95; p=0.0226) and greater "normal" bed area (OR/SD 0.55, 95% CI 0.41–0.75; p=0.00012).
Performance: NVC-only accuracy 0.764, sensitivity 0.685, F1 0.703; NVC+biomarkers accuracy 0.821, sensitivity 0.796, F1 0.803.
Conclusions. AI-assisted NVC independently discriminates IIM activity and augments routine biomarkers. A reproducible microangiopathy signature megacapillaries, hemorrhages, ramification, and caliber enlargement with reduced capillary density/"normal" area – mirrors clinical activity. ILD and serologic patterns add complementary context. Findings support integrating standardized, quantitative NVC into multimodal assessment and clinical-trial enrichment, with prospective antibody-stratified validation.
Key words: nailfold capillaroscopy, idiopathic inflammatory myopathies, disease activity

P-23

PREDICTORS OF LONG-TERM RADIOGRAPHIC CHANGES AND MORTALITY IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES USING QUANTITATIVE IMAGING ANALYSIS: REAL WORLD EXPERIENCE FROM A SINGLE-CENTER LONGITUDINAL COHORT

Sangmee Bae, Daniela Marcovic, Augustine Chung, Jessica Channick, Andrea Oh, Tiffany De Leon, Fereidoun Abtin, Lila T. Pourzand, Grace Hyun Kim, Jihey Lee, Sangwook Bae, Donald Tashkin, Jonathan Goldin, Christina Charles-Schoeman
[1]UCLA Rheumatology, Los Angeles, USA

Background. To evaluate chest High-Resolution CT (HRCT) images from a real-world cohort of patients with idiopathic inflammatory myositis (IIM) using both quantitative CT scoring and radiologist visual review.
Methods. Retrospective analysis of a single-center longitudinal cohort was performed using HRCT images with thin-section, full inspiration non-contrast images available for review. Quantitative imaging analysis (QIA) scored the extent of ground glass (QGG), fibrosis (QLF) and total ILD (QILD). Baseline images were also visually reviewed by an expert group to determine the presence and pattern of ILD. QIA, pulmonary function tests (PFTs) and clinical variables were compared in patients with and without ILD on imaging ('visual ILD'). Linear regression was used to analyze the correlation between QIA and PFTs. Twelve-month and long-term (5 years) trends of QIA and PFTs were calculated in patients with 2 or more measurements within the specified time frame using mixed-effects models. Cox regression models were used to assess associations with all-cause mortality.
Results. A total of 277 patients with a mean age of 51 years, 74% female, 61% white, 11% Black, 16% Asian, 22% Hispanic, were included in our analysis. 77% of the cohort had dermatomyositis (DM) and 22% had antisynthetase syndrome (AsyS). HRCT images were available for visual review and QIA in 168 patients, of which ILD was identified by visual review in 51%. Mixed nonspecific interstitial pneumonia with organizing pneumonia (NSIP/OP) was noted in 35% of patients with visual ILD, followed by OP in 25% and NSIP alone in 18% of patients. QIA scores were significantly higher in patients with visual ILD and minimal in most patients with no visual ILD. QLF and QILD had strong associations with FVC (standardized regression coefficients β= -0.70 and -0.59) and DLCO (β= -0.75 and -0.64) across all patient-visits ($p<0.0001$ for all). Higher baseline QIA scores and increasing QLF and QILD trends in the first 12 months were associated with higher mortality (HR 1.04 to 1.09, $p<0.05$ for all).
Conclusions. We report our results of HRCT review in a real-world IIM cohort. QIA scores correlated with physiologic indices of disease severity and both baseline and early longitudinal QIA trends demonstrated associations with all-cause mortality.
Key words: interstitial lung disease, high resolution computed tomography (HRCT), quantitative imaging analysis

P-27

DYSREGULATED PATHWAYS AND POTENTIAL BIOMARKERS IN DERMATOMYOSITIS PLASMA-DERIVED EXTRACELLULAR VESICLES

Avital Baniel[1,2,3], Mariko Momohara-Ogawa[2,3], Victoria P. Werth[2,3]
[1]Dermatology, Tel Aviv Medical Center, Tel Aviv, Israel, [2]University of Pennsylvania, Philadelphia, USA, [3]VA Medical Center, Philadelphia, USA

Background. Extracellular vesicles (EVs) have been implicated in autoimmune disease pathogenesis. Plasma-derived DNA containing EVs have been shown to induce STING-mediated proinflammatory responses in dermatomyositis (DM), but their protein content is not well characterized.
Methods. We collected EVs from plasma of 16 DM patients and 5 controls. EVs were isolated using sequential ultracentrifugation and size- exclusion chromatography, and their content analyzed by mass spectrometry. Protein biomarkers that distinguish patients with DM from controls were assessed using the random forest algorithm. Protein abundance was validated in a second cohort by ELISA.
Results. Sixty-seven proteins were uniquely detected in the patient cohort. Thirty-five proteins were significantly differentially expressed, of which 13

were upregulated and 22 downregulated. Over-representation analysis found unique and upregulated proteins enriched for myeloid mediated immunity, glutathione metabolism, nucleic acid synthesis and vesicle transport pathways. Downregulated proteins were enriched for the classical and lectin complement pathways. The diminution of complement components in vesicles may reflect its abundance in target tissues but may also reflect host inability to circulate these molecules to damaged tissue, which in a chronic stage of disease may have a protective role. Using machine learning (random forest algorithm) 15 proteins were identified as biomarkers that distinguish patients with DM from controls. Of these, the following were validated by ELISA in a separate cohort: The antioxidant enzyme glutathione peroxidase 3 (GPX3) was significantly less abundant in patients' EVs (p=0.04) suggesting DM patients may be susceptible to oxidative stress due to defective transport of GPX3 by EVs. Two complement proteins, Ficolin-2 (FCN2) and SERPING1 were significantly less abundant in patients' EVs (p=0.007 and 0.006 respectively). Finally, surfactant protein B (SFTPB) was expressed almost exclusively in patients with lung disease, rendering it a possible marker for pulmonary involvement. Its assessment in plasma of DM patients with ILD revealed significantly higher abundance than in plasma of both healthy controls and DM patients without pulmonary disease (p<0.0001).
Conclusions. Our findings indicate GPX3, FCN2 and SERPING1 as biomarkers of disease in DM. SFTPB is a potential biomarker for pulmonary involvement in DM. This finding, along with a growing body of evidence, suggests roles for EVs as disease biomarkers and prompts further mechanistic studies not only in plasma, but also in muscle and skin.
Key words: extracellular vesicles, biomarker, dermatomyositis

P-29

SIGLEC1 IS A BIOMARKER OF DISEASE ACTIVITY IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Nathan Barreth[1], Valérie Leclair[2], Marie Hudson[2], Cristina Moran Toro[1], Yvan St. Pierre[2], Ashley Clarke[1], Paul Sciore[3], Mark Tarnopolsky[4], Sasha Bernatsky[2], Marvin Fritzler[3], Eugene Krustev[1], May Choi[1]
[1]University Of Calgary, Calgary, Canada, [2]McGill University, Montreal, Canada, [3]Mitogen Diagnostics Laboratory, Calgary, Canada, [4]McMaster Children's Hospital, Hamilton, Canadaù

Background. Sialic acid-binding Ig-like lectin 1 (SIGLEC1) is a monocyte-expressed adhesion molecule, a surrogate marker of the type I interferon pathway, and a candidate biomarker for several autoimmune diseases. Here, we investigated serum SIGLEC1 levels as a novel biomarker for overall disease activity and extramuscular organ disease activity in idiopathic inflammatory myopathies (IIM).
Methods. Baseline sera and clinicodemographic data from IIM patients enrolled in a multi-centre registry with routine bio-banked serum samples were included. SIGLEC1 concentrations were tested using a capture immunoassay (Aviva Systems Biology, San Diego CA). The physician global disease activity assessment (PGA) ranges from 0 (no disease activity) to 10 (very severe disease) and classified IIM patients as having active (PGA ≥2) or inactive (PGA <2) disease. Patients were also classified on the presence (≥1.0 cm) or absence (<1.0 cm) of disease activity for six extramuscular organ systems included in the myositis disease activity assessment visual analog scales tool (MYOACT): constitutional, cutaneous, skeletal, gastrointestinal, pulmonary, and cardiac. Mean SIGLEC1 concentrations (ng/mL) were compared between patients with active and inactive disease and between those with and without disease activity in each extramuscular organ system using t-test.
Results. The study cohort consisted of 87 IIM patients (67.8% female, mean age 55.4±14.3 years) with dermatomyositis (DM, n=31), polymyositis (PM, n=4), antisynthetase syndrome (ASyS, n=9), immune-mediated necrotizing myopathy (IMNM, n=6), inclusion body myositis (IBM, n=9), and overlap myositis (OM, n=28). Higher mean SIGLEC1 concentration differentiated active from inactive disease in IIM (difference 2.7 ng/mL, 95% CI 0.7-4.8) and DM (difference 4.0 ng/mL, 95% CI 0.3-7.5). Mean SIGLEC1 concentrations were significantly higher in IIM patients with cutaneous (difference 1.7 ng/mL, 95% CI 0.1-3.4), skeletal (difference 2.0 ng/mL, 95% CI 0.1-3.9), and gastrointestinal (difference 2.2 ng/mL, 95% CI 0.5-3.9) disease activity compared to patients without disease activity in these extramuscular organs.
Conclusions. SIGLEC1 levels are a promising biomarker for assessing disease activity in IIM and DM and are associated with cutaneous, skeletal, and gastrointestinal manifestations. The candidacy of SIGLEC1 as a novel biomarker of disease activity in patients with IIM requires further investigation and validation in a larger cohort. Future studies are underway to confirm these findings and evaluate SIGLEC1 as a predictor of overall IIM disease activity over the disease course. Ultimately, the study's results could help improve personalized treatment for patients with IIM.
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Key words: biomarker, myositis, clinical research

P-38

TYPE-I INTERFERON-STIMULATED GENE EXPRESSION IS ASSOCIATED WITH TREATMENT RESPONSE TO BARICITINIB IN UK ADULT IDIOPATHIC INFLAMMATORY MYOPATHY PATIENTS

Luke Tomlinson[1], Sarah Sugden[1], Nicholas Scott[1], Gillian Rice[1], Maria Christofi[1], Alexander Oldroyd[1,2], Hector Chinoy[1,2], Janine Lamb[1]
[1]University Of Manchester, Manchester, UK, [2]Salford Royal Hospital, Salford, UK

Background. Evidence implicating interferon signaling in the pathogenesis of idiopathic inflammatory myopathy (IIM) has highlighted the therapeutic potential of Janus kinase (JAK) inhibitors. The MYOJAK trial demonstrated the efficacy of the JAK1/2 inhibitor Baricitinib in adult IIM patients, resulting in improvements in skin and muscle disease as well as physical function. This study aimed to identify novel biomarkers of treatment response to Baricitinib in IIM in longitudinal biological samples collected from participants throughout the MYOJAK trial.
Methods. Longitudinal samples of whole blood and sera were collected throughout the MYOJAK trial from 15 UK adult IIM patients. To investigate the expression of interferon-related genes, expression levels of 32 interferon-related mRNAs were quantified with a custom-designed nCounter panel from Nanostring. The concentrations of 250 inflammation-related proteins were measured in sera samples with the NULISAseq™ Inflammation Panel 250 from Alamar Biosciences. Statistical analyses were carried out using R 4.5.1 software and 'lme4' and 'lmerTest' R packages were used to perform linear mixed modeling and multiple linear regression.
Results. Targeted mRNA expression analysis found that IIM patients exhibited significantly elevated expression of type-I (p<0.001) and type-II (p=0.035) interferon-stimulated genes prior to Baricitinib treatment, compared to healthy controls matched by age, sex and ethnicity. Analysis of longitudinal samples revealed that expression of the type-I interferon-stimulated gene ISG15 associated positively with physician and patient disease activity measures (p=0.001), and negatively with Total Improvement Score (p=0.045). Patients' type-I interferon signature at baseline positively correlated with their Total Improvement Score achieved after 24 weeks of Baricitinib treatment (β=3.77x10-4, p=0.016). Additionally, proteomic analysis of longitudinal samples revealed that serum levels of IFNβ protein positively associated with physician measures of disease activity (p=0.016).
Conclusions. This study demonstrates the potential of ISG15 and IFNβ as biomarkers for monitoring treatment response to Baricitinib in IIM patients, as well as the utility of a type-I interferon-stimulated gene signature in predicting treatment response to Baricitinib. Ultimately, the identification of several potential biomarkers of treatment response provides a basis for the personalisation of Baricitinib therapy in IIM.
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Key words: JAK inhibition, biomarker, interferon, precision medicine, clinical trial

P-75

NAILFOLD VIDEOCAPILLAROSCOPY FINDINGS IN PATIENTS WITH ANTI-AMINOACYL-TRNA SYNTHETASE ANTIBODIES

Yasuhito Hamaguchi[1], Naoki Mugii[1], Natsumi Fushida[1], Ko Fujii[1], Jiro Nishio[1], Kenta Kudo[1], Goro Sakurai[1], Sho Horie[1], Takashi Matsushita[1]
[1]Kanazawa University, Kanazawa, Japan

Background. Antisynthetase syndrome (ASyS) is characterized by common clinical features, including myositis, interstitial lung disease, and cutaneous manifestations. However, data on microvascular involvement assessed by nailfold videocapillaroscopy (NVC) in relation to specific anti-aminoacyl-tRNA synthetase (anti-ARS) antibodies (Abs) remain unclear. The aim of this study is to characterize NVC abnormalities in patients with ASyS and to compare microvascular patterns among individual anti-ARS Ab subtypes.
Methods. We retrospectively analyzed 66 Japanese patients positive for one of six anti-ARS Abs (Anti-Jo-1, EJ, PL-7, PL-12, KS, or OJ Abs). Each anti-ARS Ab was identified using RNA- and protein-immunoprecipitation assays. Seven NVC abnormalities were systematically evaluated: enlarged capillaries, reduced capillaries, hemorrhages, capillary ramifications, disorganization of the vascular array, capillary loss, and giant capillaries. Clinical data and serological profiles were also compared among subtypes.
Results. Enlarged and reduced capillaries, as well as hemorrhages, were frequent findings across most anti-ARS Ab subtypes. In contrast, patients with anti-KS Abs displayed significantly fewer NVC abnormalities, particularly hemorrhages (25% *vs*. 75–100% in other subtypes; $p<0.05$). Capillary ramifications, disorganization, and capillary loss were uncommon throughout all groups. The anti-KS antibody–positive subgroup also tended to exhibit milder clinical involvement, with lower serum CK levels and less frequent use of immunosuppressants compared with other subtypes.
Conclusions. NVC findings in ASyS are not uniform but vary according to the specific anti-ARS Ab present; anti-KS Abs identify a subset with milder microvascular involvement. Recognizing anti-ARS Ab specificity may help in understanding vascular heterogeneity in ASyS.
Key words: antisynthetase syndrome, anti-aminoacyl-tRNA synthetase antibody, videocapillaroscopy, nailfold capillary change

P-86

LONGITUDINAL SERUM PROTEOMIC PROFILES – A STEP CLOSER TO PERSONALIZED MONITORING IN DERMATOMYOSITIS

Natasha Le Blanc[1], Marie Hudson[1], Ana Cristina Gonzalez Sanchez[2], Lina Marcela Diaz-Gallo[2], Valérie Leclair[1]
[1]McGill University, Montreal, Canada, [2]Karolinska Institutet, Stockholm, Sweden

Background. Dermatomyositis (DM) is an immune-mediated disease characterized by heterogeneous clinical features. Disease activity relies on biomarkers such as creatine kinase (CK), which may be unreliable, particularly in patients with extra-muscular manifestations. Novel proteomic platforms have the potential to identify biomarkers that enable personalized disease monitoring. The objective of this study was to identify proteins associated with disease activity in DM using the Olink Target 96 Inflammation panel.
Methods. Six DM patients from a multicenter inflammatory myopathy registry with available longitudinal biobanked serum samples were identified. All patients met the 2017 EULAR/ACR classification criteria for adult idiopathic inflammatory myopathy. Disease activity was categorized according to the International Myositis Assessment and Clinical Study (IMACS) physician global assessment (PhGA) as low (PhGA 0–3) or moderate/high (PhGA 4–10). The IMACS core set measures required to calculate the 2016 ACR/EULAR Total Improvement Score were extracted. Serum samples were analyzed using proximity extension technology (Olink Proteomics Inc., Watertown, MA), simultaneously quantifying 92 proteins involved in inflammatory processes. Results were expressed as normalized protein expression (NPX) values (log2 scale), with higher NPX representing higher protein concentrations. Mean NPX differences (ΔNPX) between moderate/high and low disease activity samples were calculated using paired t-tests with Benjamini-Hochberg correction for multiple testing.
Results. Six female DM patients aged 34–53 years were included. Clinical features at timepoint 1 included rash (n=6), muscle weakness (n=5), interstitial lung disease (n=5), Raynaud's phenomenon (n=3), arthritis (n=1), and dysphagia (n=1). CK values ranged from 37–6039 U/L. Detected autoantibodies included anti-MDA5, -TIF1γ, -Mi2, -Ro52, and -Ku. At timepoint 1, five patients had moderate/high disease activity, and at timepoint 2, five had low activity. Eleven proteins were significantly upregulated when comparing moderate/high versus low activity. The largest ΔNPX values were observed for monocyte chemoattractant proteins MCP-2 (3.0), MCP-1 (2.4), MCP-4 (2.2) (all adj. p=0.02), and C-X-C motif chemokine 11 (CXCL11, –3.0, adj. p=0.05). Other upregulated proteins included CX3CL1 (1.57), CCL11 (1.42), PD-L1 (1.27), IL-4 (1.1), CD40 (0.92), IL-15RA (0.9), and CSF-1 (0.61) (all adj. p=0.05).
Conclusions. Using serum inflammatory profiles, we identified proteins upregulated in DM patients with moderate/high disease activity compared to low disease activity in a small exploratory cohort. Those included chemokines involved in monocyte and T-cell recruitment that could represent potential biomarkers for disease activity monitoring. Further studies on a larger number of DM patients are required to understand the potential of longitudinal proteomic analyses to improve personalized monitoring in DM.
Key words: dermatomyositis, biomarkers, disease activity, proteomics, inflammatory myopathy

P-90

POTENTIAL ROLE OF AN INCREASED INTERFERON GENE SIGNATURE SCORE AT BASELINE FOR THE PREDICTION OF A POSITIVE RESPONSE TO ANIFROLUMAB IN REFRACTORY JUVENILE DERMATOMYOSITIS

Razvan-Ionut Mihai[1], Tanja Hinze[2], Oliver Wiemann[1], Claas Hinze[3], Daniel Windschall[2], Peter Korsten[1]
[1]Department of Rheumatology and Clinical Immunology, St. Josef-stift Sendenhorst, Sendenhorst, Germany, [2]Department of Pediatric Rheumatology and Immunology, University Hospital Münster, Münster, Germany, [3]Department of Pediatric and Adolescent Rheumatology, St. Josef-stift Sendenhorst, Münster, Germany

Background. Dermatomyositis (DM) also occurs in pediatric patients (juvenile DM, JDM). In contrast to adult patients, there are no approved therapies, and some patients may be refractory to commonly used therapies. In DM, an increased interferon (IFN) gene signature (IFNGS) has been demonstrated (1). It is unclear whether an increased IFNGS can be used as a biomarker to predict the response to interferon-directed therapies. Here, we report two patients refractory to multiple therapies with increased IFNGS scores and a positive response to anifrolumab (ANI), a monoclonal antibody against the interferon-alpha receptor.
Methods. We report two cases of refractory JDM in which we determined IFNGS scores before applying an off-label therapy with ANI. We analyzed clinical, laboratory, and imaging data. The type-I-IFN score was calculated after extraction of RNA from whole blood after reverse transcription to cDNA. The expression of six IFN-stimulated genes (ISGs), ISG15, RSAD2, IFIT1, IFI44L, IFI27, and SIGLEC1, was measured with real-time PCR against RNA controls of healthy individuals with GAPDH and RPL as housekeeping genes. The final score was calculated as the median expression level of all six ISGs.
Results. The first patient was a 19-year-old male diagnosed five years prior. Previous therapies included GC, hydroxychloroquine (HCQ), baricitinib, methotrexate (MTX), tofacitinib, mycophenolate mofetil (MMF), and IVIg. Initially, antibodies against Mi2, Ro52, and TIF1 had been positive. His symptoms included erythema, skin ulcers, and widespread myositis with a decreased MMT-8 of 122/150. His IFNGS was increased. Three months after initiating ANI, we observed a marked improvement in his MMT-8 to 133, corresponding to a complete resolution of muscle edema on whole-body MRI. His skin changes also markedly improved to near-resolution.
The second patient was a 24-year-old female diagnosed 8 years before the initiation of ANI. Previous therapies consisted of GC, HCQ, azathioprine, MMF, IVIg, MTX, and cyclosporine A (CsA). She was positive for anti-TIF1g antibodies at the time of diagnosis, and symptomatic with skin changes (periungual erythema, calcinosis) and muscle weakness (MMT-8 of 131). After adding ANI to her MTX and CsA, muscle strength normalized after three months. We did not observe a clear decrease in the IFNGS in response to therapy.
Conclusions. In summary, we demonstrated the usefulness of increased IFNGS at baseline as a potential predictor for a response to ANI. It remains unclear whether a decrease in IFNGS correlates with the therapeutic response.

Key words: juvenile dermatomyositis, biomarker, interferon, monoclonal antibody

Reference

1. PINAL-FERNANDEZ *et al*.: Identification of distinctive interferon gene signatures in different types of myositis. *Neurology* 2019

P-110

NEWLY DEVELOPED ELISA FOR DETECTION OF CIRCULATING CALPROTECTIN IN SERUM AND PLASMA

Kathrin Hoffmann[1], Victor Herbst[1], Marko Silvestric-Scheel[2], Miriam Mende[1], Tanja Seifert[1], Viola Borchardt-Lohölter[1], and Pierre Lukas[3].
[1]Institute for Experimental Immunology, affiliated to EUROIMMUN Medizinische Labordiagnostika AG, Lübeck, Germany, [2]IDS Immunodiagnostic Systems, Tyne & Wear, UK, [3]Department of Clinical Chemistry, University of Liège, Belgium

Background. Circulating calprotectin is a biomarker that reflects activation of the innate immune system. Measuring its concentration in serum or plasma is relevant for diagnosis and monitoring of systemic inflammations, autoimmune diseases, and infections. Here we introduce a newly developed enzyme-linked immunosorbent assay (ELISA) from Euroimmun by presenting results of circulating calprotectin measurements in samples from healthy individuals and patients. Furthermore, the results of the ELISA are compared with those of a newly developed calprotectin chemiluminescence assay (ChLIA) from Immunodiagnostic Systems Ltd (IDS).
Methods. To determine the reference interval of the Circulating Calprotectin ELISA, calprotectin levels were measured in 136 paired serum and K3 EDTA samples from healthy adults (74 male, 62 female, age range: [19-71] years). For assessment of inflammatory status, calprotectin concentrations were measured in a panel comprising 441 serum samples from 136 healthy adults, 25 healthy children, 80 rheumatoid arthritis (RA) patients, 50 systemic lupus erythematodes (SLE) patients, 50 Sjögren's syndrome (SS) patients, 50 systemic sclerosis (SSc) patients, and 50 idiopathic inflammatory myopathy (IIM) patients with both the Circulating Calprotectin ELISA (Euroimmun) and the IDS Fluid Calprotectin ChLIA. Quantitative results (n=305) of both immunoassays were compared, and possible bias was estimated with Passing-Bablok regression.
Results. The upper 95% reference limit of the Circulating Calprotectin ELISA was higher for serum (2.29 µg/mL) than for plasma samples (1.31 µg/mL). Compared to healthy individuals, calprotectin concentrations were elevated in patient sera. Passing-Bablok regression indicated small constant and proportional differences between calprotectin concentrations measured with ELISA versus ChLIA (n = 305, regression: y = -0.13+1.33x, 95% confidence interval (CI) intercept: [-0.14, -0.10], CI slope: [1.32, 1.34]). In comparison, the calprotectin concentrations were lower when measured with ELISA.
Conclusions. Calprotectin concentrations measured with the Circulating Calprotectin ELISA (Euroimmun) aid in the serological assessment of inflammation status in rheumatic diseases. Despite the high agreement between the Circulating Calprotectin ELISA (Euroimmun) and the IDS Fluid Calprotectin ChLIA, the results showed differences. It is therefore necessary to emphasize that the quantitative results must be evaluated with respect to the assay-specific reference intervals. Soon, the newly developed ELISA will be applied in clinical studies set out to determine reference values, likelihood ratios, and correlation with disease states of different systemic inflammations. Future research will determine whether circulating calprotectin is a more specific biomarker of inflammation than C-reactive protein (CRP).
Key words: circulating calprotectin, myopathy, ELISA

P-120

VARIABLE ANA ASSOCIATIONS AMONG PATIENTS WITH MYOSITIS SPECIFIC AND ASSOCIATED ANTIBODIES: REAL WORLD EXPERIENCE FROM AN AUSTRALIAN TESTING CENTRE

Nicholas Villaluz[2], Chris Bundell[1,2], Kelly Beer[3,4], Anna Brusch[1,2,3]
[1]PathWest Laboratory Medicine, Perth, Australia, [2]University of Western Australia, Perth, Australia, [3]Perron Institute for Neurological and Translational Research Research, Perth, Australia, [4]Murdoch University, Perth, Australia

Background. Idiopathic inflammatory myopathies (IIM) are often initially investigated with anti-nuclear antibody (ANA) testing via indirect immunofluorescence (IIF). Subsequent tests include myositis-specific (MSA) and myositis-associated antibodies (MAA) that help define clinical subtypes. ANA patterns associated with various MSA and MAA have been mostly reported from cohort studies of specific disease subgroups. However, larger studies examining the prevalence of ANA and pattern type in relation to MSA and MAA using real-world data remain limited. This study aimed to examine the relationship between ANA results and myositis antibody profiles in a large diagnostic laboratory.
Methods. A retrospective study of ANA and myositis antibody results among 3,007 adult patients tested at PathWest Laboratory Medicine, Perth, Western Australia between 2018 & 2023 was conducted. ANA IIF was performed on HEp-2000 cells, with International Consensus on ANA patterns (ICAP) ANA staining pattern and fluorescence intensity recorded. The myositis panel tested for 16 MSA/MAA (Euroline16 Ag myositis profile, Euroimmun). Frequency of MSA/MAA detection, ANA intensity, nuclear and cytoplasmic staining patterns were assessed.
Results. Myositis antibodies were detected in 703 patients (23.4% of all patients tested). Of these, 589 (84%) were positive for a single MSA/MAA and 114 (16%) had two or more antibodies. Patients with antibodies typically associated with overlap myositis had the highest frequency of nuclear ANA detection (71% for Ku, 66% for PM-Scl75, and 54% for PM-Scl100). Cytoplasmic staining was most frequent among patients with anti-synthetase antibodies but was only detected in 27-40% of patients with these antibodies. ANA patterns were highly heterogeneous. Five or more different ANA nuclear patterns were recorded for 13 of 16 myositis antibody specificities and no single ANA pattern reliably associated with a particular myositis antibody.
Conclusions. To our knowledge, this is the largest study to integrate ANA results with comprehensive myositis antibody profiling. While the frequency of positive ANA tests segregated with myositis antibodies associated with particular IIM subtypes, ANA patterns were highly heterogenous with numerous patterns identified for the majority of myositis specificities. These data suggest that ANA associations of myositis antibodies are variable and further study is required to assess their significance alongside clinical findings.
Key words: anti-nuclear antibody, ANA, myositis antibodies, anti-synthetase, immunofluorescence

P-131

MICROVASCULAR INVOLVEMENT IN THE IDIOPATHIC INFLAMMATORY MYOPATHIES

Tabitha John[1,2], Joanne Manning[3], Graham Dinsdale[3], Nikola Wilk[4], Hector Chinoy[1,2,3], Janine Lamb[5], Andrea Murray[1,2,3]
[1]Division of Musculoskeletal and Dermatological Sciences, School of Biological Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK, [2]Rheumatic and Musculoskeletal Disease Theme, NIHR Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK, [3]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [4]Department of Medicine, Division of Rheumatology, The Ottawa Hospital, University of Ottawa, Ottawa, Canada, [5]Division of Population Health, Health Services Research and Primary Care, School of Health Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK

Background. Microvascular abnormalities are a hallmark of autoimmune diseases such as the idiopathic inflammatory myopathies (IIMs) and systemic sclerosis (SSc). In SSc, non-invasive imaging techniques including nailfold capillaroscopy (NC) and thermal imaging with a cold challenge are routinely used to evaluate capillary morphology and assess whether rewarming ability is affected by Raynaud's phenomenon. In contrast, the nature and extent of microvascular involvement in IIMs remain poorly defined, with existing data limited and often conflicting. This study aimed to characterise and compare microvascular abnormalities in two subtypes of IIMs: anti-synthetase syndrome (ASyS) and dermatomyositis (DM), and in SSc.
Methods. Participants underwent NC (8 fingers) and baseline skin temperature imaging using infrared thermography, an indirect measure of perfusion. Where possible, patients underwent cold challenge (both hands in 15°C water for 1 min, followed by rewarming for 15 mins at 23°C). Outcome measures included capillary density and dimension, thermal distal dorsal difference (DDD), and area under the rewarming curve.
Results. This interim analysis of a 3-year study included 31 patients: 8

ASyS (median [range] age 49.8 [24.5-65.4] years, all female), 10 DM (58.1 [24.1-69.4] years, 9 female) and 13 SSc (64.4 [40.1-82.4] years, 12 female). Median [range] disease duration was 8.0 [0.6-17.5] years in ASyS, 5.1 [1.3-19.4] years in DM and 10.1 [4.9-35.3] years in SSc.
NC outcomes of mean capillary density and dimensions did not differ significantly between groups. The mean number of giant capillaries per finger was significantly lower in ASyS (0.03±0.02) *vs*. SSc (0.87±0.26, p=0.046), while DM patients demonstrated the greatest within-group heterogeneity (1.14±0.59) which did not reach statistical significance. The mean DDD at 23°C was significantly lower in the SSc patient group (-2.65±0.34°C) compared with ASyS (-0.66±0.47°C, p=0.015). The DM group showed intermediate values (-1.52±1.46°C), which were not significantly different from either group. Whilst patterns were evident between groups in rewarming imaging outcomes, no measures reached statistical significance.
Conclusions. Measures of microvascular involvement and dysfunction were more pronounced in SSc compared to ASyS patients. DM patients demonstrated the greatest within-group variability, with no significant differences compared to other groups. Ongoing analyses with increased patient numbers will further clarify disease-specific microvascular patterns and enable correlation with clinical features and autoantibody profiles.
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Key words: microvascular abnormalities, nailfold capillaroscopy, infrared thermography

P-138

OPTOACOUSTIC IMAGING AS A POTENTIAL NON-INVASIVE BIOMARKER IN INCLUSION BODY MYOSITIS

Stefanie Meyer[1,2], Hannah Bruex[1,2], Alica Stobbe[1,2], Stefanie Glaubitz[1,2], Janek Gröhl[3], Ferdinand Knieling[4], Roman Raming[4], Frauke Alves[5,6], Dörthe Malzahn[7], Stephan von Haehling[8], Jana Zschuentzsch[1,2]
[1]University Medical Center Goettingen, Clinic for Neurology, Goettingen, Germany, [2]University Medical Center Goettingen, Heart & Brain Center Goettingen, Goettingen, Germany, [3]European Neuroscience Institute, Working Group Quantitative Molecular Imaging, Goettingen, Germany, [4]University Medical Center Erlangen, Pediatric Experimental and Translational Imaging Laboratory, Department of Pediatric and Adolescent Medicine, Erlangen, Germany, [5]Max Planck Institute for Multidisciplinary Sciences, City Campus, Translational Molecular Imaging, Goettingen, Germany, [6]University Medical Center Goettingen, Clinic for Haematology and Oncology, Goettingen, Germany, [7]mzBiostatistics, Statistical Consultancy, Goettingen, Germany, [8]University Medical Center Goettingen, Department of Cardiology and Pneumology, Goettingen, Germany

Background. Diagnosis of inclusion body myositis (IBM) presents an ongoing challenge, due to heterogenous phenotypes and rareness of disease. Muscle biopsy remains pivotal for diagnostic certainty. Diagnostic yield is dependent on biopsy location and can be obscured by lack of typical features (1), emphasizing the need for additional biomarkers. Multispectral optoacoustic tomography (MSOT) exploits the photoacoustic effect to provide ultrastructural tissue information and has been able to detect structural muscle changes in several neuromuscular diseases (2,3,4).
Methods. MSOT examinations of skeletal muscle of 10 IBM patients (n=8 male, n=2 female, mean age 71.9 years) were compared to 10 age- and sex-matched healthy volunteers (HV) assessing intramuscular levels of lipid (MSOT_LIP) and collagen (MSOT_COL). Association of MSOT-results with standardized clinical outcome measures were evaluated.
Results. MSOT_LIP was increased in skeletal muscle in IBM compared to HV (effect 1.10, p=0.0038) whereas MSOT_COL showed significant reduction in IBM (effect -0.65, p=0.0016). Increased MSOT_LIP was significantly associated with decreased muscle strength (effect 0.029, p=0.014) as well as reduced mobility (6-minute walking test: effect -0.0021, p=0.0034). Patient reported outcome measures (IBM functional rating scale, functional disability index) were found to be associated with changes in MSOT_LIP and MSOT_COL as well.
Conclusions. This first study exploring the use of MSOT in IBM. Structural changes in skeletal muscle tissue of IBM patients were identified using optoacoustic imaging, with MSOT_LIP and MSOT_COL providing robust readout parameters. Association with functional outcome measures supports their clinical meaningfulness. Further studies are needed to evaluate the effects in a larger, more diverse population and explore intraindividual changes in optoacoustic properties longitudinally.
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Key words: inclusion body myositis, optoacoustic imaging, biomarker

P-145

DISTRIBUTION PATTERNS AND PREDICTIVE VALUE OF IGG, IGA AND IGM AUTOANTIBODY ISOTYPES IN ANTI-SYNTHETASE SYNDROME AND INTERSTITIAL LUNG DISEASE

Charlotta Preger[1], Ceke Hellstrom[4], Edvard Wigren[1,2], Johan Ronnelid[5], Helena Persson[4], Susanne Gräslund[1,2], Ingrid E. Lundberg[1,2,3], Per-Johan Jakobsson[1,2,3], Antonella Notarnicola[1,2,3]
[1]Division of Rheumatology, Department of Medicine, Solna, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, [2]Center for Molecular Medicine, Karolinska University Hospital, Stockholm, Sweden, [3]Department of Gastroenterology, Dermatology and Rheumatology, Theme Inflammation and Aging, Karolinska University Hospita, Stockholm, Sweden, [4]KTH Royal Institute of Technology, Department of Protein Science, SciLifeLab, Stockholm, Sweden, [5]Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden

Background. Anti-synthetase syndrome (ASyS) is a rare systemic autoimmune disease, within Idiopathic Inflammatory Myopathies (IIM), distinguished by the presence of autoantibodies against aminoacyl-tRNA synthetases (anti-aaRS), most commonly anti-Jo1. Clinically, ASyS presents with a triad of manifestations, namely myositis, interstitial lung disease (ILD), and arthritis. According to Connors criteria, positivity for at least one of the eight anti-aaRS autoantibodies is required for ASyS classification. Currently, only autoantibodies of IgG isotype are analyzed in the clinical setting, potentially missing patients with anti-aaRS IgM or IgA. The aim of the study was to investigate the presence of anti-aaRS autoantibody isotypes in patients with IIM and correlate with clinical manifestations.
Methods. Sera from patients with IIM (n=303) including 69 with ASyS (60 anti-Jo1+), followed at Karolinska University Hospital, and population controls (PC, n=156) were screened for IgG, IgA, and IgM autoantibodies against all aaRS using a multiplex bead array assay. Correlations with clinical manifestations was performed.
Results. We identified 65 IIM patients (21.5%) with autoantibodies targeting full-length HisRS, the target of anti-Jo1. Of these, 27 (41.5%) had both IgG and IgM, while 24 (36.9 %) had only IgG. Anti-Jo1 IgA were detected in 12 patients, together with IgG and/or IgM. Reactivities against the HisRS-WHEP, the major autoantigenic epitope of anti-Jo1, were identified in 70 patients of which 40 (57.1%) had all three isotypes. Of the four other more common anti-aaRS autoantibodies, 34 individuals (11.2%) were positive for anti-PL12, 23 (7.6%) for anti-PL7, 18 (5.9%) for anti-EJ, and 12 (3.9%) for anti-OJ. In contrast to anti-Jo1, most individuals with these autoantibodies had only one isotype present.
When investigating the predictive value of having more than one isotype for anti-Jo1, we found that the best prediction of having ASyS is given to the combination of all three isotypes against the WHEP domain (AUC=0.92) compared to only IgG (AUC=0.88, p=0.04). Moreover, within the IIM cohort, the combination of all three isotypes against the WHEP domain of Jo1 had the highest predictive value for ILD (AUC=0.77) compared to only IgG (AUC=0.73, p=not significant).
Conclusions. Most patients with anti-Jo1 reactivity harbour autoantibodies of IgG, IgA and IgM isotypes in contrast with patients reactive to other anti-aaRS with usually only one isotype. Presence of the three isotypes for anti-Jo1 increases the prediction of having ASyS and ILD, as compared to only anti-Jo1 IgG. Our preliminary results would support also testing for anti-Jo1 IgM and IgA to improve diagnostic accuracy of ASyS.
Key words: autoantibody isotypes, anti-synthetase syndrome, anti-Jo1 autoantibodies

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CARDIAC MRI T1 AND T2 MAPPING CHANGES IN MYOSITIS FOLLOWING IMMUNOSUPPRESSIVE THERAPY: A PROSPECTIVE OBSERVATIONAL STUDY

Soeren Jæger Rahbek[1,2], Redi Pecini[2,3], Søren Jakobsen[1,2], Andreas Knage[1], Kasper Søltoft Larsen[5], Kasper Yde Jensen[1], Kateryna Yurchenko[1], Eva Søndergaard[4], Pil Højgaard[6], Louise Pyndt Diederichsen[1,2]

[1]Copenhagen Research Center for Autoimmune Connective Tissue Diseases (COPEACT), Center for Rheumatology and Spine Diseases, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark, [2]Department of Clinical Medicine, Faculty of Health and Medical Science, University of Copenhagen, Copenhagen, Denmark, [3]Department of Cardiology, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark, [4]Department of Cardiology, Odense University Hospital, Odense, Denmark, [5]Department of Clinical Rheumatology, Odense University Hospital, Odense, Denmark, [6]Department of Clinical Rheumatology, Frederiksberg University Hospital, Copenhagen, Denmark

Background. Cardiac involvement in myositis is often subclinical but a major contributor to disease-related mortality. Cardiac magnetic resonance imaging (CMRI) with T1 and T2 mapping enables non-invasive quantification of myocardial inflammation, but longitudinal data during early immunosuppressive therapy are limited. This study aims to assess changes in myocardial tissue characteristics after four months of immunosuppressive treatment in newly diagnosed treatment naive myositis patients.

Methods. We conducted a prospective observational cohort study including 20 newly diagnosed treatment naive myositis patients. CMRI was performed at baseline and after four months of immunosuppressive therapy assessing native T1, T2, late gadolinium enhancement (LGE) and left ventricular ejection fraction (LVEF) measurements.

Treatment response was evaluated using the Total Myositis Improvement Score (TIS) incorporating manual muscle testing, patient and physician global activity scores, physician-assessed extra-muscular activity score, Health Assessment Questionnaire, and muscle enzyme levels. Additional cardiac assessments included electrocardiograph (ECG), a cardiac questionnaire, and cardiac troponins (TnI and TnT). Myositis subtype, autoantibody profile, and immunosuppressive therapy was recorded (n=19 with follow-up data).

A t-test on paired differences or Wilcoxon signed-rank test was used, as appropriate, to evaluate the changes from baseline to 4-month-follow-up, with $p<0.05$ considered statistically significant.

Results. Patients had a mean age of 55±15,6 yrs; 13(65%) female. Myositis subtypes included; dermatomyositis (n=5), anti-synthetase syndrome (n=8), immune-mediated necrotizing myopathy (n=6), and inclusion body myositis (n=1).

After baseline measurements, all patients except two received high dose prednisolone supplemented with methotrexate (n=9), mycophenolate mofetil (n=9), hydroxychloroquine (n=2), rituximab (n= 5) or infliximab (n= 1). Following four months of immunosuppressive therapy, native T1 and LVEF decreased significantly ($p=0.05$, $p<0.01$, respectively). There was no significant changes in T2 or ECG parameters. LGE was present in 3 patients at baseline; at follow-up, LGE had resolved in 1 patient.

Disease activity improved significantly across all TIS components ($p<0.01$). Mean TIS was 55 ±17,9: 9 major-, 4 moderate-, 4 minimal- and 2 patients with no improvement.

Conclusions. To our knowledge this is the first study to examine myocardial inflammation by CMRI in newly diagnosed treatment naive myositis patients. We observed marked clinical improvement alongside a significant decrease in native T1 and LVEF following 4 months of immunosuppressive treatment, The observed reduction in native T1 may reflect a decrease in subclinical myocarditis. However, CMRI changes did not correlate with overall disease activity, highlighting the need for further research into cardiac-specific biomarkers in myositis.

Key words: CMRI, native T1, myocarditis, myositis, idiopathic inflammatory myopathies

P-151

ASSESSING THE DIAGNOSTIC UTILITY OF BASELINE CREATINE KINASE LEVELS IN PATIENTS WITH SUSPECTED IDIOPATHIC INFLAMMATORY MYOPATHIES AND NEUROMUSCULAR DISORDERS

Nikola Wilk[1], Filipe O. Pinheiro[2], Catherine Ivory[1], Nancy Maltez[1,3], James B. Lilleker[4,5], Hector Chinoy[5,6,7]

[1]Department of Medicine, Division of Rheumatology, The Ottawa Hospital, University of Ottawa, Ottawa, ON, Canada, [2]Department of Rheumatology, Centro Hospitalar Universitário de São João, Porto, Portugal, [3]Clinical Epidemiology, The Ottawa Hospital Research Institute, Ottawa, ON, Canada, [4]Manchester Centre for Clinical Neurosciences, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [5]Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, The University of Manchester, UK, [6]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [7]National Institute for Health Research Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, The University of Manchester, Manchester, UK

Background. The use of serum creatine kinase (CK) is universally utilized in the diagnostic evaluation of neuromuscular disorders (NMD), including idiopathic inflammatory myopathies (IIM). As most laboratories use the central 95% of observations in white people as a reference range for serum CK, abnormal CK levels are frequent in otherwise healthy individuals. We sought to investigate the predictive role of patients baseline CK at various cutoff values in patients referred with a suspected IIM or NMD diagnosis.

Methods. We performed a retrospective chart review of consecutive adult patients attending a Neuromuscular clinic at a tertiary hospital in Salford, UK, from January 2018 to June 2022. We investigated the test characteristics of CK based on several a priori defined thresholds, including our laboratory-defined cutoffs, the 97.5th percentile for serum CK and the thresholds recommended by European Federation of Neurological Societies (EFNS). Additional predefined thresholds (>1000 IU/L, >1500 IU/L, and >2000 IU/L) were pragmatically evaluated, irrespective of ethnicity and sex, to assess whether higher universal cut-offs improve the predictive value of the baseline CK for IIM and other NMD.

Results. We identified 277 IIM cases, 69 with a non-inflammatory myopathy and 135 had benign/reassuring etiology. The baseline CK levels were significantly higher in the IIM and non-inflammatory myopathy groups when compared to the benign/reassuring group ($p<0.01$). The laboratory-defined cutoffs for CK yielded a sensitivity of 75.7%, a specificity of 60.7% and a PPV of 83.2% for either an IIM or NMD, which only marginally improved when evaluating the 97.5th percentile (sensitivity 74.6%, specificity 62.2% and PPV 83.5%). A slight improvement of the specificity (73.6%) and PPV (86.3%) was observed when using the threshold of 1.5 times the upper limit of normal (ULN). A more pronounced alteration of the test characteristics could be observed when evaluating our prespecified cut-offs of >1000IU/L, with an expected decline in sensitivity (49.7%), and increase of the specificity (88.9%) and PPV (92.0%). These changes continued to accrue with the >1500IU/L and >2000IU/L thresholds.

Conclusions. The current thresholds defined by the EFNS guidelines to pursue investigations for elevated CK has only moderate sensitivity (67.6%), specificity (73.6%) and PPV (86.3%). A CK threshold of 2000 IU/L corresponds to fewer than 5% false negatives. This study highlights the role of baseline CK levels in suspected IIM and neuromuscular disorders, clarifying its diagnostic value and limitations.

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AI ANALYSED FDG PET/CT AS A MARKER OF TEMPORAL CHANGES IN MUSCLE INFLAMMATION IN NEWLY DIAGNOSED IDIOPATHIC INFLAMMATORY MYOPATHIES: A PROSPECTIVE COHORT STUDY

Niclas Hansen[5,8], Jane Angel Simonsen[1,2], Thomas Lund Andersen[9], Helle Hjorth Johannesen[9], Lars Edenbrandt[3,4], Annika Loft[9], Louise Pyndt Diederichsen[5,6,7]

[1]Department of Nuclear Medicine, Odense University Hospital, Odense, Denmark, [2]Department of Clinical Research, University of Southern Denmark, Odense, Denmark, [3]Molecular and Clinical Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden, [4]University of Gothenburg, Gothenburg, Sweden, [5]Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark, [6]Department of Rheumatology,

Odense University Hospital, Odense, Denmark, [7]Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark, [8]Department of Rheumatology, Slagelse Hospital, Slagelse, Denmark, [9]Department of Nuclear Medicine, Rigshospitalet, Copenhagen, Denmark

Background. We aim to show proof of concept that artificial intelligence (AI)-assisted analysis of fluorodeoxyglucose positron emission tomography-computed tomography (FDG PET/CT) can be used in monitoring muscle inflammation in newly diagnosed idiopathic inflammatory myopathies (IIM).
Methods. In this prospective cohort study, 21 newly diagnosed IIM patients were enrolled at two tertiary myositis centers in Denmark. FDG PET/CT scans were performed at baseline and after 4 months of immunosuppressive treatment, complemented by clinical assessments and blood tests. FDG uptake as a surrogate of muscle inflammation was quantified using the RECOMIA platform, an AI tool that segments skeletal muscles in CT scans and extracts corresponding FDG uptake values. Changes in FDG Standardized Uptake Value (SUV) and muscle volumes were correlated with clinical improvement, as measured by Total Improvement scores (TIS).
Results. There was a significant reduction in SUVmean (p=0.006) at 4 months, consistent with clinical improvements with TIS showing 10 patients (50%) with Major Response, 5 (25%) with Moderate Response, 4 (20%) with Minimal Response and 1 (5%) with No Response. A positive correlation was found between reductions in SUVmean and improvements in TIS (p=0.003). There was no significant correlation between changes in muscle volume and TIS
Conclusions. AI-assisted FDG PET/CT may offer a reproducible and quantitative marker of muscle inflammation in IIM, demonstrating correlations with clinical improvement over time. This imaging approach holds promise for monitoring treatment response within a clinically relevant timeframe.
Acknowledgments. We thank the departments of Nuclear Medicine at Rigshospitalet and OUH for their invaluable work in making the PET-CT scans possible. We also thank the team working with the RECOMIA platform for developing the tools necessary for making this research possible.
Key words: FDG PET/CT, positron emission, tomography computed, tomography antisynthetase syndrome, dermatomyositis, inflammatory myopathies, myositis, polymyositis, therapeutic assessment, monitoring artificial intelligence RECOMIA

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A PREDICTIVE MODEL FOR LIVER ENZYME ELEVATIONS BASED ON CREATINE KINASE IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Tanya Chandra[1], Shiri Keret[2], Nantakarn Pongtarakulpanit[1,3], Kaushik Sreerama Reddy[1,4], Siamak Moghadam-Kia[1], Jesse Wilkerson[5], Dana P. Ascherman[1], Chester V. Oddis[1], Rohit Aggarwal[1]
[1]University of Pittsburgh Medical Center, Pittsburgh, USA, [2]Bnai-Zion Medical Center, Technion, Israel, [3]Division of Allergy, Immunology and Rheumatology, Department of Medicine, Faculty of Medicine Ramathibodi Hospital,Mahidol University, Bangkok, Thailand, [4]Division of Infectious Diseases and International Health, Duke University School of Medicine, Durham, USA, [5]DLH,LLC, Bethesda, USA

Background. Idiopathic inflammatory myopathies (IIM) are characterized by elevated muscle enzymes, including creatine kinase (CK), aldolase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH). While CK is a relatively specific marker of muscle injury, AST and ALT are also indicators of liver damage, complicating interpretation- particularly in patients receiving potentially hepatotoxic medications. We aimed to develop a predictive model for estimating liver enzyme levels based on CK values in IIM patients, to differentiate between muscle-derived enzyme elevations and true hepatotoxicity.
Methods. We studied adults in the Rituximab in Myositis (RIM) trial, a multicenter, randomized, double-blind, placebo-controlled trial of patients with refractory dermatomyositis (DM) or polymyositis (PM). Patients with known liver disease were excluded. Data on CK, AST, and ALT were collected across 11 visits (44 weeks). Enzyme values were standardized as multiples of the upper limit of normal (xULN). Concurrent medication use, including potentially hepatotoxic agents such as methotrexate, acetaminophen, and NSAIDS, was documented. All enzyme values were incorporated into a repeated measures mixed model as $\log_{10}$-transformed variables to normalize distributions. Predicted enzyme levels were derived from the model and subsequently back-transformed to xULN
Results. The study included 147 patients (49% DM, 51% PM), with a mean age of 49 ± 11.3 years; 75% were female and 71% were White. Muscle enzyme-to-CK ratios remained stable over time (median range 0.19-0.87). There were no significant differences in CK, AST, ALT, or enzyme-to-CK ratios between patients receiving hepatotoxic medications and those who were not (Example: AST/CK ratios were 0.32 *vs*. 0.41, (p-value 0.32) respectively). Similar results were observed in a sub-analysis comparing methotrexate users to non-users. ALT and AST levels were predicted from CK using model-derived formulas: ALT = $0.480 \times \log_{10}(CK) + 0.186$ ($R^2 = 0.78$) and AST = $0.598 \times \log_{10}(CK) + 0.204$ ($R^2 = 0.82$). For example, for CK levels between 2 and 3 times the ULN, the estimated ALT and AST values were 1.0 and 0.96 xULN, respectively. Estimated AST and ALT based on CK levels were similar in DM *vs*. PM patients.
Conclusions. A CK-based predictive model can allow reliable estimation of AST and ALT in IIM patients, providing a valuable framework for distinguishing muscle-related enzyme elevations from potential liver injury. The use of hepatotoxic medications did not significantly influence liver enzyme levels in this cohort. This model can potentially aid clinicians in interpreting liver enzyme elevations in the context of active muscle disease.
Key words: muscle enzymes, transaminases

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CELL-FREE DNA PLASMA LEVELS IN IDIOPATHIC INFLAMMATORY MYOPATHIES AS A POTENTIAL BIO-MARKER OF MUSCLE INVOLVEMENT

Hana Wünsch[1], Sabína Oreská[1], Kristina Svobodová[1], Lucia Vernerová[1],. Dana Dlouhá[2], Karel Pavelka[1], Jiří Vencovský[1], Ladislav Šenolt[1], Michal Vráblík[3], Jaroslav Alois Hubáček[2], Michal Tomčík[1]
[1]Institute of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, [2]Experimental Medicine Center, Institute for Clinical and Experimental Medicine, Prague, [3]3rd Department of Internal Medicine, General University Hospital and 1st Faculty of Medicine, Charles University, Prague

Background. Idiopathic inflammatory myopathies (IIM) are characterized by inflammatory muscle injury. Circulating cell-free DNA (cfDNA), including nuclear (cfnDNA) and mitochondrial (cfmtDNA) DNA, increases after exercise primarily due to apoptosis or necrosis and might be a biomarker for muscle injury in IIM. The aim was to explore the association between cfnDNA/cfmtDNA and muscle involvement in IIM.
Methods. 66 patients with IIM were included: 22 men; mean age 57.6; disease duration 2.27 years; 21 dermatomyositis (DM)/ 29 polymyositis (PM), both without statin history/ 16 statin-induced immune-mediated necrotizing myopathy (IMNM). Follow-up at 6 months of immunosuppressive therapy included 15 patients (6 DM, 6 PM, 3 IMNM). Basal laboratory parameters, clinical features, current treatment, and body composition (by bioelectric impedance analysis (BIA-2000-M)) were evaluated. cfDNA was isolated using the Plasma/Serum Cell-Free Circulating DNA Purification Mini Kit (Norgen Biotek). Two independent markers for cfnDNA (IL6 and CTO), and cfmtDNA (ND5 and CO3) were analyzed by qPCR. Data are present-ed as mean (SD).
Results. There were no significant differences in plasma concentrations of selected cfnDNA/cfmtDNA markers among the IIM subtypes. Elevated expression of both cfnDNA and cfmtDNA was associated with worse disease damage (MDI), decreased muscle strength (MMT8), higher body fat percentage (BF%), reduced basal metabolic rate (BMR), and decreased capacity for physical activity (higher ECM/BCM, lower phase angle). There was a positive correlation was between cfnDNA expression and disease activity (MITAX), and cfmtDNA and age and plasma glucose levels ($p<0.05$ for all). Six-month follow-up after im-munosuppressive treatment initiation in 15 IIM showed statistically significant reductions in disease activ-ity,muscle injury markers (CK, LD, myoglobin), and glucocorticoid dose, and increased muscle strength ($p<0.05$ for all). However, the decrease in both cfnDNA and cfmtDNA expression was not significant. Low-er baseline expression of cfnDNA (IL6) predicted a trend to an increased muscle strength (MMT8) (p=0.09).
Conclusions. Expression of both cfDNA did not significantly vary among the IIM subtypes, but was associ-ated with disease activity and damage, muscle weakness, and physical function. Despite the significant improvement in muscle impairment and the reduction in glucocorticoid dose in 15 IIM patients 6 months after immunosuppressive treatment initiation, the expression of cfnDNA and cfmtDNA did not change significantly. There was a promising prediction of increased muscle strength by baseline expression of cfnDNA (IL6). Both cfnDNA and cfmtDNA deserve further studies aimed at their potential role as a marker of muscle involvement, or treatment response in IIM.

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Key words: myositis, biomarker, cell-free DNA

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MULTI-ANCESTRY GENOME-WIDE ASSOCIATION STUDY OF CREATINE KINASE HIGHLIGHTS THE GENETIC BASIS OF MUSCLE DAMAGE

Gang Chen[1], Sizheng Zhao[2,3], Hector Chinoy[2,3,4], James Lilleker[2,5], Weijie Liu[2], Yuhui Li[1,2,6], Andrew Morris[2,3], Janine Lamb[1]
[1]Epidemiology and Public Health Group, School of Health Sciences, The University of Manchester, Manchester, UK, [2]Centre for Musculoskeletal Research, Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK, [3]NIHR Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK, [4]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [5]Manchester Centre for Clinical Neuroscience, Manchester Academic Health Science Centre, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Salford, UK, [6]Department of Rheumatology and Immunology and Beijing Key Laboratory for Rheumatism and Immune Diagnosis, Peking University People's Hospital, Beijing, China

Background. Serum creatine kinase (CK) is a routinely measured biomarker of muscle damage, yet the genetic factors underlying inter-individual variation in CK levels remain poorly defined.
Methods. We performed the largest multi-ancestry genome-wide association meta-analysis of serum CK to date (n=237,255), spanning Admixed American, African American, East Asian, European and Middle Eastern populations. Genome-wide significant loci were identified at p<5×10-8. We assessed tissue/cell-type and pathway enrichment, overlap with Mendelian myopathy genes, and conducted integrative quantitative trait locus (QTL)-based Mendelian randomization and colocalization to prioritize causal genes. Genetic correlations with related traits were estimated to characterize pleiotropy.
Results. We identify 107 independent loci at genome-wide significance (p<5x10-8), 98 of which are previously unreported, with pronounced enrichment for genes expressed in skeletal and cardiac muscle and overlap with pathways related to muscle structure and function. Notably, eight loci map to genes implicated in Mendelian myopathies, underscoring a continuum from common regulatory variation to rare pathogenic mutations. Integrative QTL-based Mendelian randomization and colocalization implicate several genes in CK regulation, most prominently SMAD3, KLF5 and STAT3 within the TGF-β signalling pathway. CK levels show positive genetic correlations with traits reflecting tissue damage and muscle mass, and negative correlations with C-reactive protein, indicating pleiotropic effects on muscle biology and enzyme clearance.
Conclusions. This multi-ancestry analysis delineates the genetic architecture of serum CK, uncovers biologically relevant pathways – especially TGF-β signaling – and links common variation to Mendelian myopathy genes. These findings inform interpretation of CK elevations across diverse populations and provide a genetic framework of muscle-damage risk and subclinical CK elevation.
Acknowledgements. We thank the participants and investigators of the BioBank Japan Project, the Million Veteran Program, the Qatar Genome Program, and the Vanderbilt University Medical Center for their invaluable contributions to this study.
Key words: creatine kinase, genetic association, muscle damage, TGF-β signaling, Mendelian myopathies

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ANALYTICAL PERFORMANCE OF COMMERCIAL MYOSITIS-SPECIFIC AUTOANTIBODY TESTS EVALUATED AGAINST IMMUNOPRECIPITATION ASSAYS AS A REFERENCE STANDARD: A SYSTEMATIC REVIEW AND META-ANALYSIS

Takahisa Gono[1,2], Albert Gil-Vila[3], Albert Selva-O'Callaghan[3], Annet van Royen-Kerkhof[4], Anett Vincze[5], Christopher Mecoli[6], Diana Gómez-Martín[7], Dörte Hamann[8], Edoardo Conticini[9], Zoltán Griger[5], Jose Jiram Torres-Ruiz[7], John D Pauling[10], Hector Chinoy[11,12], Latika Gupta[13,14], Levente Bodoki[15], Noreen Nasir[16], Pallavi Pimpale Chavan[17], Raju Khubchandani[18], Ernesto Trallero-Araguás[19], Yasuhito Hamaguchi[20], Lisa G Rider[21], Rohit Aggarwal[22], Sarah Tansley[23], Johan Rönnelid[24], Masataka Kuwana[1,2], Neil J. McHugh[23]
[1]Department of Allergy and Rheumatology, Nippon Medical School, Tokyo, Japan, [2]Scleroderma/Myositis Center of Excellence, Nippon Medical School Hospital, Tokyo, Japan, [3]Systemic Autoimmune Diseases Unit, Department of Internal Medicine, Vall d'Hebron General Hospital, and Department of Medicine, Universitat Autònoma, Barcelona, Spain, [4]Department of Neurology, Amsterdam University Medical Centre, Location AMC, Amsterdam, The Netherlands, [5]Division of Clinical Immunology, Department of Internal Medicine, Faculty of Medicine, University of Debrecen, Debrecen, Hungary, [6]Johns Hopkins University, Department of Medicine, Division of Rheumatology, Baltimore, USA, [7]Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico, Mexico, [8]Central Diagnostic Laboratory/Center for Translational Immunology, UniversitMedical Center Utrecht, Utrecht, The Netherlands, [9]Department of Rheumatology, Siena University Hospital, Viale Mario Bracci, Siena, Italy, [10]Department of Rheumatology, North Bristol NHS Foundation Trust, Bristol, UK, [11]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [12]Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK, [13]Department of Rheumatology, Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, UK, [14]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham Francis Crick Institute, London, UK, [15]Department of Rheumatology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary, [16]Department of Medicine, Aga Khan University, Karachi, Pakistan, [17]National Human Genome Research Institute, National Institutes of Health, Bethesda, USA, [18]Section of Pediatric Rheumatology, NH SRCC Children's Hospital, Worli, Mumbai, India, [19]Department of Rheumatology, Vall d'Hebron Universitary Hospital, Barcelona, Spain, [20]Department of Molecular Pathology of Skin, Faculty of Medicine, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University, Kanazawa, Ishikawa, Japan, [21]Environmental Autoimmunity Group, Clinical Research Branch, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, USA, [22] Division of Rheumatology, University of Pittsburgh, Pittsburgh, USA, [23]Department of Life Sciences, University of Bath, Bath, UK, [24]Department of Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden

Background. Myositis-specific autoantibodies (MSAs) are detected in over 60% of patients with idiopathic inflammatory myopathies (IIMs), which is a heterogenous group of diseases characterized by inflammation and damage of skeletal muscle in association with autoimmunity. Individual MSAs are useful adjunctive laboratory tests in the diagnosis of IIMs and are closely associated with different clinical manifestations of IIMs. Thus, accurate assessment of MSAs is pivotal to support diagnosis, predict prognosis, and formulate therapeutic strategies, leading to a personalized medical approach for IIM patients. However, the accessibility, cost and reliability of MSA testing depend on individual assays employed. Commercial assays, such as enzyme immunoassay (EIA) and immunoblots such as line blot assay (LBA), have become available as a tool for detection of MSAs in clinical practice across the world. We aimed to evaluate the analytical performance of commercial MSA assays against "gold-standard" immunoprecipitation (IP) assays.
Methods. A systematic literature search was conducted in PubMed, Web of Science, and Scopus through July 2024. Data were extracted on study design, participant characteristics, index tests, and 2×2 contingency tables for diagnostic performance. Study quality was assessed using the QUADAS-2 tool. Sensitivity and specificity were calculated for each dataset and presented as paired forest plots and summary receiver operating characteristic (SROC) curves. A hierarchical SROC model was used to estimate pooled sensitivity and specificity for meta-analysis.
Results. Of 3,156 articles, 23 met inclusion criteria and included both a commercial assay and IP performed on the same samples. Those articles were judged to have low risk of bias across all QUADAS-2 domains. The most frequently evaluated commercial assay was the line blot assay (LBA; 16 studies), followed by enzyme immunoassay (EIA; 9 studies). In the meta-analyses, the highest pooled sensitivity was observed for anti-MDA5 with EIA (95.7%), followed by anti-SAE with LBA (88.3%), anti-PL-12 with LBA (87.2%), and anti-Jo-1 and anti-MDA5 with LBA (82.8%). Lower sensitivities were observed for anti-Mi-2 (67.4%), anti-NXP2 (69.7%), and

anti-TIF1-γ (63.8%) with LBA. Pooled specificity ranged from 94.7% to 99.3% across MSA assays, but a false-positive result was a common concern for LBA, except for anti-EJ.
Conclusions. False-positive and false-negative results remain a significant challenge in the use of commercial MSA assays.
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Key words: autoantibody, diagnostic accuracy test, myositis, systematic review, meta-analysis

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T1/T2 MAPPING AS POTENTIAL IMAGING BIOMARKERS FOR EARLY IDIOPATHIC INFLAMMATORY MYOPATHIES: AN EXPLORATORY CROSS-SECTIONAL STUDY

Michael Dallo[1], Girish Dwivedi[1], Adil Rajwani[2], Zakir Hossain[1], Merrilee Needham[1,3], Helen Keen[1,2], Shereen Paramalingam[1,2]
[1]Fiona Stanley Hospital, Murdoch, Australia, [2]University of Western Australia, Nedlands, Australia, [3]Perron Institute of Neurological and Translation Science, Nedland, Australia

Background. Cardiovascular involvement in idiopathic inflammatory myopathies (IIM) remains inadequately characterised, despite its association with increased morbidity and mortality (1-2), underscoring the importance of early screening. We aimed to explore the utility of T1, T2 and extracellular volume (ECV) mapping of the cardiovascular system in IIM patients, and the relationship with standard outcome measures.
Methods. This is a prospective cross-sectional study involving patients with IIM (excluding overlap myositis) and healthy controls (HC). Clinical assessments including manual muscle testing (MMT26), patient and physician visual analogue scale (ptVAS and phyVAS), health assessment questionnaire (HAQ) and myositis disease activity assessment tool (MDAAT), creatinine kinase (CK), troponin and brain natriuretic peptide (BNP) were collected. All participants underwent cardiac MRI (cMRI) to identify subclinical myocardial dysfunction (ventricular mass, strain, and ejection fraction, T1,T2, ECV mapping) across six-segments, short axis model.
Results. Ten participants had IIM (dermatomyositis=3, anti-synthetase syndrome=2, necrotising autoimmune myopathy=2, polymyositis=1 and inclusion body myositis =1) and eight participants were HC. There were twelve females and six males. Median age was 48.00 (IQR: 36.000-63.500). The IIM cohort had a higher MMT26 (249.111 *vs*. 260.000, p=0.045), MDAAT (1.807 *vs*. 0.000, p=0.000), ptVAS (2.428 *vs*. 0.000, p=0.000), phyVAS (4.990 *vs*. 0.038, p=0.000), HAQ (111.461 *vs*. 0.000, p=0.000), CK (513.444 *vs*. 122.625, p=0.743), BNP (18.286 *vs*. 15.125, p=0.349) and Troponin (2.111 *vs*. 1.813, p=0.158). No statistically significant difference was noted between T1, T2 and ECV mapping values between IIM and HC (>p=0.082). Within the IIM cohort, significant correlations emerged between left ventricular mass (LVM)(ml) and BNP (r=0.815, p=0.026), LVM(g) and BNP (r=0.815, p=0.026), LVM(g/m2) and ptVAS (r=-0.741, p=0.035), LVM (g/m^2) and BNP (r=0.855, p=0.014), RVEF (%) and troponin (r= -0.756, p=0.018), segmental2 T1Pre mapping and HAQ (r= -0.652, p=0.041), segmental2 T1Pre mapping and phyVAS (r=-0.758, p=0.011), segmental6 T2 mapping and phyVAS (r=0.634, p=0.049), segmental5 T2 mapping and MMT26 (r=0.642, p=0.045).
Conclusions. Our small-cohort study showed that within the IIM cohort, there were significant associations between cMRI parameters and outcome measures suggesting subclinical cardiac involvement and potential biomarkers. Although definitive conclusions could not be made due to participant numbers, our findings support further investigations into the role of cMRI as an early diagnostic tool in IIM.
Acknowledgements. The study was funded by Arthritis Australia
Key words: cardiac MRI, idiopathic inflammatory myositis, Troponin, muscle, T1/T2 mapping

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WHOLE-BODY MAGNETIC RESONANCE IMAGING CHARACTERIZATION AND CLINICAL FEATURES OF ANTI-HMGCR IMMUNE-MEDIATED NECROTIZING MYOPATHY

Belen Miguel-Ibañez[1], Angeles S. Galindo-Feria[2,3,4], Ingrid E. Lundberg[2,3,4], Maryam Dastmalchi[2,3,4]
[1]Department of Rheumatology. Complejo Asistencial Universitario Salamanca, Spain, [2]Division of Rheumatology, Department of Medicine, Karolinska Institutet, Solna, Sweden, [3]Center for Molecular Medicine, Karolinska University Hospital, Sweden, [4]Department of Gastroenterology, Dermatology and Rheumatology, Theme Inflammation and Aging, Karolinska University Hospital, Sweden

Background. Anti-HMGCR immune-mediated necrotizing myopathy (IMNM) is a rare and severe autoimmune disease characterized by progressive muscle weakness and markedly elevated creatine kinase (CK) levels. Its management relies on glucocorticoids (GC) and other immunomodulatory therapies. Magnetic resonance imaging (MRI) enables non-invasive assessment of muscle inflammation, atrophy, and fatty infiltration. This study aimed to characterize MRI patterns in anti-HMGCR IMNM and explore their clinical correlations.
Methods. A retrospective cohort study included 15 patients with anti-HMGCR IMNM who underwent whole-body MRI within one month of diagnosis and before initiation of any treatment. The aim was to identify muscle regions most consistently involved and potentially useful for MRI evaluation or muscle biopsy. STIR or T2-weighted sequences were used to detect muscle, subcutaneous, and visceral edema, and T1-weighted sequences were used to assess atrophy or fat infiltration. Follow-up MRI was available in four patients (two with and two without intravenous glucocorticoids [IVGC]) and was analyzed to assess changes in muscle edema according to treatment.
Results. The mean age was 68 years (range 48–82), with a female predominance (80%). All patients had prior statin exposure, and hypertension was the most frequent comorbidity (80%). Myocardial infarction was the most common severe event (30%).
Muscle weakness was present in all patients. Baseline MRI showed muscle edema in all cases. Subcutaneous edema (n=5), atrophy (n=4), and fat infiltration (n=1) were less frequent. The most affected regions were the shoulder (n=12), medial leg compartment (n=11), and gluteal region (n=10), with the gluteus medius being the most commonly involved muscle (n=9).
Clinical evolution was favorable in all patients. In the four available follow-up MRI (two with intravenous glucocorticoids and two without). All cases showed improvement of the initial muscle edema, with no observable differences between groups.
Conclusions. MRI is a valuable tool for characterizing muscle involvement in IMNM. Predominant shoulder and leg compartment involvement may indicate optimal biopsy sites. More follow-up MRIs are needed to further define its role in monitoring therapeutic response.
Acknowledgements. This study received funding from the FER grant of the Spanish Society of Rheumatology. The work was carried out with the support and research infrastructure of the Department of Rheumatology, Karolinska Institutet, Stockholm, Sweden.
Key words: immune-mediated necrotizing myopathy, magnetic resonance imaging, intravenous glucocorticoid

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NEWLY DEVELOPED ChLIA FOR DETECTION OF FLUID CALPROTECTIN IN SERUM

Marko Silvestric-Scheel[1], Heather Pham[1], Kathrin Hoffmann[2], Victor Herbst[2], Tanja Seifert[2], Viola Borchardt-Lohölter[2], Pierre Lukas[3,4], Etienne Cavalier[3,4]
[1]IDS Immunodiagnostic Systems Ltd, Tyne & Wear, UK, [2]Institute for Experimental Immunology, affiliated to EUROIMMUN Medizinische Labordiagnostika AG, Lübeck, Germany, [3]Department of Clinical Chemistry, University of Liège, Liège, Belgium, [4]Centre Hospitalier Universitaire de Liège, Liège, Belgium

Background. Calprotectin present in circulation serves as a biomarker indicative of the systemic activation of neutrophile granulocytes and monocytes. Measuring its level in serum is relevant for diagnosis and monitoring of systemic inflammations in autoimmune diseases and

infections. We present a newly developed chemiluminescence assay from Immunodiagnostic Systems Ltd (IDS), IDS Fluid Calprotectin, by reporting the results of calprotectin measurements in serum samples from healthy individuals and patients. Furthermore, the results of the IDS Fluid Calprotectin are compared with those of a newly developed Circulating Calprotectin ELISA from Euroimmun.
Methods. To establish the reference limit for the IDS Fluid Calprotectin, calprotectin levels were measured in 235 serum samples from healthy adults and 51 serum samples from healthy children (age range: 1-19). To assess inflammatory status, calprotectin concentrations were quantified in a cohort comprising 378 serum samples from 50 healthy adults, 48 healthy children, 80 rheumatoid arthritis patients, 50 systemic lupus erythematodes patients, 50 Sjögren's syndrome patients, 50 systemic sclerosis patients, and 50 idiopathic inflammatory myopathy patients. Quantitative results were compared with the Euroimmun Circulating Calprotectin ELISA, and agreement was assessed with Passing-Bablok regression.
Results. The reference limit for adults at 2.8 µg/mL was established as the 95% right side upper limit of normality following the guidance of CLSI C28-A3 robust method. Compared to healthy individuals, calprotectin concentrations were elevated in patient sera. Passing-Bablok regression indicated constant and proportional differences between calprotectin concentrations: (Euroimmun = 0.75 (95% CI: [0.73, 0.78]) x IDS Fluid Calprotectin + 0.1 ([0.05, 0.014]); correlation coefficient r = 0.94; n=305
Conclusions. The finding indicated high correlation with a quantitative bias between the results of the IDS Fluid Calprotectin and the Circulating Calprotectin ELISA (Euroimmun), which make it necessary to evaluate results with respect to the assay-specific reference limits. The IDS Fluid Calprotectin will be applied in studies aimed at exploring, for instance, the correlation with disease states associated with various systemic inflammations. Future research will determine whether fluid calprotectin is a more specific biomarker of inflammation than C-reactive protein (CRP).
Key words: circulating calprotectin, myopathy, chemiluminescence immunoassay

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PLASMA EXPRESSION OF SELECTED MIR-133A-3P AND MIR-1-3P IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES COMPARED ASSOCIATES WITH DISEASE-RELATED FEATURES AND PREDICTS TREATMENT RESPONSE

Martin Klein[1], Sabína Oreská[1], Kristina Svobodová[1], Lucia Vernerová[1], Dana Dlouhá[2], Hana Wünch[1], Karel Pavelka[1], Jiří Vencovský[1], Ladislav Šenolt[1], Michal Vrablík[3], Jaroslav Alois Hubáček[3], Michal Tomčík[1]
[1]Institue Of Rheumatology and Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, [2]Experimental Medicine Center, Institute for Clinical and Experimental Medicine, Prague, Czech Republic, [3]3rd Department of Internal Medicine, General University Hospital and 1st Faculty of Medicine, Charles University, Prague, Czech Republic

Background. miR-133a-3p and miR-1-3p, as muscle-specific microRNAs (MyomiRs), are crucial in gene regulation and muscle repair. Their dysregulated expression contributes to idiopathic inflammatory myopathies (IIM) pathogenesis. This study evaluates their plasma expression in IIM *vs*. healthy controls (HC), and the association with disease-related features and therapy.
Methods. 60 patients with IIM were included: 19 males; mean age 59.1, disease duration 2.5 years; 20 dermatomyositis (DM) / 25 polymyositis (PM), both without statin history / 15 statin-induced immune-mediated necrotizing myopathies (IMNM), and 33 age-/sex-matched HC (10 males, age 58.3). Follow-up at 6 months of initial immunosuppressive therapy included 13 patients (5 DM, 5 PM, 3 IMNM) with early disease (duration 0.9 years). Basal laboratory parameters, clinical features, current treatment, and body composition (by bioelectric impedance analysis (BIA-2000-M)) were evaluated. Total RNA was extracted from plasma with miRNeasy Serum/Plasma Advanced kit (Qiagen). Quantitative PCR was performed using 6 miRCURY LNA miRNA PCR assays (Qiagen) with miR-103-3p, miR-191-5p, and let-7a-5p as endogenous controls. miRNA concentration analysis was performed using GenEx software (Multid Analysis AB). Data are presented as mean (SEM).
Results. The expression of miR-133a-3p and miR-1-3p was significantly higher in IIM *vs*. HC, in all IIM subsets *vs*. HC, and particularly in IMNM *vs*. DM and PM ($p<0.01$ for all) and correlated significantly with increased muscle injury markers (CK, LD, myoglobin), decreased muscle strength (MMT-8), and shorter disease duration. After 6 months of immunosuppressive therapy, miR-133a-3p and miR-1-3p levels significantly decreased, alongside disease activity (MYOACT) and muscle injury markers, while muscle strength (MMT-8) improved ($p<0.05$ for all). A greater miR-133a-3p decrease correlated with a larger decrease in CK ($p=0.003$; $r=0.780$) and LD ($p=0.030$; $r=0.623$), and strength improvement ($p=0.043$; $r=0.591$). Similarly, larger miR-1-3p reduction correlated with greater CK decrease ($p=0.010$; $r=0.705$). Higher baseline miR-133a-3p and/or miR-1-3p predicted greater muscle strength improvement ($p=0.043$; $r=0.591$) and larger reductions in CK ($p=0.007$; $r=0.727$ and $p=0.017$; $r=0.671$), LD ($p=0.010$; $r=0.707$ and $p=0.075$; $r=0.532$), and myoglobin ($p=0.059$; $r=0.584$), respectively.
Conclusions. The expression of miR-133a-3p and miR-1-3p was significantly higher in IIM *vs*. HC, particularly in IMNM, than in DM and PM, reflecting greater muscle involvement. The levels were highest in early active disease and declined after 6 months of initial immunosuppressive therapy. Both miR-133a-3p and miR-1-3p have a potential as a biomarker of disease activity and muscle involvement, and a predictor of initial treatment response in IIM.
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Key words: myositis, biomarker, miRNA

P-300

REAL-TIME MRI WITH DEEP-LEARNING BASED LUNG SEGMENTATION FOR ASSESSING RESPIRATORY INVOLVEMENT IN INCLUSION BODY MYOSITIS

Rachel Zeng[1], Omar Al-Bourini[2], Laura Plantenberg[1], Ulrike Olgemöller[3], Leonie Lettermann[1], Leon Lettermann[4], Sabine Hofer[1], Jens Frahm[5], Martin Uecker[2,6], Ali Seif Amir Hosseini[2], Jens Schmidt[1,7]
[1]Department of Neurology, University Medical Center Goettingen, Goettingen, Germany, [2]Department of Clinical and Interventional Radiology, University Medical Center Goettingen, Goettingen, Germany, [3]Department of Cardiology und Pneumology, University Medical Center Goettingen, Goettingen, Germany, [4]BioQuant and Institute for Theoretical Physics, University of Heidelberg, Heidelberg, Germany, [5]Biomedical NMR, Max Planck Institute for Multidisciplinary Sciences, Goettingen, Germany, [6]Institute of Biomedical Imaging, Graz University of Technology, Graz, Austria, [7]Department of Neurology and Pain Treatment, Immanuel University Hospital Ruedersdorf, Brandenburg Medical School Theodor Fontane, Ruedersdorf bei Berlin, Germany

Background. Inclusion body myositis (IBM) typically presents with chronic progressive weakness and atrophy of muscles of arms, legs and pharynx. While respiratory muscle involvement is considered uncommon, several case reports have described respiratory impairment in IBM, including mild diaphragmatic dysfunction. Reliable detection of breathing impairment is critical for therapeutic patient management, but standard diagnostics such as pulmonary function tests reach their limits in the early and mild stages of the disease. Real-time MRI (RT-MRI) enables dynamic evaluation of complex respiratory motion without triggering or breath holding. Combined with U-Net-supported lung segmentation, RT-MRI can detect early signs of respiratory muscle weakness, as demonstrated in a pilot study involving patients with Pompe disease (manuscript under review). The aim of this study was to assess respiratory muscle involvement in IBM and to characterize a potential disease-specific pattern of breathing impairment.
Methods. Patients with clinically and histologically confirmed IBM and healthy controls (matched for age and BMI) underwent RT-MRI with a temporal resolution of 50 milliseconds. This technique was combined with U-Net-supported lung segmentation for quantification of diaphragmatic and thoracic excursion, sniff velocity and synchronicity between diaphragm and chest wall motion. Study participants also underwent diaphragm ultrasound and standard pulmonary function tests (PFT).
Results. 22 patients with IBM (mean age 68.0 y; 27% female) and 22 healthy controls (mean age 67.4y; 27% female) were included. PFT showed no signs of restrictive ventilatory impairment in this cohort. Diaphragm ultrasound showed a slight decrease in diaphragmatic motion in IBM patients, but this finding was not reproducible on RT-MRI. Analysis of deep breathing and sniff maneuver obtained by RT-MRI failed to reveal evidence of diaphragmatic weakness in patients with IBM. Compared to the control group, IBM patients demonstrated a slight increase in thoracic excursion, which may indicate alterations in breathing mechanics without clear evidence of respiratory muscle involvement.
Conclusions. This study provides a comprehensive analysis of respiratory function in IBM patients and did not identify evidence of respiratory muscle

involvement in IBM. RT-MRI allows the visualization of different respiratory muscles at a high temporal and spatial resolution, offering a reliable, broad and unbiased assessment of respiratory involvement in patients with neuromuscular diseases.

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Key words: myositis, swallowing, cricopharyngeal bar

P-313

INTERLABORATORY AGREEMENT IN THE IDENTIFICATION OF MYOSITIS-SPECIFIC AND MYOSITIS-ASSOCIATED AUTOANTIBODIES BY IMMUNO-PRECIPITATION-BASED TECHNIQUES

Georgina Harvey[1], Hui Lu[1], Akira Yoshida[2], Birthe Michiels[3], Mei Cheng[4], Xavier Bossuyt[3], Masataka Kuwana[2], Ira Targoff[4], Neil McHugh[1], Sarah Tansley[1]

[1]University Of Bath, Bath, UK, [2]Nippon Medical School Graduate School of Medicine, Bunkyo-ku, Japan, [3]University Hospitals Leuven, Leuven, Belgium, [4]Oklahoma Medical Research Foundation, Oklahoma City, USA

Background. Sera from patients with suspected idiopathic inflammatory myopathy (IIM) are typically tested for myositis-specific and myositis-associated autoantibodies (MSA/MAA), which may aid diagnosis and prognosis. Immunoprecipitation (IP) based assays are widely considered to be the reference standard for MSA/MAA detection, although the type of IP, and methodological details, can vary between laboratories.

Objective. To directly compare concordance of MSA/MAA assay results determined using the variety of IP techniques employed by different centres.

Methods. Surplus single-draw patient sera previously submitted to Bath Diagnostic Serology Service for detection of MSA/MAA by Radio-IP and retained as quality-control samples were selected by volume. Fifteen participant laboratories detected MSA/MAA using their available techniques: four included an IP-based assay.

Results. Our own and three additional laboratories were included in this study of IP-based techniques: one used radiolabelled protein-IP (Radio-IP), RNA-IP and IP-Western blotting (IP-WB), one used RNA-IP and IP-WB, and one used IP directly coupled to mass spectrometry (IP-MS). Apart from the Bath lab, which uses K562-cell extracts as the antigen source, HeLa cell-extracts were utilised.

For certain sera, two sets of results could be directly compared by: (1) Radio-IP, (2) IP-WB, (3) RNA-IP:

1. Radio-IP

13 samples specifically tested for 12 MSA/MAA specificities by 2 labs:
Agreed: 13/13 (100.0%) (9 None, 1 anti-Zo, 1 anti-OJ, 1 anti-SAE, 1 anti-PM/Scl)

2. IP-WB:

10 samples specifically tested for anti-Tif1γ and anti-NXP2 antibodies by 2 labs
Agreed: 10/10 (100%) (7 None, 2 anti-NXP2, 1 anti-Tif1γ).

3. RNA-IP:

11 samples specifically tested for 7 MSA/MAA specificities by 2 labs: Agreed: 7/11 (63.6%) (5 None, 2 anti-Ro60/La RNP); Consistent: 1/11 (9.0%) (anti-ARS *vs*. anti-PL-7); Discordant: 3/11 (27.3%) (None *vs*. anti-EJ, None *vs*. anti-Ro60/La RNP), anti-SRP *vs*. anti-Th/To & anti-Sm).

Finally, IP-MS was compared with Radio-IP (Bath only):

4. IP-MS *vs*. Radio-IP:

15 samples were tested by 2 labs. Agreed: 5/15 (33.3%) (1 None,1 anti-Tif1γ, 1 anti-Zo, 1 anti-OJ, anti-Th/To); Consistent: 7/15 (46.7%) (6 None (IP-MS) *vs*. UIB (Radio-IP), 1 anti-U1RNP & anti-AGO-2 (97 kDa) (IP-MS) *vs*. anti-U1RNP & anti-90-kDa UIB (Radio-IP)); Discordant: 3/15 (20.0%) (1 anti-PSIP1/LEDGF (IP-MS) *vs*. 138-kDa UIB (Radio-IP),anti-Ro60/La, anti-65-kDa UIB & anti-Jo-1 (Radio-IP), 1 anti-Dbt & anti-gp210 (IP-MS) *vs*. anti-OJ & anti-UIBs (Radio-IP)).

Conclusions. These preliminary data suggest excellent agreement of MSA/MAA testing between centres for both Radio-IP and IP-WB. The RNA-IP results may in part reflect RNA instability. Variation between Radio-IP and IP-MS warrants further clarification while IP remains the reference standard technique.

Key words: myositis, autoantibodies, immunoprecipitation

P-315

ANTI-TRIM72 ANTIBODIES IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Eugene Krustev[1,2], Tiara N. Safaei[3], Daniela Trejo-Zambrano[1], Lisa Christopher-Stine[1], Andrew Mammen[1,4], Julie J. Paik[1], Jemima Albayda[1], Christopher A. Mecoli[1], Brittany L. Adler[1], Brendan Antiochos[1], Eleni Tiniakou[1,5]

[1]Johns Hopkins School of Medicine, Baltimore, USA, [2]Departments of Medicine and Microbiology, Immunology and Infectious Diseases, Cumming School of Medicine, University of Calgary, Calgary, Canada, [3]Johns Hopkins Department of Chemical and Biomolecular Engineering, Baltimore, USA, [4]National Institute of Arthritis and Musculoskeletal Diseases, NIH, Bethesda, USA, [5]University of Texas Health Sciences Houston, McGovern Medical School, Houston, USA

Introduction. Tripartite motif-containing protein 72 (TRIM72) is expressed in muscle and lung and mediates tissue-repair (1, 2). Autoantibodies directed against TRIM72 (anti-TRIM72) have been identified in patients with idiopathic inflammatory myopathies (IIM) and may contribute to disease pathogenesis by disrupting the repair functions of TRIM72 (2). We hypothesized that IIM patients positive for anti-TRIM72 antibodies would have more severe clinical phenotype.

Methods. Sera from patients meeting a clinical diagnosis of IIM (antisynthetase syndrome [ASyS], immune mediated necrotizing myopathy [IMNM], and dermatomyositis [DM]) and healthy controls (HC) were included. Anti-TRIM72 autoantibodies were tested using enzyme-linked immunosorbent assay. Anti-TRIM72 testing was positive if value was >2 standard deviations above the mean for HC. Clinicodemographic features were identified through chart review and were compared between anti-TRIM72 positive (anti-TRIM72[+]) and negative (anti-TRIM72[-]) groups.

Results. There were 469 IIM patients (ASyS, n=182; IMNM, n=170; DM, n=117) and 67 HC included. When Anti-TRIM72[+] was compared to HC (n=0/67, 0.0%), anti-TRIM72[+] was significantly more common in ASyS (n=46/182, 25.3%; p<0.0001) and IMNM (n=32/170, 18.8%; p<0.0001), but not in DM (n=5/117, 4.3%; p=0.16).

In ASyS, when anti-TRIM72[+] and anti-TRIM72[-] patients were compared there were no significant differences in sex, White race/ethnicity, age at diagnosis, highest recorded CK, lowest recorded DLCO, or lowest recorded FVC. There were significantly more anti-TRIM72[+] ASyS patients with normal DLCO (>75%) when compared to anti-TRIM72[-] (32.6% *vs*. 14.2%; p=0.007).

In anti-HMGCR[+] IMNM, anti-TRIM72[+] was associated with a lower proportion of females (33.3% *vs*. 60.8%; p=0.029) and were older age at time of diagnosis (66.1 *vs*. 58.3; p=0.041). There was no significant difference in White race/ethnicity, statin exposure, and highest recorded CK in anti-HMGCR[+] IMNM patients when anti-TRIM72[+] and anti-TRIM72[-] groups were compared.

Conclusions. Anti-TRIM72 antibodies are positive in a subset of patients with ASyS and IMNM, but rarely in DM. The presence of anti-TRIM72 antibodies was not associated with a more severe phenotype in ASyS or anti-HMGCR[+] IMNM. Anti-TRIM72[+] may actually correlate with milder pulmonary disease in ASyS, as there were more ASyS patients with normal DLCO in the anti-TRIM72[+] group. Future studies are needed to assess if anti-TRIM72 antibodies are associated with other measures of disease activity in ASyS and IMNM.

Key words: anti-TRIM72, myositis, antibodies

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P-322

PERFORMANCE OF PARTICLE-BASED MULTI-ANALYTE TECHNOLOGY FOR THE DETECTION OF MYOSITIS-SPECIFIC ANTIBODIES IN BOTH SELECTED AND UNSELECTED COHORTS

Thomas B. Martins[1], Arevik Ghazaryan[1,2], Merina Toninelli[3], Leo Lin[1,2,3], Dorota Lebiedz-Odrobina[5,6], Tammy Smith[1,2,3,4,6], Lisa Peterson[1,2,3]
[1]ARUP Institute of Clinical and Experimental Pathology, Salt Lake City, USA, [2]Department of Pathology, University of Utah, Salt Lake City, USA, [3]ARUP Laboratories, Salt Lake City, USA, [4]Geriatric Research Education and Clinical Center, George E. Whalen Department of Veterans Affairs Medical Center, Salt Lake City, USA, [5]George E Wahlen Department of Veteran Affairs Medical Center, Salt Lake City, USA, [6]Department of Neurology, University of Utah, Salt Lake City, USA, [7]Division of Rheumatology, University of Utah, Salt Lake City, USA

Background. Myositis specific antibodies (MSA) represent important diagnostic and stratification tools in myositis patients. However, variability exists between methods used to detect these antibodies. Testing for MSA by IP is currently only performed by a small number of labs, while others report results based on LIA or PMAT alone despite concerns over false positives and false negatives for the LIA assay and a paucity of data on the PMAT assay in an unselected cohort. The aim of this study was to evaluate a recently developed particle-based multi-analyte technology (PMAT) assay for the detection of MSA in comparison to immunoprecipitation (IP) and/or line immunoblot assay (LIA).
Methods. For the initial validation of the PMAT assay in a selected cohort, samples were collected at ARUP Laboratories based on routine testing which included a combination of LIA, IP, multiplex bead assay (MBA) and ELISA. Specimens previously tested as negative for a particular marker that were positive by IP, MAFD or ELISA for other MSA or myositis associated antibodies were included as disease controls, along with sera from self-proclaimed healthy donors. To further evaluate the performance of the PMAT and/or LIA assays in comparison to IP and each other, retrospective analysis was performed on consecutive samples received at ARUP Laboratories for myositis antibody testing using a combination of IP, PMAT and/or LIA. Clinical data for University of Utah antibody-positive patients were sought to confirm diagnosis.
Results. We report on the frequency of detection of MSA in a reference laboratory setting, the agreement between PMAT, IP and/or LIA for the detection of these antibodies and the presence of co-existing MSA. We also describe the clinical characteristics of University of Utah patients found positive for MSA using these methods
Conclusions. Identification of MSA is important for diagnosis, prognosis and disease management in patients with myositis. Combined use of IP and PMAT or LIA improves reliability for the diagnosis of myositis
Key words: myositis, antibodies, immunoassay

P-330

PREVALENCE OF SARCOPENIA IN A COHORT OF DANISH PATIENTS WITH MYOSITIS: A CROSS-SECTIONAL STUDY

Kasper Yde Jensen[1,2], Lene Terslev[2,3], Bente Appel Esbensen[2,3], Henriette Ytting[3,4], Charlotte Suetta[3,5], Louise Pyndt Diederichsen[1,3]
[1]Copenhagen Research Center for Autoimmune Connective Tissue Diseases (COPEACT), Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark, [2]Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Centre for Head and Orthopaedics, Copenhagen University Hospital Rigshospitalet, Valdemar Hansens Vej 17, 2600, Glostrup, Denmark, [3]Institute of Clinical Medicine, Faculty of Health and Sciences, University of Copenhagen, Copenhagen, Denmark, [4]Department of Digestive Diseases, Transplantation and General Surgery, Section for Liver Disease, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [5]Geriatric Research Unit, Copenhagen University Hospital, Bispebjerg and Frederiksberg Hospital, Copenhagen, Denmark

Background. Sarcopenia, defined as the progressive loss of skeletal muscle mass and strength, is increasingly recognised as a comorbidity in chronic inflammatory diseases and is strongly correlated with increased morbidity and mortality across different populations and clinical settings. Though, data on sarcopenia in idiopathic inflammatory myopathies (myositis) remain limited. Given the direct muscle involvement in myositis, we hypothesised a high prevalence of sarcopenia in this patient group.
Methods. We conducted a cross-sectional study involving adult patients diagnosed with myositis. Patients were included from the outpatient clinic at Center for Rheumatology and Spine Diseases, Rigshospitalet, Denmark. Sarcopenia was assessed using the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) criteria, incorporating measurements of appendicular lean mass via dual-energy x-ray absorptiometry, handgrip strength and physical performance (including the 30s Sit-to-stand and 10-meter maximum walking tests). Clinical data including disease duration, disease activity scores, and immunosuppressive treatment. Group comparisons between sarcopenic and non-sarcopenic patients were performed using independent t-tests. Results are presented as mean group difference with 95% confidence intervals, and a p-value <0.05 was considered statistically significant.
Results. A total of 24 patients with myositis (Antisynthetase syndrome: 8, dermatomyositis: 7, inclusion body myositis (IBM): 4, polymyositis: 3, and immune mediated necrotizing myopathy: 2) were included. The mean disease duration was 7.3 ± 6.3 years and 79% received immunosuppressive treatment. The overall prevalence of sarcopenia was 25% (6/24) and 66% (4/24) in patients with IBM. There was no difference in disease duration between patients with and without sarcopenia (-1.0 [-7.4, 9.4], p=0.78). The patients with sarcopenia exhibited lower mean handgrip strength (-14.8 kg [-6.3, -23.3], p<0.01), lower 30s Sit-to-stand performance (-11.4 reps [-7.2, -15.6], p<0.01), slower 10-meter maximum walking speed (3.2 seconds [0.3, 6.4]) and lower appendicular lean mass (-3.5 kg [-0.6, -8.4], p=0.03). There was a trend of creatine kinase being higher in patients without sarcopenia (p=0.07), while C-reactive protein did not differ between the groups (p=0.26).
Conclusions. One in four myositis patients suffer from sarcopenia with a notably higher prevalence in patients with IBM compared to those with non-IBM. Our findings highlight the importance of early detection since sarcopenia is a potentially modifiable condition in this group. These results emphasize the need for systematic screening for sarcopenia in this high-risk population, as early detection enables reversal through targeted exercise interventions.
Acknowledgements. We wish to thank Gigtforeningen for financial support and the patients for their participation in the study.
Key words: DEXA, clinical assessment, muscle strength, physical impairment

P-338

IS THE PRESENCE OF CONCOMITANT MYOSITIS-RELATED AUTOANTIBODIES ASSOCIATED WITH DISEASE SEVERITY?

Maria João Cadório[1], João Oliveira[1], Sara Alves Costa[1], Filipa Canhão André[1], Fabiana Gouveia[1], André Pinto Saraiva[1,2], Mariana Luís[1,2], Tânia Santiago[1,2]
[1]Local Health Unit of Coimbra, Coimbra, Portugal, [2]Faculty of Medicine of University of Coimbra, Coimbra, Portugal

Background. Myositis-specific (MSA) and myositis-associated (MAA) autoantibodies define distinct subsets of idiopathic inflammatory myopathies (IIM). Although MSA are commonly mutually exclusive, some patients present with concomitant myositis-related autoantibodies, whose clinical relevance remains unclear.1 We aimed to characterize demographic, clinical, and laboratory features of IIM patients according to myositis-related antibody pattern
Methods. We conducted a cross-sectional study including consecutive adult IIM patients fulfilling 2017 EULAR/ACR classification criteria with extended antibody testing. Antinuclear antibodies (ANA) were assessed by indirect immunofluorescence on HEp-2 cells (cut-off ≥1:160). Myositis-related autoantibodies were analyzed by immunoblot, including anti-Mi-2, Jo-1, PL-7, PL-12, EJ, MDA5, TIF1γ, HMGCR (MSA), and anti-SSA-60, SSA-52, SSB, Ku, Scl-70, RNP, PM-Scl, Th/To, among others (MAA). Patients were grouped as: (1) single antibody (MSA or MAA); (2) ≥2 MAA; (3) ≥2 MSA; and (4) one MSA plus one MAA. Those without detectable antibodies were excluded. Continuous variables were compared using one-way ANOVA or Kruskal-Wallis tests and categorical variables by χ^2 or Fisher's exact test. Logistic regression adjusted for age and sex explored associations between antibody burden and disease severity. p<0.05 was considered significant.
Results. Among 75 IIM patients, 47 (63%) were antibody-positive (66% females; mean age at diagnosis 38.5±17.0 years) (Table 1): 37 (79%) were single antibody; 6 (13%) ≥2 MAA; 3 (6%) ≥2 MSA; and 1 (2%) one MSA plus one MAA. Patients with ≥2 MSA were older (62±8 years) than single antibody cases (45±15 years, p=0.02). Sex distribution, muscle enzyme

levels, inflammatory markers, DLCO, and FEVE were similar among groups, as were cutaneous, articular, and lung involvement (all p>0.05) (Table 2). Raynaud phenomenon and dysphagia were more frequent in multiple MAA cases, without statistical significance. Severe baseline disease (defined by ≥1 severe organ involvement: dysphagia, myocarditis, dyspnea, or marked proximal weakness) occurred in 81% overall, with no group differences (χ^2=0.12, p=0.88). Solid (9%) and hematologic (1%) malignancies were infrequent and unrelated to antibody pattern (p>0.3). In multivariable models, concomitant antibodies (*vs*. single) were not associated with severe disease (OR=1.03, 95% CI 0.29–3.47, p=0.96), solid cancer (OR≈1.00, p=0.999), or lung involvement (OR=1.78, 95% CI 0.38–8.21, p=0.43).

Conclusions. Multiple myositis-related antibody positivity was uncommon (21%) and occurred mainly in older patients. Concomitant autoimmunity, particularly within the MAA spectrum, was not associated with more severe disease or malignancy at diagnosis, likely reflecting broader immune activation rather than a distinct clinical phenotype. Larger studies are needed to validate these findings.

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Key words: idiopathic inflammatory myopathies, myositis-related auto-antibody profile, disease severity

P-371

FOLLOWING FERRITIN TO FOLLOW THE LUNGS: MONITORING ILD IN ANTI-MDA5 DERMATOMYOSITIS

Silvia Grazzini[1], Chiara Rizzo[5], Marco Fornaro[6], Maria Rosa Pellico[4], Ting-yuan Lan[2], Pei-Hsinq Lai[3], Nicoletta Del Papa[4], Lidia La Barbera[5], Florenzo Iannone[6], Luca Cantarini[1], Bruno Frediani[1], Edoardo Conticini[1]

[1]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, Siena University Hospital, University of Siena, Siena, Italy, [2]Division of Rheumatology, Department of Internal Medicine, National Taiwan University Hospital Hsin-Chu branch, Hsinchu, Taiwan, [3]Department of Internal Medicine, Taipei City Hospital Zhongxiao Branch, Taipei, Taiwan, [4]Unit of Clinical Rheumatology, ASST Gaetano Pini - CTO, University of Milan, Milan, Italy, [5]Rheumatology Unit, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, University of Palermo, Palermo, Italy, [6]Unit of Rheumatology, Department of Precision and Regenerative Medicine and Ionian Area (DiMePre-J), University of Bari, Bari, Italy

Background. Serum ferritin is a specific biomarker for anti-MDA5 dermatomyositis (DM): not only it can be useful for distinguishing it from other IIM, but it is also a key marker of disease activity and prognosis, being associated with poorer outcome. Nevertheless, its longitudinal trajectory remains unclear, as does its role during follow-up. The aim of this study was therefore to evaluate whether ferritin could be useful for the long-term monitoring of interstitial lung disease, where imaging and functional assessments alone may not be sufficiently reliable.

Methods. We retrospectively enrolled anti-MDA5-positive DM patients from the Myositis Clinics of Siena, Palermo, Bari (Italy) and Taipei (Taiwan) who had documented pulmonary involvement at baseline and clinical data at least at three timepoints.

Results. A total of 21 patients (Italy n=11, Taiwan n=10; mean age 51.4 ± 13.9 years) were included. At baseline, median values of ferritin, CRP, and ESR were 700 μg/L (IQR 204–1523), 0.35 mg/dL (IQR 0.23–1.56), and 23 mm/h (IQR 18–44.5), respectively, whereas mean values of DLCO, FVC, and FEV1 were 57.1 ± 21.6%, 74.9 ± 22.0%, and 76.3 ± 20.5%. Ferritin tended to be higher in the Taiwanese cohort (p=0.072) and, in general, was inversely correlated with FVC (ϱ=–0.615) and FEV1 (ϱ= -0.660).

Linear mixed models showed a significant decrease in ferritin over time (p<0.001), with an average reduction of 41 μg/L per month (95% CI -62.8 to -19.9). At the same time, pulmonary function parameters demonstrated progressive improvement: DLCO increased by 0.95 percentage points/month (p<0.001), FEV1 by 0.68 (p=0.012), and FVC by 0.83 (p=0.004). CRP showed a mild but non-significant decline (p=0.12).

Conclusions. Ferritin can be considered a potentially useful biomarker of disease activity in anti-MDA5 DM with lung involvement. Its reduction likely reflects the downregulation of interferon-γ–driven immune activation typical of the early disease, and may play a crucial role in cases where extensive lung involvement and fibrosis render repeated HRCT scans unreliable for monitoring. In this context, ferritin could help distinguish patients with established lung damage and no ongoing inflammatory activity from those with persistent inflammation

Key words: ferritin, biomarker, anti-MDA5 dermatomyositis, ILD

P-376

CORRELATION OF AUTOANTIBODY PROFILE AND SOFTWARE ANALYSIS OF WELL-AERATED LUNG IN MYOSITIS PATIENTS AFFECTED BY INTERSTITIAL-LUNG DISEASE

Angela Ceribelli[1], Fabrizio Angeli[1,2], Paolo Semeraro[1,2], Andrea Borghesi[3], Matteo Riva[3], Franco Franceschini[1,2], Ilaria Cavazzana[1,2]

[1]Rheumatology and Clinical Immunology Unit, ASST Spedali Civili di Brescia, Italy, [2]Department of Clinical and Experimental Sciences, University of Brescia, Italy, [3]Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Spedali Civili, Brescia, Italy

Background. Interstitial lung disease (ILD) is a common extra-muscular manifestation in myositis patients (up to 43%) (1), with more severe prognosis and higher mortality (2). It is more frequent in anti-synthetase syndrome patients with anti-Jo1, -PL7 and -PL12 antibodies (with and without anti-Ro52) and in anti-MDA5 rapidly-progressive ILD in dermatomyositis patients (3, 4). High-resolution CT (HRCT) is the gold standard for ILD characterization, together with clinical features and lung function tests. Our goal is to use a quantitative CT parameter called well-aerated lung (WAL) (5, 6) and check correlations with myositis symptoms, autoantibody profile, and lung function tests for a better assessment of ILD and more personalized therapeutic choices.

Methods. We retrospectively evaluated 228 myositis patients followed in our Unit (1982-2025) to collect clinical, laboratory, radiological, lung function tests data. Patients with ILD were included in this study when they had a baseline (T0) and a follow-up (T1) CT scan together with concomitant lung function tests. CT images were processed with a dedicated software (Syngo CT Pulmo 3D, Siemens). Statistical analysis was done by IBM-SPSS v. 30.0 (significance: p<0,05).

Results. ILD was diagnosed in 87/228 (38%) patients with myositis, particularly in anti-synthetase syndrome (OR 11.28, IC 95% 5,08 – 25.05; p=0.0018) with anti-Jo1 (27%), -PL7 (27%), -PL12 (13%), -MDA5 (17%) antibodies. Anti-Ro52 were positive in 49% (43/87) of ILD patients, with significant correlation (OR 2.72, IC 95%, 1, 4–4.78; p=0.001). In ILD myositis patients we identified 33 cases (33/87, 38%) with 2 HRCT scans at T0 and T1 and concomitant lung function tests. Mean WAL values are significantly lower at baseline in anti-synthetase syndrome patients (p=0.001) compared to other myositis patients, in particular in anti-PL7 positive patients (p=0.07), reflecting a more severe and earlier lung disease in these patients. In anti-Ro52+ patients we noticed a significant reduction in lung function tests and WAL from T0 to T1 (p=0,048), showing loss of aerated lung overtime. From a clinical point of view, mechanic's hand and arthritis are associated with risk of ILD (OR 6.84; IC 95% 3.13–14,93, p<0.0001 and OR= 2.55 (IC 95% 1.39–4.67; p=0.002), while myositis is negatively correlated (OR= 0.19, IC 95% 0.09–0.36; p<0.001).

Conclusions. The analysis of CT lung parenchyma by WAL in myositis patients with ILD shows a significant correlation with lung function tests and autoantibody profile, mainly in patients with anti-synthetase syndrome, thus allowing more precise and early diagnosis of ILD.

Key words: interstitial lung disease, anti-synthetase syndrome, well-aerated lung

Cancer Myositis

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EPIDEMIOLOGY OF CANCER IN IDIOPATHIC INFLAMMATORY MYOPATHIES: A SYSTEMATIC REVIEW AND PROPORTIONAL META-ANALYSIS

Joost Raaphorst[1], Katinka Rasch[1], Minoesch Min[1], Hans Bogaards[2], Luuk Wieske[1], Dieta Brandsma[1,3], René Spijker[4], Johan Lim[1], Marianne de Visser[1], Alexander Oldroyd[5,6], Anneke van der Kooi[1]
[1]Department of Neurology, Amsterdam University Medical Centre, Amsterdam, The Netherlands, [2]Department of Epidemiology and Data Science, Amsterdam University Medical Centre, Amsterdam, The Netherlands, [3]Netherlands Cancer Institute – Antoni van Leeuwenhoek, Department of Neuro- oncology, Amsterdam, The Netherlands, [4]Amsterdam University Medical Centre, Medical Library, Amsterdam Public Health, University of Amsterdam, Amsterdam, The Netherlands., [5]The University of Manchester, Manchester, England, UK, National Institute for Health Research Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, University of Manchester, Manchester, UK, [6]Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK

Background. The disease classification of idiopathic inflammatory myopathies (IIM) has changed over the last decades with identification of new subgroups (*e.g.* immune mediated necrotising myopathy, antisynthetase syndrome). Updated cancer risks for IIM subgroups and subtypes based on myositis specific antibodies (MSA) may better inform patients and clinicians.
Methods. A systematic literature search was carried out via Medline and Embase. Cohort studies reporting incidence and prevalence of cancer during at least three years after diagnosis in IIM patients, with or without MSA, were included. The main outcome was the pooled cumulative incidence of cancer within three years of IIM diagnosis with associated 95% confidence interval (95%-CI). The study was registered in PROSPERO (no. CRD42021193314).
Results. Fifty-eight studies, of which 43 reported IIM subgroups with a total of 4888 patients (70% female), were included. Thirty-six studies (n=1970 patients, 73% female) included MSA data. Fifty-five articles were included in the meta-analysis. The pooled cumulative incidence of cancer within three years after an IIM diagnosis was 15·3% [95%CI: 12.0-19.3] in dermatomyositis (DM); 9.3% [95%CI: 4.0-20.3] in immune mediated necrotizing myopathy (IMNM), and 2.3% [95%CI: 0.7-7.3] in anti-synthetase syndrome (ASyS). DM patients with anti-transcriptional intermediary factor-1 gamma (anti-TIF1-γ) antibodies had the highest incidence of cancer (cumulative incidence of 42.1% three years after DM diagnosis; 70·8% of cancers diagnosed within one year of DM diagnosis). In patients with IMNM and anti-3-Hydroxy-3-methyl-glutaryl-coenzyme A reductase (anti-HMGCR) antibodies the pooled cumulative incidence of cancer three years after diagnosis was 9.0% [95%CI: 4.7-16.6].
Conclusions. Based on more recent IIM disease classifications, updated estimates of cancer risks are presented for subtypes of IIM, including DM, ASyS, IMNM and PM. We present a more accurate estimate of the high risk for malignancy in DM patients with anti-TIF1-γ antibodies and the risk of IMNM patients with anti-HMGCR antibodies. More evidence is required to quantify the cancer incidence of a number of MSA-based IIM subgroups.
Key words: cancer, epidemiology, risk, meta-analysis

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REVISITING "TRIPLE M": EVIDENCE AGAINST NEUROMUSCULAR JUNCTION INVOLVEMENT IN IMMUNE CHECKPOINT INHIBITOR TOXICITY

Elke Schipani[1], Teerin Liewluck[1], Eelco Wijdicks[1]
[1]Department of Neurology, Mayo Clinic, Rochester, USA

Background. When in the presence of ocular and limb weakness and cardiomyopathy, immune checkpoint inhibitor (ICI) toxicity is often labeled as "Triple M syndrome": myopathy, myocarditis, and myasthenia gravis (MG). Oculobulbar findings, such as ptosis, ophthalmoparesis, dysarthria, and dysphagia can occur in ICI myopathy (ICIM), mimicking symptoms of MG. However, fluctuations or fatigability are rarely present. We hypothesized that patients diagnosed with "Triple M syndrome" exhibit manifestations attributable solely to a primary myopathy, without concomitant defect of neuromuscular transmission.
Methods. We conducted a retrospective cohort study at a single tertiary referral center, identifying patients with the diagnosis ICI-related "Triple M syndrome" seen between January 2016 and February 2025. Demographics, clinical history, diagnostics (including labs, pathology, imaging, and electrodiagnostic testing), treatment, and outcomes were reviewed. A single patient with a preceding history of untreated AChR antibody-positive MG was excluded.
Results. We identified 27 patients with a diagnosis of ICI-related "Triple M syndrome," in their medical record, 24 of whom endorsed weakness, with ocular (n=19), bulbar (n=12), and proximal muscle weakness (n=22) on neurologic examination. Eight patients developed dysphagia requiring tube feed supplementation, and six developed respiratory failure requiring intubation. Median creatine kinase and troponin T were elevated (1697 ± 702 and 889 ± 586, respectively). Cascading MG serologies showed positivity to AChR binding (5/26), AChR modulating (1/6), striational (1/3) but not to MuSK (0/22) or P/Q VGCC (0/7) antibodies. Repetitive nerve stimulation was normal in all patients. Single fiber EMG (SFEMG) was abnormal in 3/9 patients, 2 of whom had severe weakness requiring feeding tube or intubation. The other patient with abnormal SFEMG had no fatigability on examination and did not respond to pyridostigmine. None of the three patients with abnormal SFEMG had positive MG antibodies. Of the 22 patients who underwent cardiac MRI, 7 had findings concerning for myocarditis. All 3 patients who underwent MSK imaging showed T2 hyperintense signal in the muscles indicating edema. Four of five patients who underwent skeletal muscle biopsy and all 6 who underwent cardiac biopsy had findings consistent with necrotizing myopathy and myocarditis, respectively.
Conclusions. Across a cohort phenotyped as "Triple M syndrome," there is no electrophysiologic finding to support a diagnosis of MG in most patients despite positive AChR antibodies. In the rare case of abnormal SFEMG, severe presentations in the absence of electrodecrement also argue that abnormal jitter is a consequence of myopathy, rather than a primary neuromuscular transmission failure.
Key words: immune checkpoint inhibitor, toxicity, myositis, myasthenia gravis, cardiomyopathy

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IMMUNE CHECKPOINT INHIBITOR-RELATED MYOTOXICITY: CLINICAL SPECTRUM, PREDICTORS OF SEVERITY, AND DEVELOPMENT OF A PRAGMATIC PROGNOSTIC SCORE

Sami Tayb-Boulahfa[1], Lucas Pacoureau[3], Marie-Claire Bretagne[2], Batoul Rostom[1], Julian Sanchez Dal Cin[1], Damien Amelin[1], Bérénice Tendrel[1], Sarah Leonard-Louis[4], Eric Ballot[5], Marie-Alexandra Alyanakian[6], Rana Al Kouri[7], Olivier Benveniste[1,8], Joe-Elie Salem[2], Yves Allenbach[1,8]
[1]Sorbonne Université, INSERM, Center of Research in Myology, UMRS 974, Paris, France, [2]Sorbonne Université, INSERM, UNICO-GRECO Cardio-oncology Program, Department of Pharmacology, GRC27, CIC-1901, AP-HP, Hôpital Pitié-Salpêtrière, Paris, France, [3]Department of Internal Medicine and Clinical Immunology, Le Kremlin-Bicêtre Hospital, AP-HP, Le Kremlin Bicêtre, France, [4]Sorbonne Université - AP-HP, Pitié-Salpêtrière Hospital, Department of Neuropathology, INSERM U974, Paris, France, [5]Unité d'immunologie, CHU Saint-Antoine, AP-HP, Paris, France, [6]Université Paris-Cité, Laboratory of Immunology, AP-HP and INEM, Necker-Enfants Malades Hospital, Paris, France, [7]Sorbonne Université, Metabolic Biochemistry Department, Pitié-Salpêtrière Hospital, AP-HP, Paris, France, [8]Department of Internal Medicine and Clinical Immunology, Pitie-Salpêtrière Hospital, AP-HP, Paris, France

Background. Immune checkpoint inhibitor (ICI)-related myotoxicity represents the most life-threatening immune-related adverse event. Its clinical spectrum is highly heterogeneous, and its outcome remains unpredictable. While the cardiac risk associated with immune checkpoint inhibitors is now well established, the burden and determinants of skeletal muscle involvement remain poorly defined. To enable early and individualized therapeutic management, it is essential to promptly recognize this entity, delineate its phenotypic spectrum, and identify the factors associated with severe outcomes.
Methods. We conducted a single-centre retrospective study including patients diagnosed with ICI-induced myositis between January 2016 and July 2024. Diagnosis required the association of muscle weakness and/or myalgia and/or elevated serum creatine kinase (CK) with myopathological evidence of muscle inflammation. Clinical, biological, and imaging data were collected.
A composite endpoint defined severe outcome as a loss of motor autonomy (modified Rankin Scale ≥4) and/or the need for mechanical ventilatory or

nutritional support. Unsupervised analyses (multiple correspondence analysis and hierarchical clustering) were used to identify homogeneous clinical phenotypes, and multivariable logistic regression to determine independent predictors of severity.
Results. A total of 102 patients were included, mainly receiving PD-1/PD-L1 mono-therapy. Clinical presentations were heterogeneous. At follow-up, most survivors had recovered full autonomy without residual weakness or relapse. Unsupervised clustering identified three distinct phenotypes correlated with disease severity. Dyspnoea, oculomotor involvement, and male sex were independent predictors of Major Adverse Muscular Events (MAME) and were combined into a pragmatic prognostic score which stratifies patients into low, inter-mediate, and high-risk groups. Its immediate bedside applicability makes it a valuable clinical tool for early risk assessment.
Conclusions. In summary, ICI-related myotoxicity carries a high risk of life-threatening muscular complications, affecting approximately a third of patients. Its clinical spectrum can be summarised into three reproducible phenotypic clusters. The proposed prognostic score enables early risk stratification and may guide clinical decision-making and therapeutic escalation in this setting.
Key words: cancer, immune checkpoints inhibitors, myotoxicity

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REAL-WORLD APPLICATION OF THE INTERNATIONAL MYOSITIS ASSESSMENT AND CLINICAL STUDIES GROUP GUIDELINES ON CANCER RISK STRATIFICATION

Silvia Cavalli[1], Maria Rosa Pellico[1,2], Cristina Bochicchio[1,2], Claudia Iannone[1,2], Ilaria Magi[1,2], Veronica Batani[3,4,5], Antonio Tonutti[6,7], Silvia Grazzini[8], Silvia Della Pina[9], Alessia Gatti[9], Manuel Sette[1,2], Antonina Minniti[2], Maria De Santis[6,7], Angela Ceribelli[6,7], Edoardo Conticini[8], Ilaria Cavazzana[9], Corrado Campochiaro[3,4], Giacomo De Luca[3,4], Roberto Caporali[1,2], Nicoletta Del Papa[1,2]
[1]Department of Clinical Sciences and Community Health, Research Centre for Adult and Pediatric Rheumatic Diseases, Università degli Studi di Milano, Milano, [2]Department of Rheumatology and Medical Sciences, ASST Gaetano Pini-CTO Institute, Milano, [3]Unit of Immunology, Rheumatology, Allergy and Rare Disease, IRCCS San Raffaele Hospital, Milano, [4]Vita Salute San Raffaele University, Milano, [5]Rheumatology Unit - Department of Medical and Surgical Sciences for Children and Adults, University of Modena and Reggio Emilia, Modena, [6]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milano, [7]Rheumatology and Clinical Immunology, IRCCS Humanitas Research Hospital, Rozzano, Milano, [8]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University of Siena, Siena, [9]Rheumatology and Clinical Immunology, ASST Spedali Civili di Brescia, Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy

Objectives. The 2023 International Myositis Assessment and Clinical Studies Group (IMACS) guidelines introduced a standardized risk-stratification model for cancer screening in idiopathic inflammatory myopathies (IIM). Despite their potential to harmonize clinical practice, real-world evidence on their performance, predictive accuracy, and feasibility remains scarce. This study aimed to evaluate the effectiveness of IMACS-based risk stratification in predicting malignancy occurrence and assess adherence to recent cancer screening recommendations in a multicentric Italian IIM cohort.
Methods. The study population included 411 IIM patients, fulfilling either the 2017 EULAR/ACR IIM classification criteria or disease-specific validated criteria (for cancer associated dermatomyositis, anti-synthetase syndrome and immune-mediated necrotizing myopathy), who were retrospectively enrolled from five Italian rheumatology centres. A minimum follow-up duration of three years and the assessment of Myositis Spacific and Associated Autoantibodies (MSA/MAA) status were mandatory criteria for inclusion. Patients were then classified into IMACS-defined risk groups (standard, intermediate, and high). Demographic, clinical, and risk factor data, as well as cancer screening methodologies, were collected at IIM diagnosis (T0) and at one (T1), two (T2), and three (T3) years of follow-up, and the last available observation (T4). Cancer occurrence within three years of IIM diagnosis was assessed, including type and site of the neoplastic disease. Screening practices prior to the implementation of IMACS guidelines were compared with the new recommendations. Logistic regression analysis was used to evaluate the predictive value of IMACS stratification.
Results. Among 411 patients, 180 (43.8%) were classified as high-risk, 156 (37.7%) as intermediate-risk, and 75 (18.2%) as standard-risk. Cancer was diagnosed in 9.2% of patients within three years of IIM onset, with high-risk patients significantly more likely to develop malignancy (OR=4.05, p=0.026). Anti-TIF1γ (OR=12.3, p<0.001) and anti-SAE1 (OR=11.9, p=0.012) were independent predictors of cancer. Evaluation of clinical practice revealed substantial variability in screening adherence, both at the time of IIM diagnosis and during the following period, with frequent underuse of enhanced screening in intermediate-risk patients and a progressive decline in surveillance intensity beyond the first year after diagnosis.
Conclusions. The IMACS cancer risk-stratification model showed strong predictive accuracy in stratifying IIM patients, supporting its validity real-world settings. However, inconsistencies in screening practices, particularly in intermediate-risk patients, highlight the need for optimization and refinement of current guidelines. Future prospective studies could help defining cost-effective, risk-adapted screening strategies for this challenging patient population.
Key words: idiopathic inflammatory myopathies, cancer screening, IMACS guidelines, risk stratification, dermatomyositis, autoantibodies, malignancy, real-world data, predictive model

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CLINICAL CHARACTERISTICS AND CANCER RISK OF ANTI-OJ ANTI-SYNTHETASE SYNDROME: A COHORT COMPARATIVE STUDY AND A SYSTEMATIC LITERATURE REVIEW

Valentin Pillot[1], Segolene Tocquet[2], Jean-Luc Charuel[3], Sarah Tansley[4], Hui Lui[4], Samia Boussouar[5], Pierre-Yves Brillet[6], Dylan Vellas[7], Sarah Leonard-Louis[8], Yurdagul Uzunhan[9], Antoine Belle[10], Pascal Cohen[11], Pascale Ghillani-Dalbin[3], Makoto Miyara[3], Miguel Hie[12], Guillaume Foulon[13], Nicolas Gambier[14], Jean-François Boitiaux[15], Piera Fuzibet[16], Bruno Crestani[17], Loïc Baudelet[18], Maxime Ilzkovitz[18], Carole Nagant[19], Anne Marie Bouvier[20], Valerie Jooste[20], Olivier Benveniste[21], Yves Allenbach[21]
[1]Department of Internal Medicine and Clinical Immunology, Hôpital Pitié-Salpêtrière, AP-HP, Sorbonne Universite, Paris, France, [2]Department of Internal Medicine, CHU Reims, Hôpital Robert-Debré, Reims, France, [3]Department of Immunology, Hôpital Pitié-Salpêtrière, AP-HP; Sorbonne Université, Paris, France, [4]Royal National Hospital for Rheumatic Diseases, Royal United Hospitals, Department of Life Sciences, University of Bath, Bath, UK, [5]Sorbonne Université, Assistance Publique-Hôpitaux de Paris, Département d'Imagerie Cardiovasculaire et Thoracique (ICT), Institut de Cardiologie, Hôpital Pitié-Salpêtrière, 47-83 Boulevard de l'Hôpital, Paris, France, [6]Department of Radiology/Thoracic Imaging, Hôpital Avicenne, AP-HP; Université Sorbonne Paris Nord, Bobigny, France, [7]Department of Internal Medicine, Centre Hospitalier Universitaire de Saint-Etienne, Saint-Etienne, France, [8]Sorbonne Université, INSERM, Department of Neuropathology, AP-HP, Hôpital Pitié-Salpêtrière, Paris, France, [9]Department of Pneumology, Assistance Publique Hôpitaux de Paris, Avicenne University Hospital, Bobigny, France; Reference center for rare pulmonary diseases, INSERM U1272, University Sorbonne Paris-Nord, Bobigny, France, [10]Department of Pulmonology, CHI Compiègne Moyon, Compiègne, France, [11]Department of Internal Medicine, National Reference Center for Rare Systemic Autoimmune Diseases, AP-HP.Centre, Hospital Cochin, Paris, France, [12]Department of Internal Medicine 2, AP-HP, Groupement Hospitalier Pitié-Salpêtrière, Centre de Référence pour le Lupus, le Syndrome des anti-phospholipides et autres maladies auto-immunes rares, Institut E3M, Paris, France, [13]Department of Pulmonology, American Hospital of Paris, Neuilly-sur-Seine, France, [14]Department of Internal Medicine, CH Général Delafontaine, Saint Denis, France, [15]Department of Pulmonology, Centre Hospitalier Hôpital NOVO, Site de Pontoise, Pontoise, France, [16]Department of Rheumatology, CHRU d'Orléans, Hôpital de la Source, Orléans, France, [17]Department of Pulmonology, Hôpital Bichat-Claude Bernard, AP-HP; Université Paris Cité/INSERM, Paris, France, [18]Department of Internal Medicine, Institut Jules Bordet, Hôpitaux Universitaire de Bruxelles (H.U.B), Université Libre de Bruxelles (ULB), Bruxelles, Belgique, [19]Department of Immunology, Laboratoire Hospitalier Universitaire de Bruxelles (LHUB-ULB), Université Libre de Bruxelles (ULB), Bruxelles, Belgique, [20]Université Bourgogne Europe-INSERM UMR1231, CHU Dijon Bourgogne, Registre Bourguignon des cancers digestifs Dijon France, Réseau français des registres de Cancers (FRANCIM), Toulouse, France, [21]Sorbonne Université, INSERM, Department of Internal Medicine, AP-HP, Hôpital Pitié-Salpêtrière, Paris, France

Background. Antisynthetase syndrome (ASyS) is a systemic autoimmune disease that primarily affects the lungs, joints, and muscles, and is associated in over 90% of cases with anti-Jo-1, anti-PL7, or anti-PL12 antibodies. ASyS is not associated with malignancy. Anti-OJ autoantibody-positive ASyS is poorly characterized, as it is a rare anti-synthetase antibody and commercial immunoassay kits lack reliability.
Methods. We conducted a retrospective comparative cohort study of anti-OJ patients. Anti-OJ was identified by immunoprecipitation. Clinical, biological, radiological, and myopathological data were collected. ASyS OJ-negative patients positive for anti-Jo-1, anti-PL7, or anti-PL12 antibodies were used as controls. Cancer incidences were compared to the aged matched general population using standardized incidence ratios. A systematic literature review of anti-OJ patients was also conducted for descriptive comparison.
Results. Anti-OJ patients (n=22) were older at diagnosis (69 years [51.5-

75], p<0.01) and exhibited lower frequencies of muscular (54.5%, p <0.01) and articular involvement (26.7%, p < 0.01) compared OJ-negative ASyS patients (n=158), while interstitial lung disease remained a prominent feature in both groups. Cancer incidence was markedly increased in the anti-OJ patients (SIR = 3.23 [95% CI: 1.21–8.62]) compared to general population, in contrast to anti-Jo-1 and anti-PL7/12 patients, where no significant difference was observed. The literature review of anti-OJ patients (n = 106) showed consistent results with our cohort.
Conclusions. Anti-OJ ASyS define a distinct clinical subset within the ASyS spectrum, and a unique increased risk of malignancy. These findings advocate for enhanced malignancy screening and dedicate serological testing in this rare subgroup.
Key words: myositis, aminoacyl-tRNA synthetases, lung diseases, interstitial, neoplasms, anti-OJ antibody

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EXPLORING MALIGNANCY IN ANTI-SYNTHETASE SYNDROME: A MULTISITE RETROSPECTIVE STUDY

Reena Yaman[1], Archit Srivastava[1], Rachel Sauls[1], Alejandro Arango Martinez[2], Caroyln Harvey[3], Luis Penaranda Bolano[1], Claire Wilson[1], Ronald Butendieck[1], Vikas Majithia[1], Florentina Berianu[1]
[1]Mayo Clinic Florida, Jacksonville, USA, [2]Universidad Pontificia Bolivariana, Medellín, Colombia, [3]Mayo Clinic Arizona, Phoenix, USA

Background. Anti-synthetase syndrome (ASyS) is a rare, heterogeneous inflammatory myopathy characterized by presence of anti-aminoacyl transfer RNA synthetase autoantibodies with multisystem disease manifestations (1). Other forms of idiopathic inflammatory myopathy, mainly dermatomyositis, are associated with increased risk of malignancy (2). Although ASyS has been presumed to have low associated malignancy risk, reports of malignancy have been presented (3). The goal of this study was to describe the incidence and types of malignancy in a cohort of ASyS patients.
Methods. A retrospective observational study was conducted by reviewing medical records of adults diagnosed with ASyS across 3 sites at the same institution. Charts were reviewed to identify whether malignancy of any type was diagnosed around the time of ASyS diagnosis defined as up to 5 years before or after. Demographic, clinical, radiologic, and immunologic data, including interstitial lung disease (ILD) patterns and myositis-specific antibodies, were collected and descriptive statistics were performed. Incidence rates per person-years are calculated for three intervals: 5 years before, 5 years after, and 5 years before and after ASyS diagnosis.
Results. A total of 236 patients diagnosed with ASyS were identified with 40 (17%) receiving a diagnosis of malignancy within 5 years of ASyS diagnosis. Of these, 18 (45%) and 22 (55%) occurred before and after ASyS diagnosis, respectively. Demographics, disease characteristics, potential malignancy risk factors, and trialed therapies of the identified cohort with concurrent malignancy were outlined. The incidence of malignancy was 1.8 per 100 person-years, slightly higher post-ASyS diagnosis (2.03/100 person-years) than pre-ASyS diagnosis (1.57/100 person-years). The most common category of malignancy was solid tumors followed by skin cancer with the most common individual cancer type being squamous cell, followed by basal cell, carcinoma of the skin.
Conclusions. Malignancy was seen in 17% of ASyS within a period of 5 years prior to and 5 years after diagnosis of their rheumatic disease with incidence 1.8 cases per 100 person-years. Comparison to rates in the general population and further elucidation of disease and treatment characteristics associated with risk of malignancy is warranted.

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MALIGNANCY SCREENING OF DERMATOMYOSITIS PATIENTS IN THE PENN STATE REGISTRY OF INFLAMMATORY MYOPATHIES (PRIMO)

Jacob Colello[1], Katrina Gonzales[1], William DeKryger[1], Deepika Saravanan[1], Esha Tulsian[1], Peri Newman[1], Galen Foulke[1], Nancy Olsen[1]
[1]Penn State Health, Hershey, USA

Background. Dermatomyositis (DM) is an immune-mediated myopathy characterized by muscle weakness and rash that carries an elevated risk of associated malignancy. While the link between DM and malignancy is well established, no consensus guidelines exist regarding advanced malignancy screening beyond age-appropriate US Preventive Service Task Force (USPSTF) and American Cancer Society recommendations. Given the variability of practices among providers, we sought to explore institutional trends to obtaining malignancy screenings for adult DM patients.
Methods. We conducted a retrospective review of patients enrolled from 2010-2020 in our previously established registry, the Penn State Registry of Inflammatory Myopathies (PRIMO). Inclusion criteria were diagnosed at age >18, DM diagnosis confirmed through ACR/EULAR criteria, and presentation within 3 years of diagnosis. Descriptive statistics were used to summarize results.
Results. Of 137 screened, 65 patients met inclusion criteria. Patients were predominantly female (78.5%), with mean age at diagnosis of 55.3 years. In 70% of initial encounters, education of malignancy risk at diagnosis was documented. CT thorax (75%) and CT abdomen/pelvis (70%) were the most commonly completed screenings with 14% undergoing PET CT. Regarding USPSTF screenings, 41% of patients completed age-appropriate screenings + advanced screenings, 14% completed all age-appropriate screenings, and 44% of patients were not up to date on their screenings. All patients with high-risk antibody profiles received advanced screening. Rheumatologists (26, 32%), dermatologists (29, 36%), and primary care physicians (19, 23%) were the most common ordering providers. Common barriers to screening included insurance coverage, poor follow up, and unclear diagnosis at presentation. Malignancy was present in 20% of patients.
Conclusions. Our data highlights variability among cancer screening practices in DM. While those with the highest risk disease subtypes were identified and screened, many others were not recommended for advanced screening and clinical judgement was not well documented. Furthermore, USPSTF screenings were not ordered by specialists, drawing attention to the need for collaboration. Given the morbidity and mortality that accompanies malignancy, efforts should be made to overcome these barriers. Future efforts should focus on collaborations to expand participant diversity, adopting insights from primary care practices, assessing patient and provider perspectives, and developing quality improvement initiatives to trial in the clinical environment.
Key words: screening, cancer, myositis

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DOES THE 2023 IDIOPATHIC INFLAMMATORY MYOPATHY CANCER SCREENING GUIDELINE ENABLE ACCURATE RISK STRATIFICATION? RESULTS FROM 18 INTERNATIONAL COHORTS

Daniel Smith[1,3], Jorge Álvarez Troncoso[4], Lilia Andrade-Ortega[5], Helena Andersson[6], Jeffrey Callen[7], Roberto Caporali[8,9], Lorenzo Cavagna[26,27], Dennis Chan[10], Hector Chinoy[1,2,3], Edoardo Conticini[11], Melissa Currence[12], Nicoletta Del Papa[8,9], Mazen Dimachkie[12], Anthony Fernandez[13], Marco Fornaro[14], Silvia Grazzini[11], Zoltan Griger[15], Florenzo Iannone[14], Masataka Kuwana[16], Patrick Man Leung Lee[17], Lucas Tsz Ho Luk[18], Elena Manna[26,27], Sergey Moiseev[19], Melinda Nagy-Vincze[15], Maria Rosa Pellico[8,9], Veronica Piccin[26,27], Sandhya Sasidharan[12], Samuel Katsuyuki Shinjo[20], Vineeta Shobha[21], Ho So[22], Iris Yan Ki Tang[23], Jiří Vencovský[24], Akira Yoshida[16], Giovanni Zanframundo[26,27], Rohit Aggarwal[25], Alexander Oldroyd[1,2,3]

[1]National Institute for Health Research Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, University of Manchester, Manchester, UK, [2]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [3]Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK, [4]Medicina Interna, Unidad Enfermedades Inmunomediadas Sistémicas, Hospital Universitario La Paz, Madrid, Spain, [5]Rheumatology Department, CMN 20 de Noviembre, ISSSTE, Mexico City, Mexico, [6]Department of Rheumatology, Oslo University Hospital, Oslo, Norway, [7]Division of Dermatology, University of Louisville School of Medicine, Louisville, USA, [8]Department of Rheumatology and Medical Sciences, ASST Gaetano Pini-CTO, Milan, Italy, [9]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy, [10]Department of Medicine, Alice Ho Miu Ling Nethersole Hospital, Hong Kong SAR, China, [11]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University of Siena, Siena, Italy, [12]Neuromuscular Division, University of Kansas Medical Center, Kansas City, USA, [13]Departments of Dermatology and Pathology, Cleveland Clinic, Cleveland, USA, [14]Rheumatology Unit, Department of Precision and Regenerative Medicine and Ionian Area, University of Bari, Bari, Italy, [15]Department of Internal Medicine, Division of Clinical Immunology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary, [16]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [17]Department of Medicine, Yan Chai Hospital, Hong Kong SAR, China, [18]Department of Medicine & Geriatrics, Kwong Wah Hospital, Hong Kong SAR, China, [19]Tareev Clinic of Internal Diseases, Sechenov University, Moscow, Russia, [20]Division of Rheumatology, Faculdade de Medicina Universidade de Sao Paulo, Sao Paulo, Brazil, [21]Department of Clinical Immunology and Rheumatology, St. John's Medical College Hospital, St. John's National Academy of Medical Sciences, Bengaluru, India, [22]Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong SAR, China, [23]Division of Rheumatology & Clinical Immunology, Department of Medicine, The University of Hong Kong, Hong Kong SAR, China, [24]Department of Rheumatology, 1st Medical Faculty, Charles University, Prague, Czech Republic, [25]Myositis Center and Division of Rheumatology and Clinical Immunology, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, USA, [26]Department of Internal Medicine and Therapeutics, Rheumatology Division University of Pavia, Pavia, Italy, [27]Division of Rheumatology, IRCCS Policlinico S. Matteo Foundation, Pavia, Italy

Background. One in four patients with adult-onset idiopathic inflammatory myopathy (IIM) are diagnosed with cancer within three years before/after disease onset. The 2023 IIM Cancer Screening Guideline recommends risk stratification according to specific combinations of IIM subtype, autoantibodies, and specific clinical features. Patients can be classified as high, moderate, or standard risk; this risk categorisation informs required screening. This study aims to assess the accuracy of the guideline's risk stratification approach in a large multi-national cohort.

Methods. Retrospective longitudinal data of participants with adult-onset IIM from 18 cohorts from 13 countries were collated (Hungary, USA, Spain, Mexico, Brazil, Japan, Russia, Norway, Italy, India, China, Czech Republic, UK).

IIM subtype, autoantibody status, and clinical features relevant to cancer risk stratification was recorded alongside cancer diagnosis information for each participant. The cancer risk group (*i.e.* high, moderate, standard) for each participant was determined according to the 2023 IIM Cancer Screening Guideline. The proportion of participants within each risk group diagnosed with cancer within three years after IIM onset was determined.

Differences of the proportion of each risk group diagnosed with cancer were determined using the Kruskall-Wallis test for continuous variables and the chi-squared test for categorical variables. Analysis was performed using R.

Results. Data of 1,498 participants (68% female, mean age 62 years) were collated. A total of 917 (61%) participants fulfilled high risk criteria, 442 (30%) fulfilled moderate risk criteria, and 139 (9%) fulfilled standard risk criteria. Cancer was detected in 226 participants (15% of whole cohort). The most common cancer was breast (n=40, 18%), followed by lung (n=32, 14%), colorectal (n=17, 8%), and nasopharyngeal (n=14, 6%). Most cancer cases occurred in the high risk group (n=179, 79%), followed by the moderate risk group (n=43, 19%), and standard risk group (n=4, 2%) (chi-squared p-value <0.01). Of the four standard risk patients diagnosed with cancer, three had lung cancer and one had colon cancer.

Conclusions. This is the first study to investigate the utility of the 2023 IIM Cancer Screening Guideline's risk stratification approach across multiple international IIM cohorts. The guideline's risk stratification approach demonstrated good performance overall, however a small number of patients classified as standard risk were diagnosed with cancers that would likely not be identified via guideline-recommended screening.

These results highlight the need to refine and optimise the risk stratification approach to enhance accuracy and cancer detection

Key words: myositis, cancer, screening

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AZATHIOPRINE-INDUCED LYMPHOMATOID GRANULOMATOSIS IN A PATIENT WITH DERMATOMYOSITIS: A CASE REPORT

Maria Diana Pascoal[1,2], Cláudia Pinto Oliveira[1,2], Eduardo Dourado[1,2]

[1]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal, [2]Aveiro Rheumatology Research Centre, Centro Académico Clínico Egas Moniz Health Alliance, Universidade de Aveiro, Aveiro, Portugal

Background. Lymphomatoid granulomatosis (LYG) is a rare Epstein-Barr virus (EBV)-associated lymphoproliferative disorder that affects immunocompromised patients and has a highly variable clinical course. The most commonly affected sites are the skin, lung, and central nervous system. Here, we describe a case of cutaneous and pulmonary LYG in a patient with anti-SAE1+ dermatomyositis treated with azathioprine.

Clinical case. A 57-year-old woman presented in 2014 with muscle weakness, photosensitive pruriginous generalized erythematous rash, dysphagia, and fatigue. Chest high-resolution computerized tomography (HRCT) showed organizing pneumonia (OP), and lung function tests showed a restrictive pattern. Her medical history included well-documented allergies to prednisolone, methylprednisolone, and several non-steroidal anti-inflammatory drugs, but was otherwise irrelevant. The patient was diagnosed with anti-SAE1+ dermatomyositis.

Cancer screening was negative at the disease onset. The patient was consecutively treated with cyclophosphamide, cyclosporin, and rituximab, and the disease had been effectively controlled with azathioprine and deflazacort without evident adverse events from December 2018 until September 2023.

In October 2023, fatigue, fever (maximum 39ºC), anorexia, and weight loss (9 kg in 10 months) ensued. Anemia, elevated C-reactive protein, erythrocyte sedimentation rate, AST, and ALT were identified. Liver injury prompted the discontinuation of azathioprine. Infectious diseases were excluded, and an extensive cancer screening revealed suspicious hepatic and pulmonary lesions suggesting metastases of unknown origin. A biopsy of a suspicious cutaneous lesion revealed an EBV-positive, angioinvasive B-cell lymphoproliferative disorder, consistent with LYG. Physical examination and a repeat CT scan 5 weeks after azathioprine suspension showed spontaneous regression of all the lesions.

In this case, azathioprine withdrawal seems to have induced LYG remission. Nonetheless, cessation of azathioprine caused a dermatomyositis flare, requiring initiation of rituximab and intravenous immunoglobulin, resulting in clinical improvement without LYG recurrence.

Conclusions. As reported in the literature, azathioprine can induce LYG in EBV-infected individuals and can be resolved with the suspension of the drug, even though some cases need targeted treatment – often rituximab.

This clinical case highlights the diagnostic challenges associated with LYG and underscores the importance of early recognition and discontinuation of the offending drug to ensure proper treatment and achieve full remission. Further research is needed to identify vulnerable patients who are at high risk of developing drug-induced LYG.

Key words: lymphomatoid granulomatosis, azathioprine, dermatomyositis

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CANCER RISK AND SURVIVAL IN IDIOPATHIC INFLAMMATORY MYOPATHY: SUBTYPE IMPACT IN A LARGE, DIVERSE COHORT

Amir Sabouri[1], Shreyas Kudrimoti[1], Janet Alexander[1], Zahra Samiezadeh-Yazd[1], Didem Saygin[2], Jafar Kafaie[3], Raymond Liu[1], Sarah Ringsted[1]
[1]Kaiser Permanente, Oakland, USA, [2]University of Pittsburg, Pittsburg, USA, [3]St Louis University, St Louis, USA

Background. Idiopathic inflammatory myopathies (IIM) are heterogeneous autoimmune disorders with variable clinical phenotypes and malignancy risk. Modern classification incorporating myositis-specific autoantibodies (MSAs) may refine cancer risk stratification. Understanding subtype-specific malignancy patterns and survival outcomes in a diverse community population is essential to optimize screening strategies.
Methods. We conducted a retrospective cohort study of adults diagnosed with IIM within Kaiser Permanente Northern California. Patients were matched to non-IIM controls by age and sex. We evaluated cancer incidence within three years before and after IIM diagnosis and analyzed associations across clinical subtypes and MSA profiles. We estimated odds ratios (ORs), hazard ratios (HRs), and adjusted HRs (AHRs) for malignancy and mortality. Survival outcomes were assessed for cancer development post-diagnosis.
Results. The study included 544 patients with idiopathic inflammatory myopathies (IIM) and 2176 healthy controls. Among the IIM patients, the most common subtype was dermatomyositis (DM, 39.7%), followed by immune-mediated necrotizing myopathy (IMNM, 26.7%) and antisynthetase syndrome (ASyS, 11.9%).CT-based malignancy screening occurred in 40.4% of IIM patients. Cancer incidence within three years before or after diagnosis was higher in IIM compared with controls (9.4% *vs*. 4.3%, p<0.001). Compared with controls, the odds of cancer prior to diagnosis was not significantly different (OR 1.08(0.79-1.48). In contrast, the cancer rate post-index was elevated for cases versus controls (HR 2.25(1.61-3.16). Subtype analysis showed increased post-diagnosis cancer risk in ASyS (HR 3.17, 95% CI 1.61–6.26), DM (HR 2.01, 95% CI 1.19–3.40), and polymyositis (HR 3.22, 95% CI 1.32–7.90). Highest MSA-associated cancer prevalence prior to IIM diagnosis occurred in non-Jo1 ASyS and Mi-2-positive DM (13.0% each), whereas HMGCR-positive IMNM and Jo-1-positive ASyS had lower rates (3.3% each). Post-index, the most frequent type of cancer was breast cancer, comprising 34.6% of cancer cases among IIM patients and 21.7% of cancer cases among controls. Mortality was higher among IIM patients *vs*. controls (HR 2.43, 95% CI 1.86–3.17). Among IIM cases, those with cancer within +/- 3 years of diagnosis had increased mortality compared to IIM cases without cancer (HR 1.94, 95% CI 1.13-3.32).
Conclusions. Cancer-associated myositis was linked to reduced survival, highlighting the need to better define and validate risk-based cancer surveillance strategies in this population. This is the first large, diverse study showing increased cancer risk in non-Jo1 ASyS.
Key words: idiopathic inflammatory myopathy, cancer risk, myositis-specific autoantibodies

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MYASTHENIA GRAVIS-MYOSITIS OVERLAP: A COMPARATIVE STUDY OF IDIOPATHIC AND IMMUNE CHECKPOINT INHIBITOR-RELATED FORMS

Antonio Lauletta[1], Elena Rossini[1], Valentina Damato[2], Francesca Beretta[2], Simone Rossi[3], Raffaele Iorio[4], Enrico Marchioni[5], Antonio Petrucci[6], Alberto Vogrig[7], Carmela Romano[8], Laura Tufano[1], Luca Leonardi[1], Stefania Morino[1], Francesca Forcina[1], Silvia Falso[4], Paola Bini[5], Antonio Lotti[2], Laura Fionda[1], Matteo Garibaldi[1]
[1]Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), Sapienza University of Rome, Rome, Italy, [2]Department of Neurosciences, Psychology, Drug Research and Child Health (NEUROFARBA), University of Florence, Florence, Italy, [3]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy, [4]Department of Neuroscience, Università Cattolica del Sacro Cuore, Rome, Italy, [5]Unit of Neuroncology, Fondazione IRCCS Mondino, Pavia, Italy, [6]Center for Neuromuscular and Neurological Rare Diseases, San Camillo Forlanini Hospital, Rome, Italy, [7]Clinical Neurology, Department of Head-Neck and Neuroscience, Azienda Sanitaria Universitaria Friuli Centrale (ASU FC), Udine, Italy; Department of Medicine (DMED), University of Udine, Udine, Italy, [8]Stroke Unit, Department of Emergency, Ospedale dei Castelli-ASL6, Rome, Italy

Background. Emerging evidence highlights that a Myasthenia Gravis-Inflammatory Myopathy (MG-IM) overlap syndrome can occur as an immune-related adverse event (irAE) following immune-checkpoint inhibitor (ICI) therapy. Before the advent of ICIs, an idiopathic form of MG-IM (i-MG-IM), often thymoma-associated, had already been described. This study compared the clinical and serological features, treatment strategies, and outcomes of i-MG-IM and ICI-related MG-IM (ir-MG-IM).
Methods. We conducted a multicenter, retrospective cohort study across eight Italian centers, including consecutive patients fulfilling established criteria for both MG and IM. Clinical features, antibody profiles, oncological history, treatments, and outcomes were systematically collected and compared. Available retrospectively collected sera were tested for reactivity against clustered adult (A) and fetal (F) AChR isoforms using live cell-based assay (L-CBA), and for complement-activating capacity using flow cytometry.
Results. Thirty-eight patients were identified (19 i-MG-IM and 19 ir-MG-IM) after excluding 13 ir-patients that did not meet MG diagnostic criteria and one i-MG-IM patient due to lack of clinical information.
Compared with i-MG-IM, the ir-MG-IM cohort was older (median 77 *vs*. 59 years, p<0.001), predominantly male (84.2% vs 47.4%), and exclusively presented with concurrent MG/IM onset, whereas i-MG-IM often manifested sequentially. Thymoma was detected in 73.7% of i-MG-IM but in none of the ir-MG-IM patients. CK levels were higher in ir-MG-IM (median 3145 *vs*. 1000 U/L, p=0.001). Myocarditis, orbital myositis, and severe bulbar/respiratory involvement were more frequent in ir-MG-IM (p<0.05).
Anti-AChR antibodies were found in all i-MG-IM but only in 68% of ir-MG-IM cases. Complement activation in vitro was observed only in i-MG-IM sera. Anti-titin antibodies were identified in 85.7% of MG-IM (all thymoma-associated) and in 50% of ir-MG-IM.
Acute mortality occurred in 36.8% of ir-MG-IM and 0% in i-MG-IM patients (p<0.01). Relapses occurred in 63.2% of i-MG-IM but were absent in ir-MG-IM (p<0.001).
At the last follow-up, functional outcomes were significantly worse in ir-MG-IM (median mRS 4 *vs*. 0, p<0.001).
Conclusions. i-MG-IM and ir-MG-IM appear to represent distinct clinical and pathological entities. Although certain features overlap, our findings underscore the need for tailored diagnostic and therapeutic approaches and raise important questions regarding the pathogenic roles of antibodies and complement activation in ir-MG-IM.
Key words: myasthenia gravis, myositis, inflammatory myopathies, immune checkpoint inhibitors, cancer

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CANCER AND ANTI-SYNTHETASE SYNDROME: DATA FROM THE CLASS PROJECT DATABASE

Thomas Moulinet[1], Laure Gallay[2], Giovanni Zanframundo[3,4], Eduardo Dourado[5,6,7], Sara Faghihi Kashani[8], Iazsmin Bauer-Ventura[9], Daphne Rivero-Gallegos[10], Francisca Bozán[11], Sangmee Sharon Bae[12], Akira Yoshida[13], Lorenzo Cavagna[3,4], Rohit Aggarwal[8]
[1]Department of Internal Medicine and Clinical Immunology, Nancy University Hospital, Nancy, France, [2]Department of Clinical Immunology, Edouard Herriot Hospital, Hospices Civils de Lyon, Lyon, Franc, [3]Department of Internal Medicine and Therapeutics, Università di Pavia, Pavia, Italy, [4]Division of Rheumatology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [5]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal, [6]Aveiro Rheumatology Research Centre, Egas Moniz Health Alliance, Aveiro, Portugal, [7]Rheumatology Research Unit, Faculdade de Medicina, Universidade de Lisboa, Portugal, Portugal, [8]University of Pittsburgh School of Medicine, Pittsburgh, USA, [9]Section of Rheumatology, Department of Medicine, University of Chicago, Chicago, USA, [10]Rheumatology Clinic, Instituto Nacional de Enfermedades Respiratorias, Ismael Cosío Villegas, Mexico, Mexico, [11]Section of Rheumatology, Department of Medicine, Hospital Clínico Universidad de Chile, Santiago de Chile, Chile, [12]Division of Rheumatology, Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, USA, [13]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan

Background. Some subtypes of myositis have been associated with cancer. Data about the association of anti-synthetase syndrome (ASyS) with cancer were scarce, relying mostly on case reports, small series, and a few retrospective studies. While recent guidelines considered ASyS to have a low risk of malignancy, some of the aforementioned literature suggests that such an association may be relevant. The objective of the present study is to further assess the association of ASyS and cancer.
Methods. ASyS cases registered in the CLASS project database, defined by

the treating physician and independently reviewed by at least two members of the CLASS core working group, were included. Cancer-associated myositis (CAM) was defined as cancer diagnosed within 3 years before or after ASyS onset. Quantitative data were summarized and compared using appropriate parametric or nonparametric tests, and qualitative data with Fisher's exact test. Clinically relevant variables associated with cancer (p<0.1) in univariable analysis were selected, followed by a backward and forward stepwise algorithm. The models with the best fit (lowest AIC) were selected as the final model.

Results. Among 1885 patients with ASyS, 1396 patients had available data regarding the history of cancer and the delay between cancer and ASyS onset. A history of cancer was noticed in 124 patients, among whom 53 responded to CAM criteria (3.8% of all ASyS patients). ASyS patients with CAM were more frequently men (47% *vs*. 26%, p=0.002) and were older (63 ± 12 *vs*. 49 ± 15 years old, p<0.001). The most represented cancers were breast cancer (n=6), melanoma (n=5), prostate cancer (n=5), other skin cancers (n=4), and thyroid cancer (n=4). Only 17% of cancers were metastatic at the time of ASyS diagnosis. On univariate analysis, CAM was associated with age at diagnosis (OR=1.07 [1.05-1.10], p<0.001), male sex (OR=2.48 [1.42-4.32], p=0.001). Skin manifestation negatively associated with CAM (OR=0.60 [0.34-1.05], p=0.07), more specifically Gottron papules (OR = 0.23 [0.04-0.78], p=0.047), while sleeve sign on upper arm was associated with CAM (OR=4.4 [0.99-13.9], p=0.02). On multivariate analysis, CAM was only significantly associated with age and sex (OR = 1.07 [1.04-1.11], p<0.001, and OR=2.41 [1.01-5.75], p=0.04, respectively).

Conclusions. Based on a large sample analysis, the association of ASyS and cancer was rare and independently associated with older age and male sex. These findings argue for risk-adapted cancer screening at ASyS diagnosis, especially in male and/or older patients.

Key words: cancer, myositis, antisynthetase syndrome

Classification of Inflammatory Myopathies

P-5

CLINICAL CHARACTERISTICS AND CONCORDANCE OF ANTI-MDA5 AUTOANTIBODIES: A MULTICENTRE AUSTRALIAN STUDY

Syed Ali[1,2], Thomas Khoo[3,4,5], Keeran Shivkumar[6], Adam Caroll[7], Lauren Hender[8], Dimitra Beroukas[8], Kim Griggs[4], Celina Jin[9], Theo De[10], Jessica Day[6], Gabor Major[7], Vidya Limaye[4]

[1]Department of Clinical Immunology, Flinders Medical Centre, Bedford Park, Australia, [2]School of Medicine and Biomedical Sciences, Flinders University, Bedford Park, Australia, [3]Department of Rheumatology, Flinders Medical Centre, Bedford Park, Australia, [4]Department of Rheumatology, Royal Adelaide Hospital, Adelaide, Australia, [5]School of Medicine and Biomedical Sciences, University of Adelaide, Adelaide, Australia, [6]Department of Rheumatology, Royal Melbourne Hospital, Melbourne, Australia, [7]Department of Rheumatology, John Hunter Hospital, New Lambton Heights, Australia, [8]Immunopathology laboratory, SA Pathology, Bedford Park, Australia, [9]Immunopathology laboratory, Royal Melbourne Hospital, Melbourne, Australia, [10]Department of Immunopathology, Newcastle Laboratory, Newcastle, Australia

Background. Anti-MDA5 autoantibodies are implicated in dermatomyositis (DM) and are associated with characteristic skin manifestations, vasculopathy, inflammatory arthritis and interstitial lung disease (ILD).

In Australia, the myositis immunoblot (MIB) is the only available diagnostic immunoassay, with enzyme-linked immunosorbent assay (ELISA) restricted to the research setting.

A retrospective study was undertaken to determine the clinical concordance of a positive MDA5 MIB (EUROIMMUNE 16 Ag kit) result across three centres from different states of Australia (John Hunter Hospital [JHH, New South Wales], Royal Melbourne Hospital [RMH, Victoria] and SA Pathology [South Australia]).

Methods. The electronic medical records of patients with anti-MDA5 antibodies detected between January 2017 and September 2024 were reviewed for clinical correlation with disease manifestations. Anti-MDA5 DM diagnosis was according to expert clinician consensus.

Results. Of the 14,126 MIB tests performed, 118 (0.84%) were positive for anti-MDA5 (JHH n=11, RMH n=15 and SA Pathology n=92). Complete clinical data were available for 108/118 patients. In twenty-one patients (19.4%) the anti-MDA5 was deemed clinically concordant with a diagnosis of DM (median age 65 years [range 13-82], 67% female); these patients had significantly higher signal intensity (52/+++) than those with clinical discordance (20/+) (p<0.0001). The cohort was predominantly of White ethnicity (n=14), followed by Southeast Asian (n=3), African (n=3) and Middle Eastern (n=1).

All patients had ILD; 7/9 patients with rapidly progressive ILD (RP-ILD) were deceased at the time of retrospective review. Patients with RP-ILD had higher ferritin (1226 *vs*. 262 ug/L, p=0.014), neutrophil: lymphocyte ratio (4.1 *vs*. 2.6, p=0.049), and LDH (403 *vs*. 235 U/L, p=0.058) than patients without RP-ILD. Three patients with RP-ILD had concurrent anti-Ro52 antibodies. Pneumomediastinum developed in 7/21 (33%), and 6/7 had RP-ILD. Notably, 4/7 with pneumomediastinum died.

Other clinical manifestations included myositis (n=10), characteristic skin manifestations (n=14), polyarthritis (n=6) and myocarditis (n=1).

Treatment was heterogeneous and included corticosteroids (n=20), rituximab (n=9), tofacitinib (n=7), intravenous immunoglobulin (n=5), plasma exchange (n=5), cyclophosphamide (n=4), mycophenolate (n=3), tacrolimus (n=1) and cyclosporine (n=1).

Conclusions. We have performed the first assessment of the clinical concordance of anti-MDA5 antibodies with MIB in Australia and described the clinical features of a cohort from three major centres across three states. Anti-MDA5 antibodies with higher signal intensity on MIB are more likely to be clinically concordant. Pneumomediastinum is common and associated with high mortality. RP-ILD is common in this disease entity and has a poor prognosis even with targeted and multimodal immunosuppression.

Key words: immunoassay, line blot, myositis, interstitial lung disease

P-6

THE HISTOLOGICAL FEATURES OF ANTI-SYNTHETASE SYNDROME

Syed Ali[1,2], Thomas Khoo[3,4,5], Bernice Gutschmidt[6], Sarah Saxon[6], Gabor Major[7], Vidya Limaye[4,5]

[1]Department of Clinical Immunology and Allergy, Flinders Medical Centre, Bedford Park, Australia, [2]School of Medicine and Biomedical Sciences, Flinders University, Bedford Park, Australia, [3]Department of Rheumatology, Flinders Medical Centre, Bedford Park, Australia, [4]Department of Rheumatology, Royal Adelaide Hospital, Adelaide, Australia, [5]School of Medicine and Biomedical Sciences, University of Adelaide, Adelaide, Australia, [6]Department of Anatomical Pathology, SA Pathology, Adelaide, Australia, [7]Department of Rheumatology, John Hunter Hospital, New Lambton Heights, Adelaide, Australia

Background. To determine whether muscle histopathology can distinguish anti-synthetase syndrome (ASyS) from other sub-groups of idiopathic inflammatory myopathies (IIM).

Methods. Muscle biopsies of patients with a clinical diagnosis of ASyS (Group 1) and a control group of non-ASyS IIM (Group 2) assessed at SA Pathology (01/2010 - 02/2023) were identified (Royal Adelaide Hospital and John Hunter Hospital). These biopsies were reviewed by an expert anatomical pathologist, blinded to the diagnosis, autoantibody profile and previous biopsy report, for the presence/absence of histological criteria for ASyS (ENMC Criteria, Stenzel et al. 2024).

Results. There were 68 biopsies; 34 in each of Group 1 and 2. Anti-Jo1 (n=21, 62%) was the most common antibody in Group 1, followed by anti-PL7 (n=7, 21%), anti-PL12 (n=4, 12%) and anti-OJ (n=2, 6%). Group 2 comprised dermatomyositis (n=11, 32.3%), polymyositis (n=7, 20.6%), immune-mediated necrotising myopathy (n=7, 21%), overlap myositis (n=5, 14.7%) and inclusion body myositis (n=4, 12%).

Comparing biopsy re-review with historical reports, reporting of fibre necrosis, regeneration, perimysial inflammation, MHC-I/II and MAC stains were highly consistent (Cohen's kappa, κ=0.8-1). Conversely, perifascicular atrophy demonstrated weak agreement (κ=0.4).

In Group 1, perifascicular atrophy was evident on H&E staining in 21/34 (62%) biopsies, although MHC-I/II staining highlighted a perifascicular localisation of pathology in a substantially higher proportion (24/31, 77%). Necrosis was present in 20/34 (59%) and perimysial inflammation in 19/34 (56%). Comparing Group 1 and 2, there were no significant differences in frequency of perifascicular atrophy, necrosis, regeneration, perimysial inflammation or MHC staining. However, a specifically perifascicular distribution of MHC staining was more frequently noted in Group 1 than 2 (24/31 *vs*. 13/29, p=0.02). Within Group 1, biopsies from patients with anti-Jo1 ASyS had similar histological features (by light microscopy) to non-anti-Jo1 ASyS, but more frequently stained positive for MHC (MHC-I: 19/19 *vs*. 9/13, p=0.02; MHC-II: 18/19 *vs*. 8/13, p=0.03).

Conclusions. We highlight the importance of immunohistochemistry in the diagnosis of ASyS: 1. MHC-I/II staining is more sensitive than traditional

histology for demonstrating perifascicular pathology; 2. A perifascicular pattern of MHC staining is more specific for ASyS than other sub-groups of IIM and (3) MHC-I/II staining is more prevalent in anti-Jo1 than non-anti-Jo1 ASyS.

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Key words: anti-synthetase, muscle biopsy, histology, immunohistochemistry

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ICD-11: THE OPPORTUNITY TO IMPROVE DISEASE CODING IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Iazsmin Bauer Ventura[1], Siamak Moghadam-Kia[2], Jens Schmidt[3], Adam Schiffenbauer[4]

[1]University of Chicago, Chicago, USA, [2]University of Pittsburg, Pittsburg, USA, [3]Universitätsmedizin Göttingen, Göttingen, Germany, [4]National Institute of Environmental Health Sciences, Bethesda, USA

Background. The International Classification of Diseases (ICD) provides a standardized language for healthcare providers to document and communicate diagnoses. ICD enables consistent health data collection across settings and countries, supporting public health monitoring, disease surveillance, and resource allocation. It also serves as the foundation for healthcare billing and reimbursement systems worldwide. ICD-11, released by the World Health Organization (WHO) in 2022, represents a major advancement with enhanced granularity and international accessibility through its internet-based platform. The IMACS (International Myositis Assessment & Clinical Studies Group) ICD Scientific Interest Group (SIG) identified opportunities to refine ICD-11 codes to better reflect current understanding of idiopathic inflammatory myopathies (IIM).

Methods. This international study was conducted through the ICD-11 SIG, an international group with over 100 participants from 5 continents, which has convened regularly (8 meetings) since 2022 to review ICD-11 coding for IIM. Through iterative discussions, the group developed recommendations aligned with the ICD-11 updating framework.

Results. The IIM Scientific Interest Group identified critical gaps in ICD-11 IIM coding and proposed several enhancements. Key recommendations included: optimizing code descriptions to capture the full clinical spectrum of IIM subtypes, with particular emphasis on myositis-specific antibodies in diagnosis and extra-muscular manifestations of IIM; code simplification by merging inflammatory and non-inflammatory inclusion body myositis into a single entity; creating new classification elements to include immune-mediated necrotizing myopathy, clinically amyopathic dermatomyositis, and anti-synthetase syndrome; and refining disease manifestation codes for conditions such as calcinosis cutis, interstitial lung disease, and associated malignancies.

Conclusions. These recommendations will form the basis for a comprehensive consultation with the broader IIM community to gather feedback and build consensus through Delphi rounds, before a formal WHO submission.

Key words: international classification of diseases, idiopathic inflammatory myopathies

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ANTI-SYNTHETASE SYNDROME AT A TERTIARY CENTRE: CLINICAL FEATURES AND AGREEMENT BETWEEN CLASS, CONNORS AND SOLOMON CRITERIA

Catarina Rua[1], Maria Oliveira[2], Tiago Beirão[1], Catarina Silva[1], Mariana Patela[1], Patricia Pinto[1], Flávio Costa[1], Sofia Neves[2], Sara Braga[3], Tiago Meirinhos

[1]Rheumatology Department, ULS Gaia Espinho, Vila Nova de Gaia, Portugal, [2]Pulmonology Department, ULS Gaia Espinho, Vila Nova de Gaia, Portugal, [3]Laboratory Medicine Department, ULS Gaia Espinho, Vila Nova de Gaia, Portugal

Background. Antisynthetase syndrome (ASSD) is a heterogeneous autoimmune disease characterized by anti-aminoacyl tRNA synthetase (anti-ARS) antibodies and variable systemic involvement. Historically, classification relied on diverse clinical frameworks, including the Connors (2010) and Solomon (2011) criteria, leading to heterogeneity in cohort definitions and trial inclusion. In 2024, the Classification Criteria for Antisynthetase Syndrome (CLASS) project introduced consensus-based, data-driven criteria. This study aimed to describe the clinical and serological features of patients with ASSD and to assess agreement and domain overlap between the CLASS, Connors, and Solomon classification systems.

Methods. We retrospectively applied the CLASS, Connors and Solomon criteria to 20 patients with clinical ASSD followed at the Rheumatology and/or Pneumology departments of a tertiary care centre from 2015 until June 2025. Only patients classified as "definite" by CLASS were considered as fulfilling the classification for comparison purposes. Concordance between criteria was analysed using Cohen's kappa coefficient (κ) with 95% confidence intervals (CI).

Results. Most patients were female (65%, n=13), with a median age at diagnosis of 63 years (range 45–82) and a median diagnostic delay of 11.1 months (range 1.4–242.1). Anti-Jo1 was the most frequent antibody (75%), followed by PL-7 (20%) and PL-12 (5%). Interstitial lung disease (ILD) was present in 90% (n=18), inflammatory arthralgias in 65% (n=13), arthritis in 40% (n=8), mechanic's hands and Raynaud's phenomenon in 35% each (n=7), clinical myositis in 20% (n=4), and dysphagia in 20% (n=4). ILD was the sole manifestation in 25% (n=5). All patients met CLASS criteria (80% definite, 20% probable); 90% met Connors and 50% Solomon criteria. Agreement was slight between CLASS and Connors (κ=0.21; 95% CI –0.28–0.70) and between CLASS and Solomon (κ=0.17; 95% CI –0.31–0.65), and substantial between Connors and Solomon (κ=0.74; 95% CI 0.39–1.00). Discordant cases included one patient lacking the mandatory laboratory criterion for Connors and Solomon and another with isolated myositis. Nine CLASS-only cases presented with isolated ILD or limited extra-pulmonary involvement, insufficient to meet Solomon requirements.

Conclusions. All patients fulfilled CLASS criteria, whereas Connors and Solomon identified narrower subsets. CLASS, by integrating weighted domains, included ILD-predominant and isolated myositis phenotypes that binary frameworks excluded. The main sources of discordance were absence of the mandatory laboratory criterion and limited domain combinations in older definitions. The small, single-centre design and retrospective nature limit generalisability, but findings underscore the need for multicentre validation of CLASS in real-world settings.

Key words: antisynthetase syndrome, classification criteria, agreement, inflammatory myositis

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THE CLINICAL CONCORDANCE OF ANTI-SAE1 ANTIBODIES TESTED WITH LINE IMMUNOBLOT ASSAY TECHNIQUES

Michelle Lin[1,2], Lauren Hender[3], Dimitra Beroukas[3], Thomas Khoo[4,5,6], Vidya Limaye[5,6], Syed Ali[1,2,6]

[1]Department of Clinical Immunology & Allergy, Flinders Medical Centre, Bedford Park, Australia, [2]School of Medicine and Public Health, Flinders University, Bedford Park, Australia, [3]Department of Immunopathology, SA Pathology, Flinders Medical Centre, Bedford Park, Australia, [4]Department of Rheumatology, Flinders Medical Centre, Bedford Park, Australia, [5]Department of Rheumatology, Royal Adelaide Hospital, Adelaide, Australia, [6]School of Medicine and Biomedical Sciences, University of Adelaide, Adelaide, Australia

Background. Autoantibodies against small ubiquitin-like modifier activating enzyme-1 (SAE1) are rare and associated with dermatomyositis (DM). Detection of anti-SAE1 antibodies in clinical diagnostic laboratories in Australia is performed using the myositis immunoblot (MIB) (Euroimmun EUROLINE Autoimmune Inflammatory Myopathies 16 Ag IgG, Lubeck, Germany). Although immunoprecipitation is recognised as the gold-standard for antibody detection, it is labour intensive and time-consuming. The MIB, however, can be fraught with false positive results. This study aimed to evaluate the clinical concordance of positive anti-SAE1 results, using the MIB, in a South Australian context.

Methods. The clinical concordance of positive anti-SAE1 antibodies detected between July 2015 and July 2025 in a tertiary referral immunopathology laboratory was retrospectively assessed.

Quantitative measurement of MIB signal intensity (SI) was categorised: weak positive (+: 15-35 units), moderate positive (++: 36-70 units), and strong positive (+++: 71-255 units). For each patient with a positive anti-SAE1, the electronic medical records were reviewed for clinical, laboratory, radiological and histopathological features supportive of a diagnosis of DM, to assess if the anti-SAE1 antibody was a clinically concordant (true positive) result.

Results. Of 12,235 samples tested, 194 samples from 161 patients were positive for anti-SAE1 antibody. 139/161 patients with complete data were

included in the analysis. A positive anti-SAE1 result was determined to be clinically concordant in only 9/139 (6.5%) patients. Patients with a clinically concordant anti-SAE1 result had higher median MIB SI compared with those who were discordant: +++ (87.4±46.7 units) *vs*. + (22.9±11.7 units) ($p<0.05$). Multiple concurrent myositis-specific antibodies were frequently present in both clinically concordant (55%, n=5) and discordant (69%, n=92) groups.
All patients with anti-SAE1 DM had cutaneous features: Gottron's papules (7/9, 78%), periungual erythema (6/9, 67%) and heliotrope rash (5/9, 56%). Proximal muscle weakness and dysphagia were present in two patients. One patient had synchronous renal cell carcinoma and interstitial lung disease (ILD).
Conclusions. Overall, anti-SAE1 testing using MIB showed low clinical concordance with a diagnosis of DM; a positive result should be interpreted with the appropriate clinical context, taking into consideration the pre-test probability of DM. Higher semi-quantitative SI is associated with a greater likelihood of a clinically concordant result. Locally appropriate cut-offs need to be explored in larger, prospective studies. Longitudinal follow-up of patients with positive anti-SAE1 will determine whether this antibody predates clinical manifestations of disease.
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Key words: dermatomyositis, myositis immunoblot, myositis specific antibody, SAE1

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CLUSTER ANALYSIS IDENTIFIES ANTI-SYNTHETASE SYNDROME AS A DISTINCT AND HETEROGENEOUS CLINICAL ENTITY: ANALYSIS FROM THE CLASSIFICATION CRITERIA FOR ANTI-SYNTHETASE SYNDROME PROJECT DATABASE

Akira Yoshida[1], Iazsmin Bauer Ventura[2], Eduardo Dourado[3,4,5], Giovanni Zanframundo[6,7], Sara Faghihi-Kashani[8], Aravinthan Loganathan[9,10,11], Daphne Rivero Gallegos[12], Francisca Bozan[13], Gianluca Sambataro[14], Sangmee Sharon Bae[15], Laure Gallay[16], Albert Selva-O'Callaghan[17], Andrew Mammen[18,19], Carlo Scirè[20,21], Carlomaurizio Montecucco[6,7], Chester Oddis[8], David Fiorentino[22], Francesco Bonella[23], Frederick Miller[24], Ingrid Lundberg[25], Jens Schmidt[26,27], Jorge Rojas-Serrano[12], Marie Hudson[28], Masataka Kuwana[1], Miguel González-Gay[29,30], Neil McHugh[10], Tamera Corte[31], Tracy Doyle[32], Victoria Werth[33], Lorenzo Cavagna[6,7], Rohit Aggarwal[8]
[1]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [2]Section of Rheumatology, Department of Medicine, University of Chicago, Chicago, USA, [3]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal, [4]Aveiro Rheumatology Research Centre, Egas Moniz Health Alliance, Aveiro, Portugal, [5]Rheumatology Research Unit, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal, [6]Department of Internal Medicine and Therapeutic, Università di Pavia, Pavia, Italy, [7]Division of Rheumatology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [8]Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, USA, [9]Royal National Hospital for Rheumatic Diseases, Bath, UK, [10]Department of Life Sciences, University of Bath, Bath, UK, [11]Arthritis Australia, Broadway, Glebe, Australia, [12]Interstitial Lung Disease and Rheumatology Units, Instituto Nacional de Enfermedades Respiratorias Ismael Cosío Villegas, Mexico City, Mexico, [13]Section of Rheumatology, Department of Medicine, Hospital Clínico Universidad de Chile, Santiago, Chile, [14]Regional Referral Center for Rare Lung Disease, Policlinico "G. Rodolico-San Marco", University of Catania, Catania, Italy, [15]Division of Rheumatology, Department of Medicine, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, USA, [16]Department of Clinical Immunology, Hôpital Édouard Herriot, Lyon, France, [17]Systemic Autoimmune Diseases Unit, Internal Medicine Department, Vall d'Hebron University Hospital, Universitat Autònoma de Barcelona, Spain, [18]National Institute of Arthritis and Musculoskeletal and Skin Disorders, National Institutes of Health, Bethesda, USA, [19]Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, USA, [20]School of Medicine, University of Milano Bicocca, Milan, Italy, [21]Rheumatology Unit, IRCCS San Gerardo dei Tintori Foundation, Monza, Italy, [22]Department of Dermatology, Stanford University School of Medicine, Redwood City, USA, [23]Center for interstitial and rare lung diseases, Pneumology Department, Ruhrlandklinik University Hospital, University of Duisburg-Essen, Essen, Germany, [24]Environmental Autoimmunity Group, Clinical Research Branch, National Institute of Environmental Health Sciences, National Institutes of Health, Durham, USA, [25]Division of Rheumatology, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden, [26]Department of Neurology, Neuromuscular Center, University Medical Center Göttingen, Göttingen, Germany, [27]Department of Neurology and Pain Treatment, Neuromuscular Center, Center for Translational Medicine, Immanuel Klinik Rüdersdorf, University Hospital of the Brandenburg Medical School; Faculty of Health Sciences Brandenburg, Brandenburg Medical School Theodor Fontane, Rüdersdorf bei Berlin, Germany, [28]Division of Medicine, McGill University, Quebec, Canada, [29]Division of Rheumatology, IIS-Fundación Jiménez Díaz, Madrid, Spain, [30]Medicine and Psychiatry Department, University of Cantabria, Santander, Spain, [31]Department of Respiratory Medicine, Royal Prince Alfred Hospital, University of Sydney, Sydney, Australia, [32]Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital, Boston, USA, [33]Department of Dermatology, Perelman School of Medicine & Corporal Michael J. Crescenz Department of Veterans Affairs Medical Center, Philadelphia, USA

Background. Anti-synthetase syndrome (ASyS) is a rare systemic autoimmune rheumatic disease (SARD) with significant clinical heterogeneity. We performed unsupervised cluster analyses on clinical and serological data of patients registered to the international, multicentre Classification Criteria for Anti-Synthetase Syndrome (CLASS) project database, to better characterize the clinical phenotype and heterogeneity of ASyS.
Methods. The CLASS database comprised 2035 ASyS and 2140 controls with mimicking conditions, namely SARDs and/or interstitial lung disease (ILD), submitted from 103 centres worldwide (1). We applied a multiple correspondence analysis followed by hierarchical clustering to aggregate ASyS and controls in the entire CLASS cohort into distinct subgroups, using 19 clinical and serological variables. Next, we repeated the cluster analysis among ASyS cases only. Clinical characteristics and survival were compared between the identified clusters. As sensitivity analyses, we repeated the cluster analyses, excluding myositis-specific autoantibodies (MSAs) and myositis-associated autoantibodies (MAAs) from the variables used for clustering.
Results. Cluster analysis of the entire CLASS cohort identified three subgroups. While Cluster 1 (n=1135) included both ASyS and controls, Clusters 2 (n=475) included almost only controls, and Cluster 3 (n 184) mostly comprised ASyS. Controls in Cluster 1 were more likely to have anti-MDA5 or PM/Scl autoantibodies than in other clusters. Four clusters emerged in the analysis of ASyS only: Cluster 1 (anti-Jo-1-positive, "full-spectrum" ASyS with myositis, ILD, and arthritis; n=495), Cluster 2 (myositis without ILD; n=146), Cluster 3 (ILD-predominant; n=312), and Cluster 4 (anti-non-Jo-1-positive; n=193). Sensitivity analyses excluding MSA/MAAs from the variables for clustering also identified clusters with similar clinical characteristics. There was no significant difference in survival between the clusters.
Conclusions. Cluster analyses identified ASyS as a distinct and heterogeneous clinical entity. Patients with anti-MDA5-positive dermatomyositis or anti-PM/Scl-positive scleroderma-myositis overlap were highlighted as strong mimickers of ASyS. Four prominent clusters emerged among ASyS, with ILD-predominant being the second most common, underscoring the critical need for classification criteria that capture these patients with isolated ILD.
Acknowledgements. The authors wish to thank all the CLASS project investigators for their invaluable role in the data collection.
Key words: anti-synthetase syndrome, interstitial lung disease, cluster analysis

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SERUM MIRNA EXPRESSION PROFILING REVEALS DISTINCT REGULATORY NETWORKS AND POTENTIAL BIOMARKERS IN DERMATOMYOSITIS

Stefano Gastaldello[1], Yi Zhong[1,2,3], Cecilia Leijding[1], Kristofer M. Andreasson[4,5], Begum Horuluoglu[2,4], Angeles S. Galindo-Feria[2,4,6], Antonella Notarnicola[2,4,6], Maryam Dastmalchi[2,4,6], Volker M. Lauschke[1,2,7,8,9], Helene Alexanderson[4,5], Ingrid E. Lundberg[2,4,6], Daniel C. Andersson[1,10]
[1]Karolinska Institutet, Department of Physiology and Pharmacology, Stockholm, Sweden, [2]Center for Molecular Medicine, Karolinska Institutet, Solna, Stockholm, Sweden, [3]Pharmaceutical Informatics Institute, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou, China, [4]Karolinska Institutet, Department of Medicine, Solna, Division of Rheumatology, Stockholm, Sweden, [5]Karolinska University Hospital, Women's Health and Allied Health Professionals Theme, Medical Unit Allied Health Professionals, Stockholm, Sweden, [6]Karolinska University Hospital, Department of Gastro, Dermatology and Rheumatology, Theme Inflammation and Aging, Stockholm, Sweden, [7]Dr Margarete Fischer-Bosch Institute of Clinical Pharmacology, Stuttgart, Germany, [8]University of Tübingen, Tübingen, Germany, [9]Department of Pharmacy, the Second Xiangya Hospital, Central South University, Changsha, China, [10]Karolinska University Hospital, Heart, Vascular and Neurology Theme, Cardiology Unit, Stockholm, Sweden

Background. Myositis encompasses a heterogeneous group of autoimmune inflammatory muscle diseases marked by chronic muscle inflammation,

weakness, and tissue injury. Dermatomyositis (DM), a major subtype, combines muscle involvement with characteristic cutaneous manifestations and immune activation. Although the immunopathogenesis of DM has been increasingly elucidated, molecular biomarkers and targeted therapies remain limited. MicroRNAs (miRNAs), key regulators of post-transcriptional gene expression, have emerged as crucial players in immune regulation and autoimmunity. This study aimed to identify circulating miRNA signatures in dermatomyositis and explore their potential regulatory relationships with mRNA expression patterns.

Methods. Serum samples from healthy donors (n=2) and dermatomyositis patients (n=5) were analyzed. Total miRNA was extracted using the miRNeasy Serum/Plasma Kit, and miRNA expression profiling was performed by Illumina NovaSeq sequencing. Both hairpin and mature miRNAs were quantified. Differential expression analysis identified significantly dysregulated miRNAs between DM and controls. Target mRNAs were predicted using miRDB and integrated with matched mRNA sequencing data. Overlapping targets were subjected to network and enrichment analyses, including topology-based analysis and Gene Set Enrichment Analysis (GSEA).

Results. Distinct profiles of upregulated and downregulated miRNAs were observed in DM serum compared with healthy controls. Several miRNAs were consistently dysregulated across both hairpin and mature datasets, indicating robust disease-associated changes. Integration with mRNA data revealed inversely correlated miRNA-mRNA pairs, suggesting functional regulatory relationships. Network and enrichment analyses identified two key subnetworks: upregulated miRNAs linked to immune activation and inflammatory pathways, and downregulated miRNAs associated with muscle differentiation, mitochondrial function, and cellular metabolism. GSEA confirmed enrichment of autoimmune-related pathways consistent with dermatomyositis pathology.

Conclusions. This study reveals a distinct serum miRNA signature in dermatomyositis and highlights key regulatory networks involved in immune and muscle dysfunction. The identified miRNAs may serve as potential circulating biomarkers for diagnosis or disease monitoring. Validation in larger cohorts is ongoing to confirm these findings and to clarify the mechanistic roles of dysregulated miRNAs in dermatomyositis.

Key words: dermatomyositis, microRNA biomarkers, autoimmune myositis, gene expression regulation, miRNA-mRNA network analysis

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RECLAIM-PM: A RETROSPECTIVE RECLASSIFICATION OF PATIENTS DIAGNOSED AS POLYMYOSITIS USING CONTEMPORARY CLINICO-SERO-PATHOLOGICAL CRITERIA

Julian Sehne[1,2], Tobias Ruck[1,2,4], Anne-Katrin Güttsches[1,2], Christopher Nelke[1,2,4], Werner Stenzel[5], Karsten Krause[1,2], Felix Kleefeld[1,2,3]

[1]Ruhr University Bochum, BG University Hospital Bergmannsheil, Department of Neurology, Bochum, Germany, [2]BG University Hospital Bergmannsheil, Heimer Institute for Muscle Research, Bochum, Germany, [3]Charité-Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt Universität zu Berlin, and Berlin Institute of Health (BIH), Department of Neurology, Berlin, Germany, [4]Department of Neurology, Medical Faculty and University Hospital Düsseldorf, Heinrich Heine University Düsseldorf, Düsseldorf, Germany, [5]Charité-Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt- Universität zu Berlin, and Berlin Institute of Health (BIH), Department of Neuropathology, Berlin, Germany

Background. Since their introduction in 1975 by Bohan and Peter, the terms polymyositis (PM) and dermatomyositis (DM) have long served as key categories in the diagnosis and classification of idiopathic inflammatory myopathies (IIM). However, at the time these definitions were proposed, diagnostic tools such as standardized myositis-specific antibody testing and advanced histopathological techniques were not yet available. The dichotomy PM and DM therefore lacks the resolution and specificity now considered essential in myositis diagnostic.

Over recent decades, a number of clinically and pathologically distinct entities – such as inclusion body myositis (IBM), immune-mediated necrotizing myopathy (IMNM), antisynthetase syndrome (ASyS), and overlap myositis (OM) – have been defined using a combined clinico-serological-histological approach. Retrospective studies suggest that a significant proportion of patients diagnosed with PM would now be classified under different disease categories. The aim of this project is to systematically re-evaluate all archived muscle biopsies originally diagnosed as PM at the University Hospital Bergmannsheil in Bochum and reclassify these cases based on current clinico-sero-pathological standards.

Methods. We performed a retrospective cohort study including all muscle biopsies diagnosed with PM between 1997 and 2025 at our institution. Each case was reviewed, taking into account histopathology, immunohistochemistry including state-of-the-art stainings (*e.g.* CD8, CD45, CD56, CD68, MHC class I, MHC class II, SQSTM1/p62 and KLRG-1), and, where available, associated clinical, genetic and serological data. All biopsies were re-evaluated by experienced neuromuscular pathologists, and a consensus process involving independent review was used.

All data were analyzed both qualitatively and quantitatively to 1) establish a diagnosis based on current classification criteria, and 2) identify patterns of misclassification.

Results. We identified 50 cases of "PM" in our cohort that were re-assessed based on current diagnostic criteria for IIM. Using these state-of-the-art criteria, the majority of "PM" cases was reclassified, with a high proportion of IBM diagnoses. Other common diagnoses after reclassification included OM and ASyS. Of note, only a minority of "PM" diagnosis were maintained after re-assessment of biopsies, and taking into account clinical, and serological data.

Conclusions. Our data indicate that most patients that received the diagnosis "PM" can be reclassified using a clinico-serological-pathological approach, with important implications for therapy and prognosis

Key words: inflammatory myopathy, muscle biopsy, polymyositis

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DISTINCT THIGH MUSCLE MRI PATTERNS ACROSS IDIOPATHIC INFLAMMATORY MYOPATHY SUBTYPES: A SINGLE-CENTER COHORT ANALYSIS

Heejae Jung[1,2], Heung-Won Kang[3], Ho Cheol Kim[4], Seokchan Hong[5], Young Chul Kim[6], Won Kim[7], Eun-Jae Lee[1], Young-Min Lim[1], Jin-Sung Park[8], Hyunjin Kim[1]

[1]Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, [2]Department of Neurology, Seoul Medical Center, Seoul, Republic of Korea, [3]Department of Medical Science, Asan Medical Institute of Convergence Science and Technology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, [4]Department of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, [5]Division of Rheumatology, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Seoul, Republic of Korea, [6]Department of Plastic and Reconstructive Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, [7]Department of Rehabilitation Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, [8]Department of Neurology, School of Medicine, Kyungpook National University, Kyungpook National University Chilgok Hospita, Daegu, Republic of Korea

Background. Idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of autoimmune muscle diseases, and their overlapping clinical phenotypes often complicate subtype differentiation. Muscle magnetic resonance imaging (MRI) is increasingly recognized as a valuable non-invasive diagnostic tool, yet direct comparative analyses across major IIM subtypes remain limited. We aimed to characterize and contrast thigh MRI patterns among anti-synthetase syndrome (ASyS), dermatomyositis (DM), inclusion body myositis (IBM), and immune-mediated necrotizing myopathy (IMNM).

Methods. This prospective single-center cohort included 47 patients with IIM (12 ASyS, 15 DM, 11 IBM, 9 IMNM). Thigh MRI (T1-weighted and STIR) was systematically evaluated. Muscle edema was semi-quantitatively graded across the gluteal, hamstring, quadriceps, and adductor compartments (0–3 per compartment; total edema score 0–12). Fatty infiltration was recorded dichotomously, and fascial and subcutaneous involvement were assessed. Group comparisons were performed using non-parametric statistical tests.

Results. Distinct MRI signatures were observed across IIM subtypes. ASyS and DM demonstrated significantly greater edema, particularly in the quadriceps and gluteal compartments, compared to IMNM (quadriceps: ASyS *vs*. IMNM, 2.0 *vs*. 0.0, p=0.033; DM vs. IMNM, 2.0 *vs*. 0.0, p=0.023, gluteal: ASyS *vs*. IMNM, 3.5 *vs*. 1.0, p=0.003; DM *vs*. IMNM, 2.0 *vs*. 1.0, p=0.007). In contrast, IBM showed markedly higher rates of quadriceps fatty infiltration (90.9%) compared with IMNM (22.2%, p=0.008) and ASyS (41.7%, p=0.027). Fascial involvement further differentiated subtypes: hamstring fascial edema was most frequent in ASyS (75.0%), followed by DM (33.3%), whereas it was uncommon in IMNM (11.1%, p=0.008) and absent in IBM (0%, p<0.001). This gradient pattern of fascial inflammation (ASyS > DM >> IMNM/IBM) served as an additional discriminator beyond muscle edema and fatty infiltration.

Conclusions. Thigh MRI reveals subtype-specific patterns of muscle and soft tissue involvement in IIMs. These distinct radiological profiles – particularly severe anterior/gluteal edema in ASyS and DM and prominent quadriceps fatty infiltration in IBM – provide clinically useful, non-invasive markers that may enhance differential diagnosis in routine practice.

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Key words: idiopathic inflammatory myopathy

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SPECTRUM AND PROGNOSIS OF ANTI-SMN ANTIBODY-POSITIVE PATIENTS: A RETROSPECTIVE COHORT STUDY AND SYSTEMATIC REVIEW OF THE LITERATURE

Adèle Carré[1], Laurent Drouot[2*], Jean-Luc Charuel[3*], Sami Tayb-Boulahfa[4], Pascale Daniel[5], Valentin Pillot[5], Olivier Boyer[2], Pascale Ghillani[3], Makoto Miraya[3], Fabienne Jouen[2], Kathy Khoy[6], Marie Limare[2], Noémie Abisror[7], Zahir Amoura[8], Fleur Cohen-Aubart[8,9], Bruno Fautrel[10], Antoine Froissart[11], Julien Haroche[8], Miguel Hié[8], Raphaël Lhote[8], Olivier Lidove[12], Alexis Mathian[8], Edouard Pertuiset[13], Sébastien Rivière[7], Céline Roussin[14], Benjamin Rossi[15], Benjamin Terrier[16], Hugo Toth[12], Yurdagul Uzuhan[17], Isabelle Brocheriou-Spelle[18], Achille Aouba[1], Teresinha Evangelista[19], Sarah Léonard-Louis[19], Anael Dumont[1†], Olivier Benveniste[4,5†], Yves Allenbach[4,5]

[1]Department of Internal Medicine and Clinical Immunology, Caen Normandie University Hospital, Caen, France, [2]Rouen Normandie University, INSERM, PANTHER UMR 1234, Mont-Saint-Aignan, France, [3]Department of Immunology, Pitié-Salpêtrière Hospital, Assistance Publique - Hôpitaux de Paris, Sorbonne University, Paris, France, [4]INSERM MRSU 974, Research Center in Myology, Sorbonne University, Paris, France, [5]Department of Internal Medicine and Clinical Immunology, Referral Center for Rare Neuromuscular Disorders, Pitié-Salpêtrière Hospital, Assistance Publique - Hôpitaux de Paris, Sorbonne University, Paris, France, [6]Laboratory of Immunology, Caen Normandie University Hospital, Caen, France, [7]Department of Internal Medicine, Saint-Antoine Hospital, Assistance Publique - Hôpitaux de Paris, Sorbonne University, Paris, France, [8]Department of Internal Medicine (Médecine interne 2), Referral Center for Rare Autoimmune Diseases of Ile-de-France, Centre and Martinique, Institut E3M, Centre d'Immunologie et des Maladies Infectieuses (CIMI-Paris), Pitié-Salpêtrière Hospital, Assistance Publique - Hôpitaux de Paris (APHP), INSERM, Paris, France, [9]Centre National de la Recherche Scientifique, Paris, France, [10]Department of Rheumatology, Pitié-Salpêtrière Hospital, Assistance Publique - Hôpitaux de Paris, Sorbonne University, Paris, France, [11]Department of Internal Medicine, Créteil Intercommunal Hospital, Créteil, France, [12]Department of Internal Medicine, Diaconesses-Croix Saint Simon Hospital, Paris, France, [13]Department of Rheumatology, Pontoise Hospital - Nord-Ouest Val d'Oise Hospital Group, Pontoise, France, [14]Department of Internal Medicine, Ouest-Réunion Hospital, Saint-Paul, La Réunion, France, [15]Department of Internal Medicine and Infectious Diseases, Robert Ballanger Hospital, Grand Paris Nord-Est Hospital Group, Aulnay-Sous-Bois, France, [16]Department of Internal Medicine, Cochin Hospital, Assistance Publique - Hôpitaux de Paris, Paris Cité University, Paris, France, [17]Department of Pneumology, Avicenne Hospital, Assistance Publique - Hôpitaux de Paris, Sorbonne University, Bobigny, France, [18]Pathology Department, UMRS 1155, Pitié-Salpêtrière Hospital, Assistance Publique - Hôpitaux de Paris, Sorbonne University, Paris, France, [19]Department of Neuropathology, Pitié-Salpêtrière Hospital, Assistance Publique - Hôpitaux de Paris, Sorbonne University, Paris, France

Background. Autoantibodies to the survival of motor neuron (SMN) complex are described since 2011 in myositis, scleromyositis and mixed connective tissue disease. They are associated with a particular fluorescence aspect on anti-nuclear antibodies (ANA) screening, but lack routine testing, limiting reported cases. This work aimed to better characterize their associated phenotype and prognosis.

Methods. This retrospective comparative cohort study included anti-SMN–positive patients, anti-SMN–negative controls, and data from a systematic literature review. Anti-SMN positivity was suggested by the characteristic indirect immunofluorescence pattern observed upon ANA testing, and was subsequently confirmed using a specific immunoassay (ALBIA, Addressable Laser Bead ImmunoAssay). Clinical features and outcomes were compared with published cases and with control cohorts of systemic sclerosis and inflammatory myopathies.

Results. Positivity of anti-SMN autoantibodies was confirmed for all 56 patients with a suggestive fluorescence pattern (100%). In this cohort, median age was 41 years [35-53], and 87% were women. Musculoskeletal involvement predominated (joint manifestations: 74%; myositis: 82%), with muscle biopsies showing endo-and perimysial inflammatory infiltrates and myonecrosis. Cutaneous vasculopathy was common (Raynaud phenomenon: 92%; fingertip ulcers or scars: 30%; digital necrosis: 11%), while skin sclerosis occurred in 42% of cases. Digestive involvement was frequent, affecting both upper (esophageal dysfunction: 90%; gastroparesis: 18%) and lower tracts (chronic intestinal pseudo-obstruction: 9%). Interstitial lung disease occurred in 54% of patients, generally moderately severe, and myocarditis in 20%. According to existing criteria, patients could be classified as inflammatory myopathy (63%), systemic sclerosis (46%), systemic lupus (41%), or Sjögren's syndrome (21%), over half (54%) met criteria for at least two of these conditions simultaneously. Our findings were consistent with the 114 previously reported cases, except for a lower rate of pulmonary hypertension. Compared with anti-SMN–negative controls (systemic sclerosis: n=75, including 35 with and 40 without myositis; inflammatory myopathies: n=239, including 100 anti-synthetase syndromes, 69 dermatomyositis, and 70 necrotizing myopathies), the anti-SMN group was younger, more often female, and had more frequent puffy fingers (40%), but milder and less extensive skin sclerosis compared to systemic sclerosis. Esophageal motor dysfunction was also more frequent. Myositis was not more severe than in the other groups. Four disease-related deaths occurred during follow-up, resulting from myocarditis and diaphragmatic failure or severe digestive complications.

Conclusions. Anti-SMN autoantibodies may define a distinct autoimmune musculoskeletal condition, whose prognosis depends on the severity of diaphragmatic and/or cardiac involvement, as well as the extent of extra-musculoskeletal manifestations.

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COMPARISON OF RULE-BASED ALGORITHMS TO THE 2017 EULAR/ACR CLASSIFICATION CRITERIA TO IDENTIFY PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES IN ELECTRONIC HEALTH RECORDS

Ana Valle[1], Amy Vo, Rochelle L. Castillo, Yumeko Kawano, Leah M. Santacroce, Daniel H. Solomon, Katherine P. Liao, Candace H. Feldman

[1]Brigham And Women's Hospital, Boston, USA

Background. Idiopathic inflammatory myopathies (IIM) are understudied due to the need for larger cohort sizes to study risk factors and outcomes. Electronic health record (EHR) data provides an opportunity to establish larger cohorts. The objective of this study was to determine the performance of published ICD code rule-based algorithms with EHR data.

Methods. We identified 8 previously published ICD code rule-based algorithms from the literature for multiple IIM subtypes. Some algorithms required mapping from ICD 9 to 10 codes; some were excluded due to interstitial lung disease and non-specific ICD codes (M60.8: Other Myositis, M60.9: Myositis, Unspecified). We identified patients seen at Mass General Brigham with >1 ICD 9/10 codes for IIM (359.7*, 710.3, 710.4, G72.4*, M33.*, M36.*) from 1/1/2000 - 9/6/2024. From this cohort, a random sample of 250 cases were selected for review. Patients were classified by chart review based on the 2017 EULAR/ACR IIM Classification Criteria with probable and definite cases considered to be true IIM. Cases were subcategorized as dermatomyositis (DM), polymyositis (PM), or inclusion body myositis (IBM). Chart review was performed by two reviewers and adjudicated by a third. Positive predictive value (PPV), specificity, sensitivity, negative predictive value (NPV) were calculated.

Results. Of 250 charts, 87 definite (47 DM, 22 IBM, 18 PM) and 28 probable (18 PM, 6 DM, 4 IBM) cases were identified (overall prevalence 46%). The highest PPV (84%) and specificity (98%) were obtained by using >2 ICD codes during hospitalization. This algorithm had a low sensitivity (14%). The algorithm of >2 ICD codes from clinic visits <2 months apart had the second highest PPV (79%), improved sensitivity (61%), and accuracy of 57%. The algorithm of >2 ICD codes between 30-365 days had a slightly lower PPV (78%) but improved accuracy (62%) and sensitivity (68%). The following algorithms had lower PPVs: 1) >1 ICD code billed by a rheumatologist, 2) >1 ICD code billed by a rheumatologist, dermatologist, or neurologist, 3) >1 ICD codes during hospitalization, 4) primary ICD code during hospitalization, 5) >2 ICD codes during hospitalization, 6) >3 ICD codes at any time regardless of setting.

Conclusions. This is the first evaluation of previously published rule-based algorithms for IIM in a US-based EHR. ICD code rule-based algorithms had PPVs ranging from 64-84% with variable sensitivity (14-77%). Limitations include modifications to adapt for use with EHR data. Future algorithms may benefit from incorporating additional EHR textual data and machine learning methods.
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Key words: algorithm, identification, myositis

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IMMUNE-MEDIATED NECROTIZING MYOPATHY IN THE PORTUGUESE POPULATION – A MULTICENTRIC NATIONWIDE STUDY

Anita Cunha[1], Maria Pontes Ferreira[1], Carolina Vilafanha[2], Bárbara Fernandes Esteves[3], João Oliveira[4], Raquel Campanilho-Marques[5,6,7,8], Ana Valido[9], Ana Teresa Melo[10], Ana Catarina Moniz[11], Daniel Melim[12], Eduardo Dourado[2], Filipa Teixeira[1], José Tavares-Costa[1], Francisca Guimarães[1]
[1]Rheumatology Department, Unidade Local de Saúde do Alto Minho, Ponte de Lima, Portugal, [2]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal, [3]Rheumatology Department, Unidade Local de Saúde de São João, Porto, Portugal, [4]Rheumatology Department, Unidade Local de Saúde de Coimbra, Coimbra, Portugal, [5]Rheumatology Department, Unidade Local de Saúde de Santa Maria, Lisboa, Portugal, [6]Pediatric Rheumatology Unit, Rheumatology and Paediatric Department, Centro Hospitalar Universitário Lisboa Norte (CHULN), Centro Académico de Medicina de Lisboa (CAML), Lisboa, Portugal, [7]Rheumatology Department, Centro Hospitalar Universitário Lisboa Norte (CHULN), Centro Académico de Medicina de Lisboa (CAML), Lisboa, Portugal,[8]Rheumatology Research Unit, Instituto de Medicina Molecular (iMM), Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa (CAML), Lisboa, Portugal, [9]Rheumatology Department, Unidade Local de Saúde do Litoral Alentejano, Santiago do Cacém, Portugal, [10]Rheumatology Department, Unidade Local de Saúde São José, Lisboa, Portugal, [11]Rheumatology Department, Centro Hospitalar de Lisboa Ocidental, Lisboa, Portugal, [12]Rheumatology Department, Hospital Dr. Nélio Mendonça, Funchal, Portugal

Background. Immune-mediated necrotizing myopathy (IMNM) is a rare idiopathic inflammatory myopathy (IIM) characterized by proximal muscle weakness and markedly elevated creatine kinase (CK). Three serological subgroups are recognized: anti-signal recognition particle (SRP), anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR), and seronegative IMNM. Geographic heterogeneity is common in IIMs, and epidemiological and clinical data about Portuguese patients were limited.
Objectives. To characterize the IMNM cohort of the Rheumatic Diseases Portuguese Registry (Reuma.pt/Myositis).
Methods. Multicentric, cross-sectional study including adult patients with IMNM diagnosis, as determined by their attending rheumatologist, registered in Reuma.pt/Myositis. Data were analyzed using SPSS v. 28.
Results. A total of 30 patients were included. Median age at onset was 59 years (IQR 21), 70% were females, and 88% Caucasian. Most patients (97%) presented with subacute or insidious symmetric proximal weakness, and median CK at diagnosis was 8357 U/L. Extra-muscular involvement included dysphagia (37%), Raynaud phenomenon (35%), cardiac (17.9%) and pulmonary manifestations (21.4%). Autoantibody subgroups included 11 anti-HMGCR, 10 anti-SRP, and 5 seronegative patients. Previous statin use was reported in 7 of 11 anti-HMGCR–positive patients. Muscle biopsy revealed myofiber necrosis with sparse inflammatory infiltrate in 90% of the patients. Electromyography and magnetic resonance imaging showed myopathic changes in most cases. Treatment included glucocorticoids (80%), IVIG (50%), rituximab (43%), and at least one conventional immunosuppressant (66.6%). Malignancy was uncommon (6.7%). Subgroup differences were significant for age at diagnosis and disease onset – anti-HMGCR-positive patients were older than anti-SRP (p=0.011 and p=0.05, respectively) – and for sex, with a female predominance in the SRP subgroup (p=0.012). Methotrexate use was more common in HMGCR than seronegative patients (p=0.036).
Conclusions. Typical IMNM findings in our cohort included subacute or insidious onset, symmetric proximal weakness, elevated CK, and biopsy evidence of myofiber necrosis with minimal inflammation. Subgroup differences mirror prior reports: anti-HMGCR–positive patients were older, whereas anti-SRP-positive patients were predominantly female. Most anti-SRP patients received glucocorticoids, intravenous immunoglobulin, and rituximab, reflecting a more aggressive treatment course. Overall, IMNM shows a heterogeneous but distinct profile within IIMs, with serological subgroups differing in demographics, clinical features, and treatment patterns. This nationwide characterization provides a foundation for prospective studies and inter-center collaboration in this rare disorder.
Key words: idiopathic inflammatory myopathy, immune-mediated necrotizing myopathy

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INCIDENCE AND CHARACTERISTICS OF ANTISYNTHETASE SYNDROME: A QUADRUPLE-SOURCE CAPTURE-RECAPTURE SURVEY USING THE AMERICAN COLLEGE OF RHEUMATOLOGY/EUROPEAN LEAGUE AGAINST RHEUMA-TISM CLASSIFICATION CRITERIA

Margherita Giannini[1,2,3], Léa Debrut[3,4], Benoît Nespola[5], Jean-Baptiste Chanson[6], Aleksandra Nadaj Pakleza[6], Béatrice Lannes[7], Klein Delphine[8], Michel Velten[8], Jean Sibilia[2,9], Bernard Geny[1,3], Alain Meyer[1,2,3,9]
[1]Service de Physiologie et Explorations Fonctionnelles, University Hospital of Strasbourg, Strasbourg, France, [2]Centre de Référence des Maladies Autoimmunes Rares, University Hospital of Strasbourg, Strasbourg, France, [3]Unité de Recherche 3072 (UR3072), Centre de Recherche en Biomédecine, University of Strasbourg, [4]Faculty of Sport Sciences, European Centre for Education, Research and Innovation in Exercise Physiology (CEERIPE), University of Strasbourg, Strasbourg, France, [5]Laboratoire d'Immunologie, Plateau Technique de Biologie, Strasbourg University Hospital, Strasbourg, France, [6]Service de Neurologie, Centre de Référence des Maladies Neuromusculaires NEIdF, ERN EURO-NMD, Strasbourg University Hospitals, Strasbourg, France, [7]Département d'Anatomopathologie, Strasbourg University Hospitals, Strasbourg, France, [8]INSERM UMR-S1113, Registre des Cancers du Bas-Rhin, Fédération de Médecine Translationnelle, University of Strasbourg, Strasbourg, France, [9]Rheumatology Department, Strasbourg University Hospitals, Strasbourg, France

Background. The ACR/EULAR criteria for antisynthetase syndrome (ASyS) have been recently developed (1). The ASyS incidence using these criteria has never been studied in a population-based cohort. Alsace (a region in Eastern France) hosts specialized centers for autoimmune, neuromuscular, and interstitial lung diseases (ILD). Universal health coverage and full reimbursement for ASyS make it an ideal setting for epidemiologic research (2, 3). This study aimed to determine the ASyS incidence in Eastern France using the ACR/EULAR ASyS criteria and to compare their performance with the 2017 EULAR/ACR inflammatory myopathies (IM) criteria.
Methods. The study covered 2006–2012, during which the IM incidence according to the 2017 EULAR/ACR criteria had been established (2). Potential ASyS cases were identified from general practitioners and community specialists, public and private hospital records, laboratory databases, pathology archives. For all potential cases, data were extracted using a standardized form after manual review of medical records. Incident cases (diagnosed between January 1, 2006, and January 1, 2013, among Alsace residents), meeting at least "possible ASyS" ACR/EULAR criteria were included. Incomplete case ascertainment across the four sources was adjusted using a capture–recapture analysis.
Results. Among 1742 potential ASyS cases identified, after excluding patients who did not meet IM or ASyS criteria (n=1030), those living outside Alsace (n=284), and those with incident IM before the study period (n=308), 28 patients were diagnosed with ASyS between 2006 and 2012 (definite=21, probable=2, possible=5).
The estimated number of cases missed by any source was 3.2 after capture-recapture analysis. Estimated incidence was 2.11 cases/million inhabitants/year (95% CI 1.37–2.85). Most patients were female (75.9%) with a median age of 57.5 years (IQR 41.8–69.5). Twenty-one patients tested positive for anti-Jo-1, 6 for anti-PL12, 2 for anti-PL7. At the last follow-up, only 8/26 patients (30.8%) showed the complete clinical triad. ILD and arthritis were isolated triad features in 5/25 (20%) and 5/27 (18.5%) patients, respectively. Myositis was always associated with arthritis in 2/14 (14.3%) or ILD in 4/15 (26.7%) patients. Only 15 of the ASyS patients (53.6%) also met the 2017 EULAR/ACR IM criteria (definite: n=9; probable: n=5; polymyositis: n=11, dermatomyositis: n=3).
Conclusions. This population-based study provides a reliable estimate of ASyS incidence and highlights the high frequency of ILD and arthritis. Half of the cases were missed by the 2017 EULAR/ACR IM criteria, emphasizing the improvement enabled by the ACR/EULAR ASyS criteria.

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THE SPECTRUM OF NON-SPECIFIC AND OVERLAP MYOSITIS: CLINICO-SERO-PATHOLOGICAL CHARACTERISTICS

Lung Jeung[1], Sanne Evers[1], Ocan Cakir[1], Ester M. M. van Leeuwen[2], Pedro Coelho[3], Sander W. Tas[4], Marianne de Visser[1], Anneke J. van der Kooi[1], Eleonora Aronica[5], Joost Raaphorst[1]

[1]Department of Neurology, AmsterdamUMC, Amsterdam, The Netherlands, [2]Department of Laboratory Medicine, AmsterdamUMC, Amsterdam, The Netherlands, [3]Serviço de Neurologia, Hospital de Santa Maria, Lisboa, Portugal, [4]Department of Rheumatology & Clinical Immunology, AmsterdamUMC, Amsterdam, The Netherlands, [5]Department of (Neuro)Pathology, AmsterdamUMC, Amsterdam, The Netherlands

Background. Non-specific myositis (NSM) and overlap myositis (OM) are frequent but poorly defined subgroups within idiopathic inflammatory myopathies (IIM). The lack of standardized classification criteria challenges diagnosis. We compared clinical, serological, and muscle pathology features of NSM and OM to identify commonalities and differences.

Methods. We retrospectively reviewed patients diagnosed with OM or NSM between 2009-2023. Diagnosis was based on proximal weakness, muscle biopsy findings, and serological testing of autoantibodies. Biopsies could show isolated features associated with specific IIM subtypes but not in a pattern diagnostic of dermatomyositis, antisynthetase syndrome, inclusion body myositis, or immune-mediated necrotizing myopathy. Serology was required to be negative for myositis-specific autoantibodies (MSAs). Connective tissue disease (CTD) diagnoses were based on American College of Rheumatology criteria. Patients were categorized as definite OM (concomitant CTD), probable OM (CTD features and/or myositis-associated autoantibodies (MAAs) without fulfilling CTD criteria), or NSM (no CTD features). Clinical features (muscle weakness, myalgia, dysphagia, arthritis/arthralgia, Raynaud's phenomenon, interstitial lung disease, myocarditis, and skin abnormalities), serology (MAA) and serum creatine kinase levels), and semi-quantified muscle biopsy parameters were compared.

Group differences were evaluated using one-way ANOVA with Bonferroni adjustment ($p<0.008$) and Chi-Square testing.

Results. Forty-six patients (mean age 50.4±14.6 years; 73.9% female; mean follow-up 35.6±31.3 months) were included: 20 definite OM (43.5%), 20 probable OM (43.5%), and 6 NSM (13.0%). Muscular and extra-muscular manifestations did not differ significantly between groups. MAAs were present in 8/20 (40%) definite OM and 12/20 (60%) probable OM. Out of 19 histopathological parameters, necrotic muscle fibres were more frequent in definite OM (17/20; 85%) and probable OM (20/20; 100%) as compared to NSM (3/6; 50%) ($p=0.006$ after correction). For two probable OM and one definite OM frozen tissue was unavailable for immunohistochemical evaluation. Perimysial alkaline phosphatase staining and fragmentation was present in five definite OM patients (5/19; 26.3%) and five probable OM patients (2/18; 27.8%) and none of the NSM patients ($p=0.063$).

During follow-up, 5/20 (25%) patients with probable OM developed definite OM (median 12 months); none of the NSM patients developed CTD.

Conclusions. OM represents a clinico-sero-pathological spectrum, ranging from definitive CTD to only CTD features. Compared with NSM, OM shows, alongside many clinical and histopathological similarities; a higher frequencies of muscle fibre necrosis and possibly, perimysial pathology, though this requires confirmation in larger cohorts.

Key words: overlap myositis, non-specific myositis

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CLINICAL SIGNIFICANCE OF ANTI-SYNTHETASE ANTIBODIES IN PATIENTS WITH RHEUMATOID ARTHRITIS OR UNDIFFERENTIATED ARTHRITIS: PRE-LIMINARY DATA FROM A MONOCENTRIC COHORT

Alberto Paladini[1], Emanuele Filippini[2], Fernanda Paolucci[2], Martina Principi[2], Victoria Bitca[2], Claudia Buongarzone[2], Gianluca Moroncini[1,2]

[1]Clinica Medica, Department of Clinical and Molecular Sciences, Marche Polytechnic University, Ancona, Italy, [2]Internal Medicine Residency Program, Marche Polytechnic University, Marche Polytechnic University, Ancona, Italy

Background. Anti-synthetase syndrome (ASyS) is a rare autoimmune disease characterized by the presence of specific autoantibodies directed against aminoacyl-tRNA synthetases. Its clinical presentation is highly heterogeneous and may include myopathy, interstitial lung disease (ILD), arthritis, Raynaud's phenomenon, fever, and mechanic's hands. These features may vary considerably in severity and combination.

The EULAR/ACR CLASS project aims to propose classification criteria for ASyS and the results have recently been anticipated.

Objectives. To explore the prevalence of anti-synthetase antibodies and the clinical characteristics of patients with rheumatoid arthritis (RA) or undifferentiated arthritis presenting extra-articular or serological features suggestive of ASyS.

Methods. In light of the early EULAR/ACR CLASS results (1), we analysed a cohort of patients with arthritis followed in an outpatient setting, selecting a subgroup according to the following criteria:

1. Confirmed diagnosis of RA based on 2010 ACR/EULAR criteria, or unclassified arthritis not meeting these criteria;
2. Presence of at least one extra-articular manifestation suggestive of ASyS according to the CLASS criteria, including suspected inflammatory myopathy (elevated CPK, EMG evidence of muscle damage, clinical weakness), ILD, Raynaud's phenomenon, mechanic's hands, inflammatory cutaneous rash, fever of unknown origin, or prior ANA positivity.

Collected data included ANA, anti-ENA immunoblot, myositis/anti-synthetase antibody panel (Alphadia Myositis Profile 12AgDot, Synthetase Profile 10AgDot); assessment for Raynaud's phenomenon, mechanic's hands, rash, muscle weakness, systemic symptoms; HRCT evaluation.

Results. Among 304 patients screened, 72 (23.7%) met the inclusion criteria: 58 (80.6%) had prior ANA positivity, 29 (40.3%) had ILD, 7 (9.7%) Raynaud's phenomenon, and 2 (2.8%) mild CPK elevation. No cases of inflammatory rash, fever, clinical myositis and mechanic's hands were reported.

Of these patients, 53 patients underwent serological testing (19 were lost to follow-up or refused testing). ANA positivity was confirmed in 40 (75.5%) cases, with a cytoplasmic pattern in 10 (18.9%). Six patients (11.3%) were positive for anti-Ro52 antibodies. The myositis/anti-synthetase panel was positive in 9 (17.0%) cases: anti-Jo1 (n=3, 5.7%), anti-PL12 (n=3, 5.7%), anti-SAE (n=2, 3.8%), and anti-ribosomal P0 (n=1, 1.9%).

According to the EULAR/ACR CLASS criteria, six patients (11.3%) could be classified as definite ASyS and three (5.7%) as probable ASyS. Among these, 7 out of 9 (77.8%) also fulfilled the 2010 EULAR/ACR criteria for definite RA.

Conclusions. Early identification of ASyS in patients with rheumatoid or undifferentiated arthritis may guide therapeutic choices and prevent extra-articular complications.

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DATA-DRIVEN SUBGROUPING OF INFLAMMATORY MYOPATHY RELATED CLINICAL AND SEROLOGICAL PROFILES IN A GREEK COHORT: MULTIPLE CORRESPONDENCE ANALYSIS AND HIERARCHICAL CLUSTERING

Nikolaos Marketos[1,2], Sylvia Raftopoulou[1], Nikolaos Michalakeas[5], Charalampos Skarlis[1], Maria Gerochristou[1,4], Theodora Douvali[4], Ilir Cinoku[5], Alexandra Koutsogianni[5], Vasilios Lainis[5], Dimitrios Ioakeimidis[2], Michalis Alevizos[2], Christos Koutsianas[6], Charalampos Papagoras[7], Efthimia Soura[8], Andreas Goules[5], Dimitrios Vassilopoulos[6], Panagiotis Vlachogiannopoulos[5], Athanasios Tzioufas[5], Vasiliki Chasapi[4], Dimitrios Boumpas[9], Alexandros Stratigos[8], George Kastis[10], Nikolaos Dikaios[10], Clio Mavragani[1,5,8]

[1]Molecular Physiology And Clinical Applications Unit, Department Of Physiology, Medical School Of Athens, Athens, Greece, [2]Rheumatology Outpatient Department, Henry Dunant Hospital Centre, Athens, Greece, [3]First Department of Propaedeutic and Internal Medicine, School of Medicine, NKUA, Athens, Greece, [4]State Department of Dermatology and Venereology NHS, "A. Syggros" Hospital for Skin and Venereal Diseases, Athens, Greece, [5]Department of Pathophysiology, School of Medicine, NKUA, Athens, Greece, [6]2nd Department of Medicine and Laboratory, Clinical Immunology-Rheumatology Unit, Hippokration General Hospital, School of Medicine, NKUA, Athens, Greece, [7]First Department of Internal Medicine, Democritus University of Thrace, University Hospital of Alexandroupolis, Alexandroupolis, Greece, [8]1st Department of Dermatology and Venereology, National and Kapodistrian University of Athens, "Andreas Syggros" Hospital of Venereal and Skin Diseases, Athens, Greece,

[9]4th Department of Internal Medicine, "Attikon" University Hospital, School of Medicine, NKUA, Athens, Greece, [10]Mathematics Research Center, Academy of Athens, Athens, Greece, Academy of Athens, Athens, Greece

Background. Idiopathic inflammatory myopathies (IIM) are systemic autoimmune disorders primarily affecting skeletal muscles but often involving the skin, lungs, and joints. Myositis-specific and myositis-associated autoantibodies (MSAs/MAAs) play a key role in diagnosis and are strongly linked to distinct clinical phenotypes and outcomes. We aim to classify patients with suspected IIM and serum MSA/MAA positivity into subgroups based on their clinical characteristics and autoantibody titers, through unsupervised multiple correspondence analysis (MCA), followed by hierarchical clustering on principal components (HCPC).
Methods. Among 888 individuals with suspected myositis who tested positive for MSAs/MAAs at our Unit between February 2017 and January 2024, 380 patients with available clinical data provided by the referring physicians were included in the analysis. MSAs/MAAs were detected using a commercial EUROLINE Autoimmune Inflammatory Myopathies 16 Ag (IgG) kit. Over 90 demographic, clinical, and serological variables were recorded. MCA and HCPC were used to form patient subgroups. Chi-square testing assessed the significance of variable distribution across clusters. All participants provided informed consent in accordance with the Declaration of Helsinki. A threshold of ≥26 on the immunoblot was applied to classify antibody titers as strong, while values of 11–25 were considered medium.
Results. Of the 380 patients included, 258 were exclusively positive for either strong (n=132) or medium titers (n=126). Among those with strong titers, three clusters were produced (n=38, 51, and 43). Skin lesions, including V-sign, Gottron papules, periungual erythema, shawl sign, heliotrope sign, facial erythema, photosensitivity, livedo reticularis, along with myalgias and muscle weakness, as well as anti-TIF-1 γ and anti-NXP-2 autoantibodies, were more frequently reported in the 1st cluster. Statin use, hypertension, coronary artery disease, and pulmonary complaints were more commonly reported in the 3rd cluster. Among the 126 patients with medium titers, four clusters were identified (n=26, 53, 27, and 20). Cluster 1 was associated with cardiovascular comorbidities, tongue ulcers, and lung involvement, and showed more frequent anti-Ku positivity. Cluster 4 showed female predominance and frequent fever, multiple cutaneous features (V-sign, periungual erythema, heliotrope sign, facial erythema, shawl sign, calcinosis cutis) and anti-NXP-2 antibodies. All patients in Cluster 3 had Raynaud's phenomenon and high frequency of anti-PM-Scl-75 antibodies, while anti-Mi-2b antibodies were more common in Cluster 2.
Conclusions. Unsupervised MCA followed by HCPC identified distinct and clinically meaningful subgroups among patients with suspected IIM and serum MSA/MAA positivity. Future steps, such as developing a decision tree or diagnostic algorithm based on these clusters, could enhance early recognition and tailored management of IIM subtypes.
Key words: myositis-associated or specific autoantibodies (MAAs/MSAs), multiple correspondence analysis, hierarchical clustering on principal components analysis, idiopathic inflammatory myopathies

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PREVALENCE OF ANTI-CCP ANTIBODY IN ANTISYNTHETASE SYNDROME, ASSOCIATION WITH CERTAIN CLINICAL MANIFESTATIONS. PRELIMINARY ANALYSIS

Maria M. Croce[1], Veronica Vargas[1], Delys Torres[1], Nadia Domínguez[2], Fernanda B. Ingenito[3], Carolina I. Leon[3], Carolina Sanchez-Andia[1]
[1]Rheumatology Section, J. M. Penna Hospital, Autonomous City of Buenos Aires, Argentina, [2]Rheumatology Section, Ramos Mejía Hospital, Autonomous City of Buenos Aires, Argentina, [3]Immunology Laboratory Section, Laboratory Division, C. G. Durand Hospital, Autonomous City of Buenos Aires, Argentina

Introduction: Antisynthetase syndrome (ASS) is a subgroup of immune-mediated inflammatory myopathy (IIM) characterized by fever, arthralgia and/or arthritis, interstitial lung disease, myositis, and mechanic´s hands. The association of anti-citrullinated peptide (anti-CCP) antibodies with this IIM subtype has been described and correlated with joint involvement similar to rheumatoid arthritis, establishing a pattern of overlap with this disease. While anti-CCP antibodies are associated with pulmonary involvement in several autoimmune diseases, it remains unclear whether they play a specific role in pulmonary behavior in this group of diseases. The objective of this study is to determine the prevalence of anti-CCP antibodies in patients with ASS.
Secondary objectives include establishing the association of anti-CCP antibodies with joint and pulmonary involvement.
Methods. This was an observational, descriptive-analytical, retrospective study (review of medical records) conducted in a public hospital in Buenos Aires, Argentina. Patients over 18 years of age who met the classification criteria for ASS (Connors Criteria) were included. A linear immunoassay method (Myositis Profile EurolineBlot test kit, Euroimmun, Lübeck, Germany) was used to perform the myopathic panel. Semi-quantitative ACPA assays detected third-generation anti-cyclic citrullinated peptide antibodies by electrochemiluminescence, and rheumatoid factor (RF) was measured using immunoturbidimetric assay. For the assessment of pulmonary involvement High resolution chest computed tomography was used.
Results. Twenty-seven patients with ASS were recruited, of whom 8 were excluded because they did not have anti-CCP antibody testing. A total of 19 patients were included, with a median age of 67 years (IQR: 58–73), predominantly female (n=12, 63.2%). The prevalence of anti-CCP antibodies in the cohort was 10.5% (95% CI: 1.3% to 33.1%), 2 of 19 patients. Joint involvement was observed in 15 patients (78.9 %), of whom (n= 8, 42.1 %) presented with arthritis. In total, 3 patients (n=3, 15.8%) met the ACR/EULAR classification criteria for rheumatoid arthritis (RA).
Interstitial lung disease (ILD) was observed in 15 patients (78.9%), with a predominance of nonspecific interstitial pneumonia (NSIP) (n=11,73.3%). Both patients with anti-CCP positivity had ILD (2/2; 100%) compared to 13/17 (76.5%) in the CCP-negative group (p=0.44), and met RA classification criteria (2/2;100%) versus 1/17 (5.9%) in the CCP-negative group (p=0.018).
Conclusions. In our study, the prevalence of anti-CCP antibodies in patients with ASS was 10.5%. An association was observed with joint involvement in a pattern similar to rheumatoid arthritis, as described in the literature. Studies with a larger number of patients and a broader representation of this population are needed to draw conclusions of greater statistical value.
Key words: antisynthetase syndrome, anti-cyclic citrullinated peptide antibodies, autoimmune myopathies, arthritis rheumatoid, interstitial lung disease

Clinical Trials

P-12

THE MIGHT TRIAL – AN EXPLORATORY CLINICAL TRIAL OF IVIG IN ANTI-HMGCR IMMUNE-MEDIATED NECROTIZING MYOPATHY

James Andrews[1], Eleni Tiniakou[2], Timothy Walton[3], James Sheets[3], Jack Lemley[3], Lisa Christhoper-Stine[4], Michael Weiss[5], Rohit Aggarwal[6]
[1]University of Alabama at Birmingham, Birmingham, USA, [2]University of Texas at Houston, Houston, USA, [3]CSI Clinical Specialty Infusions, Plano, USA, [4]Johns Hopkins University, Baltimore, USA, [5]University of Washington, Seattle, USA, [6]University of Pittsburgh, Pittsburgh, USA

Background. The lack of randomized, placebo-controlled trial (RCT) data on HMGCR immune mediated necrotizing myopathy (IMNM) treatment is a critical barrier to improving outcomes for patients. Observational data suggest that intravenously administered pooled human immunoglobulin (IVIG) may be effective in treating anti-HMGCR IMNM. In addition, we demonstrated that HMGCR-specific CD4+ T cells may play a key role in anti-HMGCR IMNM disease propagation and response to treatment. Our overarching goal is to conduct a pilot RCT testing the hypothesis that IVIG is an effective anti-HMGCR IMNM treatment in improving both key clinical outcomes and immunologic markers of disease pathogenesis.
Methods. The MIGHT Trial is a hybrid, decentralized, phase 2, double-blinded, placebo-controlled RCT of Octagam IVIG in anti-HMGCR IMNM. Participants (n=12) are randomized to either 2g/kg Octagam IVIG or normal saline placebo monthly home infusions for 3 months. Infusions are administered at home in a blinded manner. The primary outcome is change in CK from baseline to week 12. After the randomized phase, all participants enter a 3-month open-label extension phase. Secondary outcomes include core set measures (CSMs) and total improvement score. We will also examine 1) whether the % of HMGCR-specific CD4+ T cells, T cell epitope specificity, and T cell phenotype (Th 1, 2, 17, 1-17) are associated with disease activity measures (CK, other CSMs); and 2) whether treatment group is associated with these same T cell measures.
Results. Using an intention-to-treat approach, serum CK will be compared between treatment groups using a linear mixed model (LMM) to test the

hypothesis that mean change in CK between weeks 0 and 12 is greater in the Octagam IVIG compared to placebo group. An LLM approach will also model 1) the associations of T cell measures with CK and other CSMs at weeks 0, 4, 8, and 12; and 2) of treatment group with T cell measures at weeks 4, 8, and 12. Enrollment for MIGHT begin in November 2025, and initial recruitment and demographic data will be presented at GCOM. Primary outcome results are anticipated by Fall 2027.
Conclusions. The MIGHT Trial innovatively examines the efficacy of IVIG in anti-HMGCR IMNM and the potential role of HMGCR-specific CD4+ T cells in the disease. Home administration of treatment infusions is a key feasibility innovation of the trial. Anticipated results will inform a future, larger phase 3 RCT.
Acknowledgements. The MIGHT Trial is supported by NIH/NIAMS grant R21AR083566 and by generous support from Octapharma.
Key words: myositis, HMGCR immune mediated necrotizing myopathy, IVIG, CD4+ T cells

P-58

CLINICAL TRIALS IN IDIOPATHIC INFLAMMATORY MYOPATHIES – A LONGITUDINAL ANALYSIS OF PATTERNS IN STUDY DESIGN, THERAPEUTIC TARGETS AND OUTCOME MEASURES

Yasaman Ahmadzadeh[1], Hridya Harimohan[3], Deepali Sen[2], Jisna Paul[1]
[1]The Ohio State University Medical Center, Columbus, USA, [2]Washington University, St Louis, USA, [3]UCLA Ken Medical Center, Bakerfield, USA

Background. Idiopathic inflammatory myopathies (IIM) are rare, heterogeneous autoimmune diseases including dermatomyositis, polymyositis, antisynthetase syndrome, and immune-mediated necrotizing myopathy. Despite increased understanding of disease pathogenesis, therapeutic development has been hindered by disease rarity, limited trial enrollment, and lack of validated outcome measures. We aimed to characterize trends in interventional trial design, therapeutic classes, and primary outcome measures in IIM trials over the past three decades using data from ClinicalTrials.gov.
Methods. We conducted a systematic review of interventional trials for IIM (excluding inclusion body myositis) registered on ClinicalTrials.gov between January 1, 1990, and February 29, 2025. Trials were analyzed for study design characteristics (*e.g.* phase, randomization, multicenter status), therapeutic class (*e.g.* IVIG, biologics, JAK inhibitors, cell therapies), and type of primary outcome. Outcomes were categorized into composite disease activity indices (*e.g.* International Myositis Assessment & Clinical Studies Group Core Set Measures (IMACS-CSM), ACR/EULAR Total Improvement Score [TIS]), muscle strength, pulmonary function, skin involvement, safety, and patient-reported outcomes (PROs). Only primary outcomes were analyzed.
Results. A total of 93 interventional trials met inclusion criteria. Trial phases were predominantly early-stage, with 65% classified as phase 1 or 2; only 17% and 8% reached phase 3 or 4, respectively. Randomization and multicenter enrollment increased after 2010 but 56% of trials remained single centered. Cell-based therapies (n=25) were the most frequently studied intervention especially in recent years, followed by IVIG (n=21), IL inhibitors (n=11), and JAK inhibitors (n=11). Use of disease activity scores as primary outcomes was reported in 37% of conventional drug trials but in only 4% of cell therapy trials. The IMACS-CSM was used in 28% of trials, while TIS appeared in 18%. Safety outcomes were dominant in cell therapy trials (92%). Pulmonary-specific outcomes (*e.g.* FVC, imaging) and skin-specific scores (*e.g.* CDASI) were rarely used (<8%). PROs such as HAQ or PROMIS were primary endpoints in only ~3% of trials. Trials with ≥100 participants increased in frequency after 2015, suggesting improving recruitment feasibility.
Conclusions. From 1990 to 2025, IIM clinical trials have evolved with increasing therapeutic diversity and a shift toward targeted and cell-based therapies. However, most trials remain in early phases, with few advancing to late-stage validation. There is underutilization of standardized, disease-specific outcome measures – particularly those capturing skin, lung, and patient-reported domains. Bridging these gaps in trial design and outcome selection is essential for translating emerging therapies into meaningful clinical benefit in this heterogeneous disease group.
Key words: clinical trials

P-71

SYSTEMATIC LITERATURE REVIEW OF THE PROPERTIES OF OUTCOME MEASUREMENT INSTRUMENTS IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Latika Gupta[1,2,3], Didem Saygin[4], Eduardo Santos[5,6], Taanya Talreja[7], Aleksandra Opinc-Rosiak[8], Ana Valle[9], Anchal Sabharwal[10], Astia Allenzara[11], Bayram Farisogullari[12,13], Christina Downey[14], Connor Buechler[15], Daniel Brito de Araujo[16], Elizabeth Chu[17], Ellen Romich[18], Hammad Ali[19,20], Joanna Makowska[21], Matilde Bandeira[22,23], Raisa Lomanto Silva[24], Shereen Paramalingam[25], Simone Appenzeller[26], Victoria Werth[27,28], Pedro M. Machado[29]
[1]University of Birmingham, Birmingham, UK, [2]Royal Wolverhampton Hospitals, London, UK, [3]Francis Crick Institute, London, UK, [4]Rush University Medical Center, Chicago, USA, [5]School of Health, Polytechnic University, Viseu, Portugal, [6]Health Sciences Research Unit: Nursing (UICiSA:E), Coimbra, Portugal, [7]Seth GS Medical College and KEM Hospital, Mumbai, India, [8]Department of Rheumatology, Medical University of Lodz, London, Poland, [9] Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Harvard Medical School, London, USA of Americs, [10]Laboratory of Immune & Neural Networks, Feinstein Institute for Medical Research, Northwell Health, London, USA, [11]Division of Rheumatology, Allergy, and Immunology University of North Carolina at Chapel Hill Thurston Arthritis Research Center, London, USA, [12]St. George's University Hospitals NHS Foundation Trust, London, UK, [13]Neuromuscular Department, University College London, London, UK, [14]Division of Rheumatology, Loma Linda University Health, Loma Linda, USA, [15]University of Minnesota, Minneapolis, USA, [16] Internal Medicine Department, School of Medicine, Federal University of Pelotas (UFPel), Pelotas, RS, Brazil, [17]Division of Rheumatology and Clinical Immunology, University of Florida, Gainsville, USA, [18]Division of Rheumatology, Department of Medicine, University of Pennsylvania, USA,[19]Department of Dermatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA, [20]Department of Rheumatology, Hoskinson Health and Wellness Clinic, Gillette, Wyoming, USA, [21]Department of Rheumatology, Medical University of Lodz, Poland, [22]Rheumatology Department, ULS Viseu Dão Lafões, Viseu, Portugal, [23]Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa (CAML), Lisbon, Portugal, [24]Massachusetts General Hospital, Department of Rheumatology, Allergy & Immunology, USA, [25] Fiona Stanley Hospital, Western Australia Perth, Australia, [26]Department of Orthopefics, Rheumatology and Traumatology, Universidade Estadual de Campinas, Campinas, Brazil, [27]Department of Dermatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA, [28]Department of Dermatology, Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, USA, [29]Centre for Rheumatology, Department of Neuromuscular Diseases, University College of London, London, UK

Background. The introduction of myositis core set measures (CSMs) in 2001 enhanced study comparability and facilitated better design of therapeutic trials in idiopathic inflammatory myopathies (IIM). Numerous additional outcome measurement instruments (OMI) have since been developed and evaluated, and limitations of the original CSMs have become evident. This SLR aimed to critically appraise, compare, and summarize the quality of measurement properties of available OMI for adults with IIM (excluding IBM [inclusion body myositis]).
Methods. This SLR was conducted according to the COSMIN approach, and reported following the PRISMA guidelines, with the protocol registered in PROSPERO (CRD420251125407). A comprehensive literature search was performed in MEDLINE (via PubMed), EMBASE, CINAHL, and Cochrane Library on April 24, 2024. Citations were managed using COVIDENCE. Two independent reviewers performed title/abstract screening, full-text review, quality assessment, and data extraction. Risk of bias was evaluated using the COSMIN-OMERACT Good Metrics Checklist. Findings were synthesized into Summary of Measurement Properties (SOMP) tables, created for each measure, assessing various domains including feasibility, reliability, validity, responsiveness, and interpretability.
Results. From 9,043 initially identified studies, 7,611 were screened after removing duplicates. After reviewing 236 full-text articles, 82 studies were included in the final analysis.
For muscle strength assessment, Manual Muscle Testing (MMT-8) demonstrated the strongest overall evidence supporting its measurement properties, though with considerable variability in types of MMT assessed across different studies. For Dermatomyositis, Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) showed the strongest overall evidence supporting its measurement properties for skin assessment in adults and children with IIM across all domains studied.
The Functional Index series (FI-2, FI-3) along with the 30-second chair stand test showed strong evidence for performance-based functional assessment in adults with IIM.
Among patient-reported outcomes, PROMIS Physical Function 8b v2.0, PROMIS Pain Intensity 6a v1.0, PROMIS Fatigue 7a v1.0 and Myositis Activities Profile (MAP) all demonstrated robust measurement properties across most domains.

Although multiple measurement properties including feasibility, reliability, validity, responsiveness, and interpretability were evaluated, data on responsiveness, meaningful thresholds and discriminant validity remained limited for most instruments. Most studies utilized small, cross-sectional samples, and the majority of instruments were examined in only 1-2 studies, limiting the strength of evidence.
Conclusions. This comprehensive review summarizes the available evidence for measurement properties of OMI in IIM. The results will inform an updated core set of domains and CSMs in adults and children with IIMs for clinical trials and real-world studies.
Key words: idiopathic inflammatory myopathies, myositis, systematic review, outcome measures, core set measures, measurement properties

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COMPARISON BETWEEN THE CAMRY AND JAMAR DYNAMOMETERS FOR MEASUREMENT OF HAND GRIP STRENGTH IN INCLUSION BODY MYOSITIS

Helena McKay[1,2], Ian Cooper[3,4], Katie Schutze[1,2], Althea Doverty[3,4], Kelly Beer[3,4], Annik Panicker[3,4], Merrilee Needham[3,4,2,5]
[1]Sir Charles Gairdner Hospital, Nedlands, Australia, [2]University of Notre Dame Australia, Fremantle, Australia, [3]Perron Institute for Neurological and Translational Science, Perth, Australia, [4]Murdoch University, Murdoch, Australia, [5]Fiona Stanley Hospital, Murdoch, Australia

Background. Long finger-flexor weakness is a defining feature of Inclusion Body Myositis (IBM) and is typically monitored via dynamometry. The Jamar hydraulic dynamometer is widely considered the criterion ("gold") standard but is heavy (~1.5 kg), requires a minimum trigger force and is relatively expensive. The Camry spring dynamometer is substantially lighter and inexpensive, and has been validated in other populations, but its performance has not been specifically assessed in IBM. We aimed to compare reliability, validity and acceptability of the Camry against the Jamar devices in people with IBM.
Methods. This is a single-visit, crossover clinical performance study recruiting up to 50 adults with IBM. Participants are randomised to one of two device sequences (Jamar→Camry or Camry→Jamar). Grip strength is measured with each device in both the dominant and non-dominant hands, performing three maximal 3-second efforts per hand, with 30-second rests between attempts. The mean of the three attempts is recorded. A 15-minute rest period separates the two device sessions to minimise fatigue. Standardised participant positioning and scripted instructions are used throughout. The Jamar test is conducted with the elbow flexed at 90°, while the Camry is performed with the elbow in neutral extension, according to manufacturer guidance. Demographic information, disease duration, and IBM Functional Rating Scale (IBMFRS) scores are collected.
Test-retest reliability is tested using Pearson correlation coefficients and intraclass correlation coefficients, as well as agreement between devices using Bland-Altman methods. The target sample size is 50 participants (minimum 29 required). Secondary analyses include an independent t-test to assess fatigue effects by crossover sequence and a thematic analysis of participant acceptability questionnaire responses.
Results. Data collection is in progress. We will report correlation coefficients, ICCs with 95% CIs, Bland-Altman bias and limits of agreement, and participant-reported device acceptability (comfort, ease of use, likelihood of home use). Subgroup analyses will consider severely weak hands where Jamar trigger force may limit sensitivity.
Conclusions. If the Camry demonstrates strong agreement and reliability relative to the Jamar and greater patient acceptability, it could offer a lower-cost, lighter, and more practical tool for routine clinic monitoring and remote self-measurement in IBM. Confirmation of equivalence would support wider adoption of the Camry for longitudinal outcome capture and decentralised data collection in IBM research and care.
Acknowledgements. We thank all the participants for their time and effort in contributing to this study.
Key words: inclusion body myositis, grip strength, dynamometry, reliability, validity

P-208

PROSPECTIVE EVALUATION OF DERMATOMYOSITIS OUTCOMES FOR MUSCLE AND SKIN (DMOMS) IN A PHASE 3 RANDOMIZED TRIAL OF BREPOCITINIB IN DERMATOMYOSITIS (VALOR)

Victoria Werth[1,2], Katharina Shaw[1,3,4], Emily Hejazi[1], Matthew Cascino[4], Paul Mudd Jr.[4], Barbara White[5], David Fiorentino[6], Lesley Saketkoo[7], Maria Dall'Era[8]
[1]Department of Dermatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, USA, [2]Corporal Michael J. Crescenz VA Medical Center, Philadelphia, USA, [3]Division of Dermatology, Children's Hospital of Philadelphia, Philadelphia, USA, [4]Priovant Therapeutics, Durham, USA, [5]Corbus Pharmaceuticals Holdings Inc, Norwood, USA, [6]Department of Dermatology, Stanford University School of Medicine, Stanford, USA, [7]New Orleans Scleroderma and Sarcoidosis Patient Care and Research Center, New Orleans, USA, [8]Division of Rheumatology, Department of Medicine, University of California San Francisco, San Francisco, USA

Background. Cutaneous involvement is a cardinal feature of dermatomyositis (DM). As such, assessment of skin disease activity should ideally be incorporated into any composite endpoint that evaluates overall disease activity in DM. The Total Improvement Score (TIS) has served as the standard primary efficacy endpoint in myositis studies to date but lacks a skin-specific component. The Dermatomyositis Outcomes for Muscle and Skin (DMOMS) was recently developed to address this limitation by integrating a validated measure of cutaneous disease activity, potentially improving sensitivity to treatment effects and facilitating inclusion of patients with skin-predominant DM into clinical trials. However, DMOMS has yet to be prospectively evaluated in a clinical trial setting. We therefore assessed the performance of DMOMS in VALOR, a Phase 3, randomized, placebo-controlled trial of brepocitinib, an oral TYK2/JAK1 inhibitor, in adults with DM.
Methods. Adults with active DM were randomized 1:1:1 to receive brepocitinib 30 mg, brepocitinib 15 mg, or placebo once daily for 52 weeks. Background therapies were continued with a protocol-defined corticosteroid taper. Mean TIS at week 52 was the primary endpoint and mean DMOMS at week 52 was a key secondary endpoint. DMOMS integrates four assessments (Cutaneous Dermatomyositis Disease Area and Severity Index-Activity score, CDASI-A; Manual Muscle Testing-8, MMT-8; Physician Global Assessment, PhGA; and Patient Global Assessment, PtGA) and was calculated using previously described methods. Least-squares mean (LSM) treatment differences are reported.
Results. At week 52, mean DMOMS was 57.9, 48.9, and 40.5 for brepocitinib 30 mg, brepocitinib 15 mg, and placebo, respectively (difference, brepocitinib 30 mg *vs*. placebo, 17.3; 95% CI 6.8-27.9; p=0.001). Brepocitinib 30 mg achieved statistical significance on DMOMS at all post-baseline assessments including week 4. These results paralleled those of other ranked endpoints including mean TIS, which also demonstrated statistical significance from week 4 through week 52 (difference, brepocitinib 30 mg *vs*. placebo at week 52, 15.3; 95% CI 6.7–24.0; p<0.001). Brepocitinib demonstrated a safety profile consistent with approved TYK2 and JAK1 inhibitors.
Conclusions. In this Phase 3 trial, DMOMS was sensitive to clinical improvement, differentiated active therapy from placebo in a dose-dependent manner, and aligned with other clinical measures. Brepocitinib 30 mg demonstrated results that were rapid, statistically significant, and sustained over time, including improvement in multiple domains such as skin, muscle, and patient-reported outcomes. These findings provide the first prospective validation of DMOMS as a DM-specific endpoint suitable for detecting therapeutic benefit in clinical trials.
Key words: brepocitinib, TYK2/JAK1 inhibitor, dermatomyositis, DMOMS, TIS

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GLOBAL PATTERNS AND CHALLENGES IN PATIENT ENROLMENT FOR IDIOPATHIC INFLAMMATORY MYOPATHY CLINICAL TRIALS: RESULTS FROM THE MCTC INVESTIGATORS' SURVEY

Iris Yan Ki Tang[1], Kaushik Sreerama Reddy[2], Aditi Gupta[3], Akira Yoshida[4], Anushka Aggarwal[5], Dhruvi Shah[6], Eduardo Dourado[7,8,9], Gabriel Wong[10], Jennier Ben Shimol[11], Laura Martinez-Prat[12], Michelle S. Min[13], Océane Landon-Cardinal[14], Pavani Battula[15], Samar Al Emadi[16], Shiri Keret[17], Daniel Brito de Araujo[18], Samuel Katsuyuki Shinjo[19], Prateek Gandiga[20], Rohit Aggarwal[2]

[1]Division of Rheumatology & Clinical Immunology, Department of Medicine, The University of Hong Kong, Hong Kong, China, [2]Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, USA, [3]Jawaharlal Nehru Medical College, Belgaum, India, [4]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [5]Department of Rheumatology, Indraprastha Apollo Hospital, New Delhi, India, [6]Dr Vasantrao Pawar Medical College Hospital and Research Centre, Nashik, India, [7]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal, [8]Aveiro Rheumatology Research Centre, Egas Moniz Health Alliance, Aveiro, Portugal, [9]Rheumatology Research Unit, Instituto de Medicina Molecular, Faculdade de Medicina Universidade de Lisboa, Lisboa, Portugal, [10]AstraZeneca, UK, [11]Department of Rheumatology, Barzilai Medical Center, Ashqelon, Isarel, [12]Myositis Support & Understanding, USA, [13]Department of Dermatology, University of California Irvine School of Medicine, Irvine, USA, [14]Division of Rheumatology, Centre Hospitalier de l'Université de Montréal, Montréal, Canada, [15]Apollo Hospital, India, [16]Medicine Department, Rheumatology Section, Hamad Medical Corporation, Doha, Qatar, [17]Rheumatology Unit, Bnai Zion Medical Center, Faculty of Medicine, Technion Israel institute of technology, Haifa, Isarel, [18]Department of internal medicine, Universidade Federal de Pelotas, Pelotas, Brazil, [19]Division of Rheumatology, Faculdade de Medicina FMUSP, Universidade de São Paulo, São Paulo, Brazil, [20]Division of Rheumatology, Emory University, Atlanta, USA

Background. Despite a growing number of idiopathic inflammatory myopathy (IIM) clinical trials, most are limited to a few centres, restricting generalizability and equitable access to novel therapies. This study aimed to identify global patterns of clinical trial enrolment and factors influencing enrolment.

Methods. The Myositis Investigators' Survey was distributed online to physicians who joined the Myositis Clinical Trials Consortium (MCTC) between July 2024 and August 2025. Data surveyed included investigator demographics; clinical and research experience; and the number of IIM patients seen for (i) routine care in the previous year and (ii) enrolment in investigational studies (including pilot, open-label, and phase 2–4 trials) over the previous three years. Multivariable logistic regression analysis was performed to identify independent factors associated with any enrolment in trials.

Results. In the 509 responses analysed, a diverse geographic distribution was observed with 147 (28.9%) investigators from Europe, 137 (26.9%) from North America, 118 (23.3%) from the Asia-Pacific region, 72 (14.2%) from Central/South America and 33 (6.5%) from the rest of the world. Respondents specialised in rheumatology (74.2%), pulmonology (8.7%), neurology (7.9%), and dermatology (5.5%). Most only treated adult patients (81.2%). 115 (22.7%) investigators had completed additional IIM training. The median duration of clinical research experience was 10 years (IQR: 5–18), with 321 (63.3%) investigators reporting experience in IIM clinical research.

Overall,194 (38.3%) physicians had enrolled patients into clinical trials over the previous three years. Among all respondents, enrolment was more common among investigators from Europe (53.1%) and North America (40.8%), compared with Central/South America (26.4%) and Asia-Pacific region (26.3%) ($p<0.001$). Enrolment was higher in dermatomyositis (DM) (30%) than anti-synthetase syndrome (ASyS) (15.2%), immune-mediated necrotizing myopathy (IMNM) (10.8%) and juvenile DM (JDM) (5.4%). Enrolment was more likely among physicians seeing >20 IIM patients/year (DM: 56.6%, ASyS: 34.3%, IMNM: 54.8%, JDM: 17.6%). Using multivariable analysis, additional IIM training (OR 1.8, 95% CI 1.1-3.0) and higher patient volume (>20/year; OR 1.9, 95% CI 1.2-3.1) were found to be independently associated with enrolment, whereas practising in the Asia-Pacific region (OR 0.51, 95% CI 0.3-0.9) and treating paediatric patients (OR 0.4, 95% CI 0.2-0.7) were associated with lower odds of enrolment.

Conclusions. Substantial disparities in IIM trial enrolment persist, with under-representation outside of Europe and North America, in non-DM subtypes and among paediatric investigators. Expanding investigator training and trial infrastructure especially in underrepresented areas might improve the feasibility and robustness of future IIM clinical trials.

Key words: clinical trials

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A MULTICENTRE, 26-WEEK, OPEN-LABEL PHASE 2 TRIAL OF THE JAK INHIBITOR FILGOTINIB IN IDIOPATHIC INFLAMMATORY MYOPATHIES: FIRST RESULTS OF THE DRIMID STUDY

Bettina Geertsema-Hoeve[2], Merve Kocyigit[1], Cesar Magro Checa[3], Jan A.M. Van Laar[4], Sander W. Tas[5], Paco M.J. Welsing[2], Robbert J. Goekoop[6], Rogier M. Thurlings[7], Nicolle H. Rekers[8], Erik Present[8], Joost Raaphorst[1], Jacob M. Van Laar[2]

[1]Department of Neurology and Clinical Neurophysiology, University of Amsterdam, Amsterdam, The Netherlands, [2]Department of Rheumatology and Clinical Immunology, University Medical Centre Utrecht, Utrecht, The Netherlands, [3]Department of Rheumatology, Zuyderland Medical Centre, Heerlen, The Netherlands, [4]Department of Internal Medicine and Immunology, Erasmus Medical Centre, Rotterdam, The Netherlands, [5]Department of Rheumatology and Clinical Immunology, Amsterdam University Medical Centre, Amsterdam, The Netherlands, [6]Department of Internal Medicine and Rheumatology, HagaZiekenhuis, The Hague, The Netherlands, [7]Department of Rheumatology, Radboud University Medical Centre, Nijmegen, The Netherlands, [8]Alfasigma Nederland BV, Utrecht, The Netherlands

Background. In idiopathic inflammatory myopathies (IIM), current immunosuppressive therapies are insufficient, with 60–70% of patients still experiencing disease activity and significant long-term side effects. Common subtypes include dermatomyositis (DM) and anti-synthetase syndrome (ASyS). In these subtypes, interferons (IFNs) have been demonstrated as major contributors to the pathogenesis, primarily through the Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway, particularly in DM and in smaller studies in ASyS. While data on efficacy of IFN-targeting therapies in ASyS are scarce, recently IFN-targeting therapy demonstrated efficacy in refractory DM. Therefore, JAK inhibitors (JAKi) may hold potential for treatment of DM and ASyS. This study aims to determine the effect of the JAKi filgotinib after 26 weeks on disease activity and quality of life in DM and ASyS.

Methods. The DRIMID study is a multicentre, investigator-initiated, prospective, open-label, phase-2 basket-trial evaluating the effects of 26-week treatment with filgotinib (1). We aim to include 20 patients with active DM or ASyS aged 18-65 years who are refractory/intolerant to immunosuppressive or immunomodulatory therapy (*e.g.* disease-modifying antirheumatic drugs, rituximab, intravenous immunoglobulins). The co-primary endpoints include change in disease activity based on a Total Improvement Score (TIS) of ≥20 after 26 weeks and quality of life (EuroQol-5D-5L). Secondary outcomes include Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) score (mean change), changes in glucocorticoid dose (GCd) and safety.

Results. Between June 2024-November 2025, 11 out of 20 patients (DM; n=5, ASyS; n=6) were included. Here we report data on TIS, CDASI, GCd and safety of the first five patients. All five patients (DM; n=3, ASyS; n=2) reached the primary endpoint with a median TIS of 65 (range: 25-67.5), including 3 patients with a TIS>60. All DM patients showed skin improvement (CDASI mean change of 4 (range 2–6)). In all patients on glucocorticoids at baseline(n=3), these could be tapered to <5 milligrams. One patient (DM) discontinued filgotinib due to non-response and side effects. No medication-related serious adverse events were reported.

Conclusions. Until November 2025, five out of eleven patients (DM; n=3, ASyS; n=2) with treatment refractory DM or ASyS completed the 26-week treatment period and all showed a positive clinical response to filgotinib. Only one patient (DM) discontinued filgotinib. Results of the 26-week primary and secondary endpoints, including TIS, EuroQol-5D-5L, CDASI, GCd and safety for the first 10 patients will be presented at the Global Conference on Myositis.

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Key words: myositis, JAKi, interferon

Reference

1. PMID: 39915014

P-358

DECENTRALIZED RECRUITMENT EFFICIENCY IN A RARE DISEASE TRIAL: INSIGHTS FROM THE MYOSITIS INTERSTITIAL LUNG DISEASE NINTEDANIB TRIAL (MINT)

Vaidehi Kothari[1], Eaman Alhassan[1,12], Kaushik Sreeram[1], Nantakarn Pongtarakulpanit[1,13], Tanya Chandra[1], Sol Dominiguez[1], Eugenia Gkiaouraki[1], Jesse Wilkerson[1], Akanksha Sharma[1], Iazsmin Bauer Ventura[2], Galina Marder[3], Tejaswini Kulkarni[4], Kevin Geoffrey Dsouza[4], Mark Hamblin[5], Mazen Dimachkie[5], Debabrata Bandyopadhyay[6], Jose Herazo Maya[6], Mary Beth Scholand[7], Elana Bernstein[8], Joshua Solomon[9], Jeffrey Swigris[9], Vivek Nagaraja[10], Ana Zamora Martinez[10], Robert Hallowell[11], Barry S. Shea[11], Shreya Sriram[1], Vladimir Liarski[1], Daniel Kass[1], Kevin Gibson[1], Didem Saygin[14], Diane Koontz[1], Siamak Moghadam-Kia[1], Chester Oddis[1], Dana Ascherman[1], Daniel Sullivan[1], Rohit Aggarwal[1]

[1]University of Pittsburgh, Pittsburgh, USA, [2]University of Chicago, Chicago, USA, [3]Northwell Health, Great Neck, USA, [4]University of Alabama, Birmingham, USA, [5]University of Kansas Medical Center, Lawrence, USA, [6]University of South Florida, Tampa, USA, [7]University of Utah, Salt Lake City, USA, [8]Columbia University, Manhattan, USA, [9]National Jewish Health, Denver, USA, [10]Mayo Clinic, Phoenix, USA, [11]Massachusetts General Hospital, Boston, USA, [12]University of San Diego, San Diego, USA, [13]Mahidol University, Phutthamonthon, Thailand, [14]Rush University, Chicago, USA

Background. Recruitment for trials in rare diseases, such as Idiopathic Inflammatory Myopathy-associated Interstitial Lung Disease (IIM-ILD), is challenging based on the limited geographic reach of traditional site-based models. The Myositis Interstitial Lung Disease Nintedanib Trial (MINT) implemented a hybrid-decentralized model to overcome this barrier, enabling remote patient participation. We aimed to: 1. evaluate the feasibility and efficiency of this hybrid model, and 2. assess the effectiveness of engaging both academic and community physicians in recruitment.

Methods. MINT is a Phase III, randomized, double-blind, placebo-controlled trial of nintedanib in progressive IIM-ILD. Patients were recruited remotely nationwide (U.S.) through a central coordinating center (University of Pittsburgh) or locally through 11 traditional in-center sites. Remote channels included physician referrals (academic/community), self-referrals, and a recruitment vendor. Local patients were recruited from populations near the participating clinical sites. We compared patient progression through enrollment milestones (pre-screening, screening, randomization) using chi-square tests. Weekly recruitment velocity (patients/week) was estimated using Poisson regression and reported as incidence rate ratios (IRR) with 95% confidence intervals (CI).

Results. Of 258 referrals (remote n=118; local n=140), referral to pre-screening conversion was higher remotely [64% remote (76/118) *vs*. 17% local (24/140); p<0.001], whereas pre-screening to screening favored local [49% remote (37/76) *vs*. 83% local (20/24); p=0.003]. Overall randomization yield from referrals was more than two-fold higher remotely (23.7% *vs*. 11.4%), indicating superior end-to-end efficiency.

Remote physician-referred recruitment velocity (patients/week) was significantly higher for both screening (IRR 2.22, 95% CI 1.29–3.83; p=0.004) and randomization (IRR 2.07, 1.12–3.83; p=0.020).

For remote referrals, community physicians performed comparably to academic physicians across all milestones: pre-screening [79% (11/14) *vs*. 63% (65/104); p=0.238]; screening [64% (7/11) *vs*. 46% (30/65); p=0.283]; and randomization [71% (5/7) *vs*. 77% (23/30); p=0.771].

Remote and local cohorts were clinically comparable with similar autoantibody profiles and predominant anti-synthetase syndrome. Demographics were largely similar, though the local cohort had more black patients (41.2% *vs*. 6.3%; p=0.012), while the remote cohort included more Hispanic participants (12.5% *vs*. 0%).

Conclusions. Remote recruitment was feasible and substantially accelerated patient enrollment by more than two-fold compared to local site-based approaches, while maintaining comparable clinical characteristics. Community physicians' referrals were as effective as their academic counterparts', highlighting community providers as critical, untapped resources for trial recruitment. These observations indicate decentralized methods can broaden access, improve diversity, and accelerate enrollment in rare-disease trials.

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Key words: idiopathic inflammatory myopathy, decentralized clinical trial recruitment, interstitial lung disease

Exercise & Rehabilitation

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HAND EXERCISE IN PEOPLE WITH INCLUSION BODY MYOSITIS – A SINGLE SUBJECT DESIGN

Malin Regardt[1,2], Ingrid de Groot[3], Åsa Lindberg[4]

[1]Women's Health and Health Professional Theme, Medical Unit Allied Health Professionals, Karolinska University Hospital, Stockholm, Sweden, [2]Department of Neurobiology, Care Sciences and Society, Division of Occupational Therapy, Karolinska Institutet, Stockholm, Sweden, [3]Spierziekten Nederland (Dutch patient association for NMD), Baarn, Netherlands, [4]Center for Rheumatology, Academic specialist center, Stockholm, Sweden

Background. Inclusion body myositis (IBM) is a chronic progressive inflammatory myopathy leading to muscle weakness. Reduced hand function is prominent in IBM and have a large impact on daily activities. Therefore, we aimed to evaluate if a 12-week hand exercise intervention had effect on hand function and activity performance.

Methods. The intervention consisted of hand strengthening exercise with focus on grasp and different pinch grip using an exercise dough. The exercise was performed 5 days/week during the 12-week intervention.

A Single Subject AB-design with average and standard deviation (SD) was used. The A-phase represents baseline and had three measure points and B-phase the intervention period with six measure points. A true change was defined as two consecutive measure points exceeding the 2SD band from the A-phase. Minimum Clinically Important Difference (MCID) was used to evaluate the results. Hand grip strength was measured by Jamar dynamometer, key grip and three-point grip strength was measured by Pinch Gauge and range of motion by the The Escola Paulista de Medicina-Range of Motion scale (EPM-ROM).

Activity performance was measured by the Disabilities of Arm, Shoulder, and Hand (DASH) and the Canadian Occupational Performance Measure (COPM). DASH includes arm and hand related activities that are performed in daily life and COPM is a patient preference measure where the participants set hand-related activity-goals and rate them in performance and satisfaction.

Results. A total of nine people with IBM (men=6, women=3) participated. Eight (88%) participants had measure points during the B-phase over or under the 2SD band regarding the hand function. Three participants had measure points that were over the 2SD band for the three-point grip and also reached a MCID which could indicate a positive improvement. The range of motion was unchanged. The activity performance with DASH was higher in six (67%) participants and one participant even improved according to the MCID.

With COPM six (67%) participants rated an improvement in performance and/or satisfaction in the hand-related activity-goals.

Conclusions. The hand exercise showed improvement in activity performance and there was an indication at an individual level that hand exercise can give positive results regarding hand function, but the results are difficult to assess because of an unstable A-phase. A combination of encouraging activities in daily living and hand exercise for persons with Inclusion body myositis is recommended.

Acknowledgements. We thank the participants for their endurance and engagement and Karolinska university hospital for enabling the study.

Key words: inclusion body myositis, single subject design, hand function, hand exercise, activity performance, occupational therapy.

P-162

FEASIBILITY OF A 16-WEEK EXERCISE INTERVENTION FOR PATIENTS WITH INCLUSION BODY MYOSITIS: ADHERENCE, SAFETY AND EXPERIENCES FROM PATIENTS AND PHYSIOTHERAPISTS

Kristine Risum[1,2], Marianne Skattør[1], Ulrika Nilsson[1], Helene Alexanderson[3,4], Helena Andersson[1], Therese Brovold[2]

[1]Oslo University Hospital, Oslo, Norway, [2]Oslo Metropolitan University, Oslo, Norway, [3]Karolinska University Hospital, Stockholm, Sweden, [4]Karolinska Institutet, Stockholm, Sweden

Background. Inclusion Body Myositis (IBM) is a progressive muscle disease with limited treatment options. Exercise may help preserve function, but evidence is scarce. We conducted a feasibility study to evaluate adherence,

safety, and acceptability of a 16-week individualized exercise intervention for patients with IBM.
Methods. Each week, patients participated in one supervised group session and one home-based exercise session, both focusing on strength and balance. Feasibility was assessed through logbooks, adherence rates, and safety reports. Post-intervention focus group interviews with patients and physiotherapists explored experiences with the intervention. Thematic analysis is ongoing.
Results. Of 24 invited patients, 15 were included and 13 (54 % men) completed the intervention. Two patients withdrew after baseline assessments due to back pain and transportation challenges. Among the 13 participants, 10 (77 %) attended ≥75 % of group sessions and completed ≥75 % (≥12 sessions) of home exercises. No falls or near-falls occurred during supervised sessions, while participants reported seven falls and 56 near-falls at home. Weekly symptom ratings (numeric rating scale 0–10) indicated low levels of pain, fatigue, and muscle soreness throughout the intervention.
Preliminary analysis of focus group interviews suggests that patients valued the opportunity to exercise alongside others with the same diagnosis, describing a sense of shared understanding and peer connection, and relief in not having to explain their condition. The presence of physiotherapists with IBM expertise was experienced as professional competence and trust, contributing to a sense of safety and motivation. Several patients emphasized that exchange of lived experiences – discussing how it is to live with IBM – was as meaningful as the physical training itself. Physiotherapists reported practical challenges and the need for adjustments, including limited space and varying support needs. These challenges led to dividing participants into two groups and adding a third physiotherapist. Time constraints hindered individual adjustment of exercise loads to some degree. Regarding assessment feedback, patients generally found the physical tests and questionnaires manageable, although some safety-related questions were perceived as difficult to interpret. These preliminary findings will be further explored through thematic analysis
Conclusions. The exercise intervention was feasible and safe for patients with IBM, with high adherence and positive experiences reported by both patients and physiotherapists. Preliminary qualitative findings suggest strong acceptability and highlight areas for refinement. The results may inform future development and implementation of tailored exercise programs for this patient group.
Acknowledgements. This study was funded by Foundation Dam. We thank all the participating patients and physiotherapists.
Key words: inclusion body myositis, exercise, experiences

P-179

CHIN TUCK AGAINST RESISTANCE (CTAR) TRAINING FOR SWALLOWING FUNCTION IN PATIENTS WITH MYOSITIS: EXPERIENCE FROM A STANDARDIZED CLINICAL INTERVENTION

Dilara Erer[1], Helene Alexanderson[1]
[1]*Karolinska University Hospital, Stockholm, Sweden*

Background. Myositis often causes dysphagia, significantly affecting quality of life, yet targeted rehabilitation strategies remain limited. The Chin Tuck Against Resistance (CTAR) exercise strengthens suprahyoid muscles and promotes hyolaryngeal elevation. CTAR has proven effective to recuse dysphagia in neurological diseases, but its effectiveness in myositis is unknown.
Methods. Eight patients with myositis and dysphagia referred for swallowing evaluation were included (IBM = 4, PM = 2, DM = 2; diagnosed 2017–2024). Median age was 71.5 years (range 48–83). All completed a 6-week structured CTAR program, three daily sessions with telephone follow-up every other week. Swallowing was assessed pre- and post-intervention using Fiberoptic Endoscopic Evaluation of Swallowing (FEES). Overall swallowing function was rated with the Dysphagia Outcome and Severity Scale (DOSS; 1 = severe limitation, 7 = normal), and airway safety with the Penetration-Aspiration Scale (PAS; 1 = no penetration or aspiration, 8 = aspiration).
Results. At baseline, median DOSS score for all patients was 5 (range 5–6) and median PAS scores 2 (range 1–3) indicating mild to moderate dysphagia. After CTAR median DOSS score was 6 (5–6) and PAS scores 2 (1–6). Two patients with IBM changed from 5 to 6 on DOSS, one of them changed from 3 to 2 in PAS score and one from 1-6 in PAS which may indicate increased aspiration risk, possibly due to reduced general condition. The patient underwent videofluoroscopy before and FEES after the intervention, which may have affected the results. Among DM patients, one changed from 5 to 6 in DOSS and from 2 to 1 in PAS, while the other changed from 2 to 5 in PAS, likely due to daily clinical variation of fatigue. One patient with PM changed from 5 to 6 in DOSS and from 2 to 1 in PAS while the other remained unchanged, patient improved and one was stable. Some performed two to three sessions per day due to fatigue or forgetfulness, and for a few, the program was extended to seven-eight weeks due to delayed follow-up.
Conclusions. The CTAR was feasible and can possibly result in mild improvements in swallowing and airway protection in selected patients with myositis. These preliminary findings from a clinical intervention highlight the need for further pilot studies to explore efficacy, optimal dosage, and underlying mechanisms.
Acknowledgements. The authors thank the participating patients and healthcare professionals who contributed to this clinical intervention.
Key words: myositis, swallowing function, CTAR

P-193

ASSESSMENT OF CARDIAC HEALTH IN STABLE PATIENTS WITH MYOSITIS FOLLOWING 16 WEEKS OF HIGH-INTENSITY RESISTANCE TRAINING

Kasper Yde Jensen[1], Søren Jæger Rahbek[1], Sofie Bech Christensen[1], Augusta Bech Diederichsen[1], Louise Pyndt Diederichsen[1]
[1]*Copenhagen Research Center for Autoimmune Connective Tissue Diseases (COPEACT), Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen, Denmark*

Background. Idiopathic inflammatory myopathies (myositis) are characterised by chronic muscle inflammation. Cardiac involvement, including arrhythmias and myocarditis, raises the concern about long-term cardiovascular risk. However, limited data exist on cardiac health in stable patients with myositis who have undergone structured exercise regimes. Therefore, this study aimed to evaluate heart health in patients with myositis following 16 weeks of high-intensity resistance training.
Methods. Post-hoc analysis based on data from a previous RCT (NCT04486261) including adult patients diagnosed with myositis (excluding inclusion body myositis) with stable disease prior to inclusion. Participants was randomly allocated to resistance training (n=14, age: 44.4 years, disease duration: 5.1 years) or control (n=16, age: 49.1, disease duration: 4.3 years). Cardiac health was measured by cardiovascular biomarkers (HbA1C, glucose, lipid profile [total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides), 12-lead Electrocardiography (ECG) outcomes (heart rate, p-wave, P-Q interval, QT and QTc [Bassett and Friderica]) and blood pressure. A Linear mixed model was used to evaluate within and between group differences. Results are presented in group means ± standard deviation.
Results. No significant between group differences were observed following the 16 weeks of high-intensity resistance exercise. Within the group of resistance trained individuals, heart rate decreased from 74±9 to 67±11 beats per second ($p=0.02$), while QT increased from 388±19 to 398±25 milliseconds ($p<0.03$), while all other cardiovascular biomarkers, ECG parameters, and blood pressure remained unchanged following the 16-week intervention. Within the control group, none of the analysed outcomes were observed to change throughout the study period.
Conclusions. Our findings suggest that patients with stable myositis exhibit a normal cardiac health profile. The surrogate marker for aerobic fitness (heart rate) improved in the group of resistance trained individuals, suggesting that 16 weeks high-intensity resistance training can potentially have a positive effect on aerobic capacity in patients with myositis. The cardiovascular risk profile remained unchanged for both the resistance-trained and the controls following the 16 weeks of intervention. Larger longitudinal studies incorporating echocardiography and other cardiac biomarkers are warranted to confirm these findings and guide long-term cardiovascular care in patients with myositis.
Acknowledgements. We are grateful for the participants in present study, as well as our patients advisory board.
Key words: cardiac health, electrocardiography, biomarkers, non-pharmacological interventions

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EFFECT OF EXERCISE ON FUNCTIONAL DECLINE IN INCLUSION BODY MYOSITIS

Alexander Ozonoff, Gary Cutter, Eesha Chakraborty, Kurt Petschke, A. David Paltiel, Bhaskar Roy
[1]*Yale University School of Medicine, New Haven, USA*

Background. Inclusion body myositis (IBM) is a rare, progressive muscle disease characterized by predominant involvement of the quadriceps and long finger flexors, leading to muscle weakness and atrophy. In the absence of curative therapy in IBM, the potential beneficial role of exercise has been implicated. However, a definitive benefit of exercise could not be established in short-duration clinical trials.
Methods. In this study, we leveraged the Yale IBM registry (IBMR) to examine the role of exercise on functional decline in IBM, based on the IBM functional rating scale score (IBM-FRS). Longitudinal data on patients with IBM, who had data available for 9 months or longer, were obtained from the IBMR, which contains details of their physical activities.
Results. We included 401 patients (68.4 ± 8.4 years, Female 139 (34.7%)), with a baseline IBM-FRS score of 26.9 ± 6.8, with longitudinal data over an average of 46 months (range 9–80 months). All patients showed a decline in IBM-FRS over time, averaging 1.58 points per year. We did not notice any significant differences in disease progression by gender or age at symptom onset. The habit of exercise was associated with a slower rate of decline (p-value <0.01), with a graded benefit for more active patients (p-value <0.001). Among different types of exercise, patients engaged in physical therapy and walking had slower deterioration (p-values 0.003 and 0.04, respectively, compared to no exercise). While patients in the exercise group had a relatively higher IBM-FRS, the benefit of exercise remained statistically significant even after adjusting for baseline IBM-FRS. Similarly, we confirmed that our findings were not confounded by patients with more severe disease at baseline being lost in the follow-up. Analyses of within-person changes emphasized the role of continuity: stopping exercise showed a less favorable subsequent slope, whereas starting exercise lacked an immediate level change, suggestive of potential benefit.
Conclusions. These findings, based on patients' self-reports, support the potential long-term benefit of remaining physically active in IBM. More work is needed to better understand the optimal duration of exercise and the most beneficial type of exercise. Given the lack of approved therapy in IBM, longer clinical trials with a component of remote monitoring, which can be feasible through the existing platform of Yale IBMR, might be necessary to delineate the actual impact of exercise on IBM disease progression.
Acknowledgements. We are thankful to patients participating in the Yale online IBM registry.
Key words: exercise, IBM

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EVALUATING CHATGPT'S ADVICE AND RECOMMENDATIONS REGARDING EXERCISE FOR PEOPLE WITH INCLUSION BODY MYOSITIS

Ian Cooper[1,2], Ruby Shehatha[1], Kelly Beer[1,2], Alethea Doverty[1,2], Tanya Smith[1], Katie Schutze[3,5], Mathew Bagg[4,6], Merrilee Needham[1,2,5,7]
[1]*Perron Institute, Perth, Australia,* [2]*Murdoch University, Perth, Australia,* [3]*Sir Charles Gairdner Hospital, Perth, Australia,* [4]*University of Notre Dame Australia, School of Health Sciences, Fremantle, Australia,* [5]*University of Notre Dame Australia, School of Medicine, Fremantle, Australia,* [6]*Centre for Pain IMPACT, Neuroscience Research Australia, Randwick, Australia,* [7]*Fiona Stanley Hospital, Perth, Australia*

Background. Artificial intelligence (AI) technologies, particularly large language models such as ChatGPT, are increasingly being integrated into healthcare education and practice. While ChatGPT has demonstrated strong performance in medical reasoning and diagnostic contexts, its potential as a source of clinical guidance for rare conditions has not been thoroughly evaluated. Inclusion Body Myositis (IBM) is a slowly progressive inflammatory myopathy affecting older adults, primarily involving weakness of the quadriceps and finger flexors. With limited pharmacological options, exercise remains the cornerstone of IBM management. Given the rarity of the condition, both patients and health professionals may rely on AI tools for disease-specific information and exercise advice. This study aimed to assess the accuracy, safety, and appropriateness of ChatGPT's recommendations relating to exercise for people with IBM.
Methods. A panel of physiotherapists from the Perron Institute (Perth, Australia) developed six clinically relevant questions covering IBM pathology, exercise safety, exercise prescription for mild and advanced weakness, hand grip exercises, and fall-prevention strategies. ChatGPT-4's responses were evaluated by 12 physiotherapists experienced in IBM management across Australia, Europe, and North America. Each response was rated using a five-point rubric ranging from "comprehensive and accurate" to "wrong and unsafe." Data were analyzed descriptively, with qualitative comments thematically reviewed.
Results. Overall, ChatGPT's responses were judged safe and mostly accurate in five of the six domains assessed. The mean ratings across all questions ranged from 1.41 (highly accurate) to 3.33 (moderately inaccurate). The most positively rated responses related to identification of muscles affected by IBM (66% rated "comprehensive and accurate") and fall-prevention advice (58% rated "comprehensive and accurate"). Responses on exercise safety and mild muscle weakness were rated as safe but basic. ChatGPT's recommendations for advanced quadriceps weakness (MRC grade 2/5) however were considered inappropriate by one-third of physiotherapists due to the inclusion of Functional Electrical Stimulation, which lacks evidence in IBM. No correlation was found between responses and participant experience or geographic location.
Conclusions. This study demonstrates that ChatGPT can generate generally safe but incomplete exercise recommendations for people with Inclusion Body Myositis. While its responses may assist inexperienced clinicians or patients seeking general guidance, they should not replace specialist physiotherapy input. Ethical considerations, particularly around reliability, validation, and patient safety remain essential. Ongoing evaluation, clinician oversight, and inclusion of patient perspectives are recommended to ensure responsible AI integration in rare disease care.
Key words: artificial intelligence, ChatGPT, inclusion body myositis, exercise prescription, physiotherapy, patient safety

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A PILOT STUDY TO EVALUATE THE EFFICACY OF AN AT-HOME THERAPUTTY® HAND EXERCISE INTERVENTION ON STRENGTH AND FUNCTION IN ADULTS WITH INCLUSION BODY MYOSITIS (IBM)

Ian Cooper[1,2], Matthew Archer[3], Raoul Oehmen[3], Alethea Doverty[1,2], Annik Panicker[1,2], Nataliya Slater[1,2], Merrilee Needham[1,2,3,4]
[1]*Perron Institute, Perth, Australia,* [2]*Murdoch University, Perth, Australia,* [3]*University of Notre Dame Australia, School of Medicine, Fremantle, Australia,* [4]*Fiona Stanley Hospital, Perth, Australia*

Background. Inclusion body myositis (IBM) is the most common idiopathic inflammatory myopathy after age 50, leading to progressive weakness of quadriceps and finger flexors. Weakness of the flexor digitorum profundus, flexor digitorum superficialis, and flexor pollicis longus markedly impairs grip and fine motor control, leading to functional loss and independence. With no effective disease-modifying therapies, accessible non-pharmacological strategies are needed. Exercise is safe, may slow disease progression and improve strength. However, most studies focus on lower limb strengthening, with few studies examining hand strength and function. This pilot study analysed the acceptability, tolerability and efficacy of an at-home TheraPutty® hand exercise intervention on grip strength and upper limb function in adults with IBM.
Methods. In this 12-week, single-arm pilot study, thirteen participants with a confirmed diagnosis of IBM were recruited to participate in a 12 week at home structured exercise programme, three times per week. The protocol required fortnightly increases in the number of repetitions and at 6 weeks a change in TheraPutty® resistance. Each participant underwent baseline, 6-week, and 12-week assessments of grip/pinch strength (hand-held dynamometry), dexterity (Nine-Hole Peg Test, Box and Block Test), and function (IBM Functional Rating Scale, Duruöz Hand Index). Use of intention-to-treat and per-protocol approaches assessed the effect of adherence on strength outcomes. Adherence (≥75% sessions), acceptability, and tolerability were assessed through weekly diaries and an end-of-study questionnaire.
Results. Thirteen participants (mean age 72.1 ± 11.4 years; 69% male) completed the study. Nine participants (69%) achieved ≥75% adherence. Intention-to-treat analysis showed no significant changes in grip or pinch strength, although Box and Block performance improved significantly bilaterally (p<0.01). In the per-protocol analysis, significant improvements

were observed in non-dominant 2-point (p=0.023) and bilateral 3-point pinch strength (p=0.049 and 0.010 respectively). No significant changes were found in DHI or IBMFRS scores. Mean Borg exertion was 13.9 ("somewhat hard"), indicating appropriate intensity. Overall programme acceptability and tolerability were rated positively (mean Likert scores = 3.52 ± 0.65 and 3.37 ± 0.80, respectively). Fatigue, pain, and difficulty using even the lowest resistance TheraPutty® limited adherence.
Conclusions. A home-based TheraPutty® programme was feasible, safe and generally acceptable by people with IBM, with potential benefits in adherent participants. Improvements in pinch measures were positively noted against a background of progressive degenerative weakness. Fatigue and difficulty with putty resistance highlight the need for individualized progression and softer resistance. Future larger, longer-term studies should refine treatment protocols to reduce fatigue and optimise efficacy.
Key words: myositis, inclusion body, sporadic, exercise therapy hand strength, theraputty

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INTEGRATING DIGITAL TECHNOLOGY IN EXERCISE IN MYOSITIS AND INTRODUCTION OF A NEW MOBILE-EXERCISE APP, MYORXERCISE

Seon Kyung Nam[1], Shivam Pathak[2], Hannah Zhang[2], Jolina Zhao[2], Mac Ajwani[2], Ankhi Banerjee[2], Ashley Niu[2], Hemesh Chadalavada[2], Joel Villarino[2], Nhi Quach[2], Pradyun Chebolu[2], Simar Rajpal[2], Tom Yuan[2], Helene Alexanderson[3], Suur Biliciler[1]
[1]University of Texas Health Science Center at Houston, Houston, USA, [2]Rice University, Houston, USA, [3]Karolinska Institutet and Department of Medicine, Stockholm, Sweden

Background. Idiopathic Inflammatory Myopathy (IIM) is a group of autoimmune conditions that encompasses dermatomyositis, inclusion body myositis (IBM), immune-mediated necrotizing myopathy, and overlap myositis, which significantly impairs patients' mobility and reduces quality of life. While aerobic and resistance exercises are recognized as safe and effective for patients, access to tailored rehabilitation resources remains limited. Most of the data on exercise in myositis is on IBM, and exercise regimens tailored to each subtype of inflammatory myopathy are yet to evolve. We developed a new mobile exercise app, MyoRxercise, which delivers personalized exercise programs to patients with IIM. The app offers a novel opportunity for remote diagnosis, monitoring, and treatment of patients.
Methods. A targeted literature search was conducted across PubMed and PMC databases to identify gaps in exercise among myositis patients and to inform the development of a free digital technology for IIM patients to monitor their disease and facilitate treatment.
Results. Digital health tools, including mobile applications, wearable devices, and online platforms, are increasingly utilized in the management of IIM, offering the potential to enhance access to care. Existing mobile applications for IIM offer general education, symptom tracking, and medication reminders, but few provide myositis-specific exercise guidance. Wearable technology, which reliably measures metrics such as daily step count, peak 1-minute cadence, and vector magnitude, has been shown to correlate moderately to strongly with validated measures of myositis disease activity, including manual muscle testing (MMT), physician and patient global disease activity, and functional tests. Although current literature supports the use of wearable devices, mobile apps, and online training prescriptions to supplement the care of myositis patients, there is a lack of myositis-specific mobile exercise tools. In response to existing gaps in digital tools in managing myositis patients, our team, in collaboration with the Karolinska Institute and Rice University, developed MyoRxercise. This mobile exercise app aims to deliver personalized exercise programs to patients with IIM. The platform features several instructional videos, customizable routines by disease subtype, progress tracking, and clinician connectivity to promote data-driven, individualized exercise rehabilitation.
Conclusions. Most of the data on exercise in IIM is on IBM. There is a need for specific exercise regimens for each myositis subtype, as well as for individual patients. Mobile apps represent a valuable and evolving toolset for myositis treatment. They provide easy accessibility and reach patients in rural areas. With the help of MyoRxercise, we plan to develop and validate individualized exercise regimens for different subtypes of myositis.
Key words: exercise, digital tool, mobile app

P-310

PERSONALIZED REHABILITATION IN SEVERELY FATIGUED MYOSITIS PATIENTS (PRO-FIT): STUDY PROTOCOL OF A PILOT RANDOMIZED CONTROLLED TRIAL

Nienke Heida[1,2], Joost Raaphorst[3], Hans Knoop[4], Annerieke van Groenestijn[1,2], Nicole Voet[5], Johanna van Dongen[6], Frans Nollet[1,2], Eric Voorn[1,2]
[1]Amsterdam UMC location University of Amsterdam, Department of Rehabilitation Medicine, Amsterdam, The Netherlands, [2]Amsterdam Movement Sciences, Rehabilitation & Development, Amsterdam, The Netherlands, [3]Department of Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam Neuroscience, Amsterdam, The Netherlands, [4]Department of Medical Psychology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands, [5]Rehabilitation Center Klimmendaal and Radboud University Medical Center, Arnhem and Nijmegen, The Netherlands, [6]Department of Health Sciences, Faculty of Science, Amsterdam Public Health Research Institute, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

Background. Despite initial benefits of immunosuppressive treatment, many patients with myositis (70-90%) suffer from severe fatigue. Fatigue reduces daily functioning, participation, and quality of life, and leads to a three- to five-fold increase in healthcare and societal costs. We aim to examine, in a pilot randomized controlled trial, the (cost-)effectiveness of personalized rehabilitation therapy, including remotely delivered cognitive behavioral therapy (CBT), exercise therapy (ET), or both, compared with usual care in myositis patients in the chronic phase (without apparent disease activity).
Methods. This multicenter trial randomly assigns (1:1 ratio) twenty participants (aged 18–68, with myositis excluding inclusion body myositis, without apparent disease activity, with severe fatigue, defined as a score ≥35 on the fatigue subscale of the Checklist Individual Strength (CIS-Fatigue)) to the intervention group (6-month personalized rehabilitation therapy) or control group (usual care). Treatment (ET, CBT, or both) is tailored through multidisciplinary consultation involving a rehabilitation physician, physiotherapist, and psychologist. The primary endpoint is the change in daily functioning, measured by the Canadian Occupational Performance Measure (COPM). Secondary outcomes include exercise testing, questionnaires, and activity monitoring.
Results. Twenty participants (17 females; mean age 51.5 years (SD 10.7)) have been randomized; baseline data have been collected between July 2024 and July 2025. The enrollment rate was 44% (20 out of 45 eligible participants). Baseline assessments showed a mean COPM performance score of 5.1 ± 1.3 (range 1–10, higher scores indicating better performance), mean CIS-Fatigue score of 43.9 ± 5.9, VO_2 peak of 20.8 ± 8.5 ml/min/kg, Manual Muscle Testing score (0–260) of 255.2 ± 6.5, and creatine kinase level of 179.8 ± 187.8 U/L. In the intervention group (n=10), eight participants were assigned to a combination of CBT and ET, while one was assigned to ET alone and one to CBT alone. To date, eight participants have completed the post-intervention assessments.
Conclusions. The trial is ongoing. At baseline, participants showed limitations in daily functioning and low physical fitness (VO_2 peak values below 20 ml/min/kg, a level associated with impaired independence). Recruitment took longer than expected due to difficulties enrolling disease-inactive participants (recent changes in immunosuppressive medication) or because participants found the study was too burdensome. Final results, expected in 2026, will provide insight into the feasibility and potential effectiveness of personalized rehabilitation in severely fatigued myositis patients and will inform future larger trials and clinical practice.
Key words: myositis, rehabilitation, fatigue

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FATTY ACID BINDING PROTEIN 3 (FABP-3) IS A POTENTIAL MEDIATOR OF MUSCLE DAMAGE IN INFLAMMATORY MYOPATHIES AND ITS SERUM LEVEL DECREASE IN RESPONSE TO A HIGH INTENSITY EXERCISE PROGRAM

Léa Debrut[1,2], Quentin Toumazeau[1], Giulia Quiring[1], Pauline Silverstrin[1], Alizée Heit[1], Anne-Laure Charles[1], Bernard Geny[1,3], Alain Meyer[1,4], Margherita Giannini[1,4]

[1]UR3072 Research Centre of Biomedecine Strasbourg, University of Strasbourg, France, [2]Faculty of Sport Sciences, European Centre for Education, Research and Innovation in Exercise Physiology (CEERIPE), University of Strasbourg, Strasbourg, France, [3]Physiology and Function Explorations Department, Strasbourg University Hospitals, France, [4]Physiology and Muscle Function Explorations Department, Referral Centre for Systemic Rare Autoimmune Diseases, Strasbourg University Hospitals, France

Background. Inflammatory myopathies (IM) are autoimmune diseases characterized by chronic skeletal muscle inflammation and weakness. In many patients, disability persists despite remission or low disease activity under immunosuppressants. This condition, termed 'damage', is frequent and correlates with disability and mortality. Although no pharmacological treatment exists, combined resistance and endurance training improves patient-reported outcomes (PRO), muscle strength and aerobic capacity (1). We showed that elevated fatty-acid binding protein 3 (FABP3) serum levels correlates with IMACS muscle damage scores in inactive IM patients (2), suggesting a role for FABP3 in IM damage pathophysiology and its potential as a biomarker.

This study investigates whether combined resistance and endurance training in IM patients with damage modify circulating FABP3 levels.

Methods. Fifty IM patients (2017 EULAR/ACR criteria) with disease duration >12 months, creatine kinase <500IU/L and stable medication for ≥6 months, were prospectively enrolled in a 12-week combined resistance and endurance training protocol: 3 sessions/week composed by 30min of aerobic exercise (70% VO_2max) followed by 20min of resistance exercise (30–40% max strength) (1).

PRO, exercise capacity, muscle strength and serum FABP3 levels were recorded at baseline and post-training.

Results. Twenty-five patients completed the protocol (15 women and 10 men; age: 59.7±17years; disease duration: 12.6±5.9years). At baseline, FABP3 serum levels did not differ by sex. Training significantly improved PRO, exercise capacity and muscle strength, while reducing FABP3 serum levels (Δ=-425.6±829.3pg/mL, p=0.025).

At baseline, FABP3 levels correlated with i) exercise capacity (VO2max: R=-0.46, p=0.021; 6-min walk test R=-0.41, p=0.034), ii) muscle strength (MMT-8: R=-0.42, p=0.038; grip strength: R=-0.38, p=0.069), and iii) muscle extent and severity MDI (both R=0.52, p=0.022), but not with PRO (HAQ: R=0.17, p=0.40; PROMIS20: R=0.28, p=0.16).

After training, FABP3 levels remained correlated with i) exercise capacity (VO2max: R=-0.49, p=0.017; 6-min walk test: R=-0.67, p=0.0005), ii) muscle strength (MMT-8: R=-0.49, p=0.018; grip strength: R=-0.50, p=0.015), and iii) muscle extent and severity MDI (respectively: R=0.53, p=0.03; R=0.64, p=0.005). Post-training FABP3 levels correlated with HAQ (R=0.57, p=0.006).

Conclusions. FABP3 serum levels is a biomarker of muscle damage, and its reduction is associated with the response to a combined resistance and endurance training program. Knowing the role of FABP3 in the transport of fatty acids to mitochondria, this myokine might contribute to damage maintenance in IM.

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P-375

PHYSICAL FUNCTION AND PATIENT-REPORTED OUTCOMES FOLLOWING A 16-WEEK EXERCISE INTERVENTION IN PATIENTS WITH INCLUSION BODY MYOSITIS: RESULTS FROM A FEASIBILITY STUDY

Skattør M.[1], Nilsson U.[1], Alexanderson H.[2,3], Brovold T.[4], Andersson H.[1], Risum K.[1,4]

[1]Oslo University Hospital, [2]Karolinska University Hospital, [3]Karolinska Institutet, [4]Oslo Metropolitan University

Background. Inclusion Body Myositis (IBM) is a rare, progressive inflammatory myopathy with limited treatment options. Strength and balance exercises may help preserve muscle strength and physical function, but evidence in IBM is limited.

Methods. Fifteen patients with IBM participated in a 16-week intervention consisting of one weekly supervised group-based session at Oslo University Hospital and one home-based session per week, both including strength and balance exercises. Physical function was assessed using the Manual Muscle Test-8 (MMT-8), grip strength, 30-second sit-to-stand test, Functional Index-3 (FI-3), 2-minute walk test (2MWT), and Berg Balance Scale. Patient-reported outcomes (PROMs) included the Inclusion Body Myositis Functional Rating Scale (IBMFRS), Health Assessment Questionnaire (HAQ), Patient-Specific Functional Scale (PSFS), and International Physical Activity Questionnaire (IPAQ). Pre- and post-intervention scores were compared using Wilcoxon signed-rank tests.

Results. Of the 15 included patients, thirteen patients completed the intervention. Two patients withdrew after baseline assessments due to back pain and transportation challenges. The median age was 71.7 years (IQR 66.8–72.9), and 54% were male. Statistically significant improvements were observed in grip strength, with the right hand increasing from median 22.0 lbs (IQR 19.0–32.3) to 23.7 lbs (20.2–34.2) (p=0.004), and the left hand from 16.7 lbs (11.4–25.5) to 19.0 lbs (14.0–32.4) (p=0.003). The number of repetitions in the 30-second sit-to-stand test increased from 8.0 (0.0–11.0) to 9.0 (2.0–13.5) (p=0.004). Participants also reported a significant increase in moderate-to-vigorous physical activity, from 100 minutes per week (53–440) to 225 minutes (110–585) (p=0.02).

Additionally, walking time increased from 60 minutes per week (IQR 5–260) to 210 minutes (54–420) (p = 0.06), and time spent sitting decreased from 600 minutes per day (450–750) to 420 minutes (315–720) (p=0.07). Other outcomes, including MMT-8, FI-3, 2MWT and Berg Balance Scale, remained unchanged or showed trends toward improvement without reaching statistical significance. PROMs such as IBMFRS, HAQ, and PSFS showed minimal changes.

Conclusions. The exercise intervention was associated with statistically significant improvements in grip strength, lower limb function, and physical activity levels. However, some of the observed changes were small and may be influenced by measurement variability. Trends toward increased walking time and reduced sedentary behavior suggest potential benefits of individualized strength and balance training for patients with IBM, but further research is needed to confirm clinical relevance.

Acknowledgements. This study was funded by Foundation Dam. We thank all participating patients.

Key words: inclusion body myositis, exercise, experiences

Extra-Muscular Organ Involvement

P-10

KL-6 PREDICTS INTERSTITIAL LUNG DISEASE AND PROGRESSION IN IDIOPATHIC INFLAMMATORY MYOPATHIES: A ONE-YEAR COHORT WITH SERIAL HRCT AND PULMONARY FUNCTION TESTING

Jorge Álvarez Troncoso[1], Elena Martínez Robles[1], Luis Gómez Carrera[2], Clara Soto Abánades[1], Ana Noblejas Mozo[1], Ángel Robles Marhuenda[1], Belén Gutiérrez Sancerni[1], Sergio Carrasco Molina[1], Isabel Esteban Rodríguez[3], Pilar Nozal Aranda[4], Juan José Ríos Blanco[1]
[1]Internal Medicine Department, Hospital Universitario La Paz, Madrid, Spain, [2]Pulmonology Department, Hospital Universitario La Paz, Madrid, Spain, [3]Pathology Department, Hospital Universitario La Paz, Madrid, Spain, [4]Immunology Department, Hospital Universitario La Paz, Madrid, Spain

Background. KL-6, a MUC1 mucin secreted by injured type II pneumocytes, reflects alveolar damage and fibrotic remodeling. In idiopathic inflammatory myopathies (IIM), interstitial lung disease (ILD) drives morbidity and mortality, yet accurate biomarkers of activity and progression remain limited. We evaluated the diagnostic and longitudinal performance of KL-6 in relation to pulmonary function and HRCT over one year.
Methods. Consecutive IIM patients with ILD or at high ILD risk were prospectively evaluated at baseline (TP-1) and one year (TP-2) with serum KL-6, pulmonary function tests (PFTs) (FVC, DLCO, KCO, TLC), and high-resolution computed tomography (HRCT). HRCT abnormalities were recorded as binary variables and categorized by predominant pattern. Statistical analyses included Spearman correlations, Mann-Whitney and ROC analyses for ILD discrimination, and multivariable and mixed-effects models to assess independent and longitudinal associations.
Results. Forty-seven patients were analyzed (85.1 % women; median age 55.9 years). Antisynthetase antibodies were most frequent (53.2%; anti-Jo-1, PL-12, PL-7, EJ, OJ), followed by Ku, PM/Scl, and MDA5. Baseline ILD prevalence was 51.1%, with NS-0.556, p<0.001) and KCO (ϱ = -0.474, p=0.0007); these strengthened at one year (DLCO ϱ = -0.711, p<0.001; KCO ϱ = -0.539, p=0.0038). The correlation with FVC was weaker (ϱ = -0.438, p=0.003). KL-6 rose in parallel with HRCT findings of ground-glass opacities, subpleural and septal thickening, and bronchiectasis, mirroring functional decline and fibrotic remodeling. Baseline KL-6 predicted ILD presence at follow-up (ϱ = 0.582, p=0.001) and ILD progression (ϱ = 0.404, p=0.005). Patients exceeding 500 U/mL had significantly lower DLCO (median 71.5% *vs*. 93.2%, p<0.001), higher KL-6 trajectories, and greater fibrotic extension on HRCT. The optimal Youden cut-off for baseline ILD was 500 U/mL (sensitivity 71%, specificity 91%; AUC 0.889), whereas 620 U/mL best predicted progression (sensitivity 55%, specificity 79%).
Conclusions. KL-6 demonstrated excellent diagnostic accuracy and reproducible longitudinal performance, bridging epithelial injury, diffusion impairment, and structural lung disease. Its robust correlation with both physiologic and radiologic domains highlights KL-6 as an integrative marker of ongoing pulmonary damage. Routine serial KL-6 testing alongside PFTs and HRCT may refine early ILD recognition, identify high-risk trajectories, monitor therapeutic response, and provide a reliable, quantifiable endpoint for personalized intervention and multicenter clinical trials in IIM-associated ILD.
Key words: KL-6, idiopathic inflammatory myopathies, interstitial lung disease, HRCT, DLCO, biomarkers

P-22

ANTI-SYNTHETASE SYNDROME (ASYS) RELATED INTERSTITIAL LUNG DISEASE (ILD) IS ASSOCIATED WITH DISTINCT PHENOTYPE AND POOR PROGNOSIS AS COMPARED TO OTHER ILDS: CLASSIFICATION CRITERIA FOR ANTI-SYNTHETASE SYNDROME (CLASS) PROJECT ANALYSIS

Sangmee Bae, Francisca Bozán, Daphne Rivero-Gallegos, Giovanni Zanframundo, Eduardo Dourado, Akira Yoshida, Iazsmin Bauer Ventura, Sara Faghihi-Kashani, Aravinthan Loganathan, Gianluca Sambataro, Francesco Bonella, Tamera Corte, Tracy Doyle, David Fiorentino, Miguel Gonzalez-Gay, Marie Hudson, Masataka Kuwana, Antonella Notarnicola, Andrew L. Mammen, Neil McHugh, Fredrick W. Miller, Carlomaurizio Montecucco, Chester V. Oddis, Jorge Rojas-Serrano, Jens Schmidt, Carlo Scire, Albert Selva-O'Callaghan, Victoria Werth, Domenico Sambataro, Carlo Vancheri, Santos Castañeda, Matthew Parker, Mayra Mejia, Lorenzo Cavagna, Rohit Aggarwal
[1]UCLA Rheumatology, Los Angeles, USA

Background. To describe the characteristics of anti-synthetase syndrome (ASyS)-related ILD (ASyS-ILD) in comparison to non-ASyS-related ILD.
Methods. We utilized an international, real-world physician-reported database to identify patients with ASyS-ILD (cases) and ILD related to other causes (controls). Demographic, clinical, radiographic, physiological data as well as hospitalization and all-cause mortality were compared between cases and controls. Comparisons were also performed with ILD disease subgroups.
Results. Among 2,385 ILD patients (1,557 ASyS-ILD, 828 controls), ASyS-ILD cases were younger, had more acute onset, and were more often symptomatic. Nonspecific interstitial pneumonia (NSIP) was the most common radiological pattern across all groups, which was 55% in ASyS-ILD followed by organizing pneumonia (OP, 19%). Among ILD patients with dermatomyositis (DM), both those with and without MDA5 antibodies, NSIP (53% and 64%, respectively) was followed by OP (32% and 11%). ILD in rheumatoid arthritis (RA) and systemic sclerosis (SSc) had NSIP (39%, 59%) followed by usual interstitial pneumonia (UIP, 36%, 14%). Compared with controls, ASyS-ILD had higher odds of hospitalization (OR 1.81, 95%CI 1.38-2.37) and higher all-cause mortality (HR 1.66, 95%CI 1.03–2.66). Five-year survival in ASyS-ILD was 94.7%. By comparison, 5-year survival was 97.4% in SSc-ILD, 97.3% in RA-ILD, 94% in IPAF, 93.5% in DM-nonMDA5-ILD and 90.3% in MDA5-ILD. Age-adjusted Cox proportional hazard models showed MDA5-ILD trended towards higher mortality compared to ASyS-ILD (HR 2.42 [0.88-6.68], p=0.13). SSc-ILD had significantly lower all-cause mortality than ASyS-ILD (HR 0.24 [0.06-0.99], p=0.047). Other control ILD subgroups were not significantly different from ASyS-ILD; DM-nonMDA5 (HR 1.29 [0.41-4.11], p=0.66), RA-ILD (HR 0.33 [0.10-1.08], p=0.06), and IPAF (HR 0.46 [0.16-1.28], p=0.14).
Conclusions. ASyS-ILD has younger, more acute onset, symptomatic ILD compared to control ILDs. ASyS-ILD has more hospitalizations and worse all-cause mortality than control ILDs. Further work is needed to identify early predictors of adverse outcomes in ASyS-ILD.
Acknowledgements. This research was generated using the Classification Criteria for Anti-Synthetase Syndrome (CLASS) project database which was funded by ACR and EULAR for the purpose of creating the Anti-Synthetase Syndrome classification criteria.
Key words: antisynthetase syndrome, interstitial lung disease

P-40

LUNG TRANSPLANT OUTCOMES IN PATIENTS WITH MYOSITIS- AND SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE COMPARED TO IDIOPATHIC PULMONARY FIBROSIS: A MULTICENTER RETROSPECTIVE ANALYSIS

Navid Saleh[1], Angela Chang[1], Alec Yu[1], Darya Jalaledin[2], Sabrina Hoa[2], Robert Levy[1], Jennifer Wilson[1], Charles Poirier[2], James Choi[1], John Yee[1], Océane Landon Cardinal[2], Hyein Kim[1], Kun Huang[1]
[1]University of British Columbia, Vancouver, Canada, [2]Centre Hospitalier de l'Université de Montréal, Montreal, Canada

Background. Lung transplantation is an option for idiopathic inflammatory myopathies (IIM)-associated interstitial lung disease (ILD) when refractory to medical treatment, but outcomes lack comparison to other diseases like systemic sclerosis (SSc) or idiopathic pulmonary fibrosis (IPF). We performed a multicenter retrospective study to compare post-transplant outcomes between IIM, SSc, and IPF patients.
Methods. ILD patients with IIM, SSc, and IPF who underwent lung transplantation (2012–2024) were identified at two Canadian centers, Vancouver General Hospital and at the Centre Hospitalier de l'Université de Montréal. Clinical, laboratory, radiographic, and pathological data were retrospectively reviewed. The primary outcome was long-term survival from transplantation to death or last follow-up.
Results. Of 118 patients (22 IIM, 32 SSc, 64 IPF), IIM subtypes included anti-MDA5 DM (45%), antisynthetase syndrome (32%), overlap myositis (14%), and other DM (9%). In SSc, 88% had pulmonary hypertension (28%

severe). IIM and SSc patients were younger, more often female, and had fewer comorbidities than IPF patients. Immunosuppressive therapy was more common in IIM/SSc, while antifibrotics were more frequent in IPF.
IIM patients more frequently required ICU admission, mechanical ventilation, ECMO, and emergency transplantation (50% due to RP-ILD, predominantly anti-MDA5 DM) than IPF. Post-transplant, patients with IIM and SSc required prolonged ICU stays compared to those with IPF (median durations: 33 days for IIM, 9 days for SSc, and 4 days for IPF). Similarly, the median total hospitalization duration was longer for IIM patients (59 days for IIM, 31 days for SSc, and 22 days for IPF). One-year survival was similar (IIM 91%, SSc 84%, IPF 92%). At the last available post-transplant follow-up (median: 2.8 years for IIM, 2.5 years for SSc, and 3.6 years for IPF), Kaplan-Meier analysis showed no differences in overall survival. Subgroup analyses of IIM (stratified by transplant urgency, ECMO support, and amyopathic subtype) and SSc (stratified by severe PH, esophageal dysmotility, and transplant urgency) showed no significant differences in long-term survival. Rates of CLAD and malignancy were similar, and no autoimmune disease recurrence was observed in IIM or SSc patients post-transplant.
Conclusions. Despite their underlying systemic autoimmune rheumatic diseases, post-transplant survival outcomes of IIM and SSc patients are comparable to those with IPF. However, their pre- and post-transplant courses are more complex, highlighting the need for tailored lung transplant strategies and multidisciplinary management in patients with IIM- and SSc-associated ILD.
Key words: idiopathic inflammatory myositis, autoimmune myopathy, systemic sclerosis, scleroderma, interstitial lung disease, lung transplant, transplant outcome, survival

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CLINICAL CHARACTERISTICS AND EVOLUTION OF INTERSTITIAL LUNG DISEASE IN SUBTYPES OF IDIOPATHIC INFLAMMATORY MYOSITIS PATIENTS WITH PREVALENT LUNG MANIFESTATION: A RETROSPECTIVE ANALYSIS

Julia Clark[1], Damon Dhillon[1], Jan Dutz[1], Gillian Goobie, Kun Huang[1]
[1]University Of British Columbia, Vancouver, Canada

Background. Interstitial lung disease (ILD) is a frequent manifestation of idiopathic inflammatory myositis (IIM), serving as a primary driver of morbidity and mortality. It is particularly prevalent in specific clinical subtypes, including antisynthetase syndrome (ASyS), anti-melanoma differentiation-associated protein 5 (MDA5) dermatomyositis (DM), and scleromyositis. A challenging clinical scenario arises when pulmonary fibrosis continues to progress insidiously despite the successful resolution of muscular and cutaneous disease activity. This phenomenon, which we term post-myopathic progressive pulmonary fibrosis (PmPPF), remains poorly characterized. Our study aims to delineate the longitudinal trajectories of ILD within these key IIM subgroups, with a specific focus on understanding the incidence, risk factors, and outcomes associated with PmPPF.
Methods. We conducted a retrospective cohort study reviewing the medical records of IIM patients from a British Columbia myositis clinic database between 2019 and 2024. Eligible patients had a confirmed diagnosis of ASyS, anti-MDA5+ DM, or scleromyositis. Collected data included detailed demographics, autoantibodies, immunosuppressive regimens, radiological patterns, and longitudinal pulmonary function trends to define ILD progression and the PmPPF state.
Results. A total of 111 patients with ASyS, anti-MDA5+ DM, and scleromyositis were identified (median age 51, median follow-up 35.5 months). ILD prevalence was highest in ASyS (87.5%), followed by anti-MDA5+ DM (84.6%) and scleromyositis (65.5%). PmPPF was identified in 13.5% of the entire cohort, occurring predominantly in anti-MDA5+ DM (19.2%) and ASyS (16.1%) patients, but was absent in the scleromyositis subgroup. Patients who developed PmPPF had significantly higher rates of historically active disease (46.7% *vs*. 9.3%, p=0.002), rapidly progressive (RP) ILD onset (33.3% *vs*. 5.3%, p=0.006), and subsequent lung transplantation (20% *vs*. 1.3%, p=0.014). Intriguingly, anti-MDA5+ DM exhibited the highest disease remission rate (88.5%) yet also the highest transplant requirement (11.5%). Radiologically, an organizing pneumonia (OP)/non-specific interstitial pneumonia (NSIP) overlap pattern on HRCT was more common in the PmPPF group (33.3% *vs*. 9.3%, p=0.03). PmPPF showed a non-significant trend toward higher mortality (20% *vs*. 4%, p=0.06), and was treated more frequently with rituximab (73.3% *vs*. 37.3%, p=0.02).
Conclusions. This study elucidates distinct ILD patterns across three IIM subtypes. The entity of PmPPF is a significant clinical outcome, particularly in ASyS and anti-MDA5+ DM, characterized by a severe disease course and high resource utilization. The persistence of progressive fibrosis independent of extra-pulmonary disease activity underscores that ILD can follow a decoupled and autonomous trajectory. These findings highlight the imperative for ongoing, vigilant pulmonary monitoring even after systemic disease control is achieved.
Key words: inflammatory myositis, interstitial lung disease, antisynthetase syndrome, anti-MDA5, scleromyositis

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ELECTROCARDIOGRAM ABNORMALITIES IN PATIENTS WITH NEW-ONSET MYOSITIS

David Makari[3], Fabricio Espinosa Ortega[1,2], Ingrid Lundberg[1,4], Daniel Andersson[3]
[1]Department of Medicine Solna, Karolinska Institutet, Sweden, [2]ME Gastro, Dermatology and Rheumatology, Theme Inflammation and Aging, Karolinska University Hospital, Sweden, [3]Department of Physiology and Pharmacology, Karolinska Institutet, Sweden, [4]Center for Molecular Medicine, Karolinska University Hospital, Sweden

Background. Patients with idiopathic inflammatory myopathies (IIM) may develop heart disease ranging from subclinical cardiac abnormalities to severe myocarditis and arrythmias (1). Electrocardiographic abnormalities have been reported in IIM (2), but data on patients with new-onset disease are scarce. The objective of this study was to characterize ECG abnormalities in patients with new-onset IIM.
Methods. Thirty-two consecutive patients with new-onset myositis and ten with established disease were enrolled at Karolinska University Hospital (March 2017 - November 2021. Measurements of PQ, QRS, QTc (according to Bazett's formula) intervals, QTc ≥450 ms (prolonged) were assessed. Notching and slurring were defined as irregularities of the QRS contour (notches or smooth transitions on its upstroke/downslope) (3). Group comparisons for the new-onset *vs*. established disease phase, steroid-treated *vs*. untreated acute patients, with and without previous myocardial infarction, and of myositis autoantibody-status. Multivariable linear regression adjusted for common explanatory factors was used to assess the association with between ECG abnormalities and serum troponin T and N-terminal pro-brain natriuretic peptide, NT-proBNP.
Results. Two new-onset patients had a PQ interval >200 ms and another 2 new-onset patients had left bundle branch block (QRS >120 ms); no previous coronary artery disease in both 2 groups. Twelve patients (28%) had elevated NT-pro-BNP. QTc showed a moderate correlation with levels of NT-pro-BNP (r=43, p=0.034). No differences on QTc depending on age, disease phase, sex, or autoantibody-status (anti- Jo1, -HMGCR, -PL12, or -Ro52) were found. Moreover, QTc was associated with levels of NT-pro-BNP (beta 11.35, p=0.04) independently of sex, age, renal function, prednisolone treatment, and previous myocardial infarction. Prolonged QTc was found in 27% of patients (n=10). The frequency of notching and slurring was comparable between new-onset and established disease groups, yet, substantially higher than expected from the background population.
Conclusions. Levels of NT-pro-BNP showed a positive correlation with QTc even in patients with new-onset disease. Moreover, this association remained after adjusting for common explanatory factors. Our findings suggest abnormal ventricular repolarization together with overload ventricular stress in patients with new-onset diagnosis and no pharmacological treatment. Our study supports the importance of ECG screening in patients with now onset myositis.
Key words: idiopathic inflammatory myopathies, electrocardiography, cardiac involvement

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INTERSTITIAL LUNG DISEASE IN SYSTEMIC AUTOIMMUNE RHEUMATIC DISEASES: RADIOLOGIC AND HISTOLOGIC CORRELATIONS

Aidan Pye[1], Darya S. Jalaledin[2], Angela Chang[1], Navid Saleh[1], Saud AlHajer[1], Béatrice Daviault[2], Arusa Shah[2], Sabrina Hoa[2,3], Alec Yu[1], Robert D. Levy[4], Jennifer M. Wilson[4], Charles D. Poirier[5], James Choi[6], John Yee[6], Océane Landon-Cardinal[2], Hyein Kim[3,7], Kun Huang[3,7,8]
[1]Department of Medicine, University of British Columbia, Vancouver, Canada, [2]Division of Rheumatology, Centre Hospitalier de l'Université de Montréal, Montreal, Canada, [3]Arthritis Research Canada, Vancouver, Canada, [4]Division of Respirology, Vancouver General Hospital, Vancouver, Canada, [5]Lung Transplant Program, Centre hospitalier de l'Université de Montréal, Montreal, Canada, [6]Division of Thoracic Surgery, Vancouver General Hospital, Vancouver, Canada, [7]Division of Rheumatology, University of British Columbia, Vancouver, Canada, [8]Surrey Memorial Hospital, Surrey, Canada

Background. High resolution CT (HRCT) guides clinical diagnosis in systemic autoimmune rheumatic disease associated interstitial lung disease (SARD-ILD). Histologic confirmation by lung biopsy is not commonly done or recommended. We evaluated the agreement between HRCT patterns and explant pathology in SARD-ILD patients undergoing lung transplantation.
Methods. We retrospectively analyzed idiopathic inflammatory myopathy (IIM), systemic sclerosis (SSc), and rheumatoid arthritis (RA)-ILD patients who underwent double lung transplant at two Canadian centers. HRCT-histology agreement was assessed using weighted kappa (κ) statistics: complete (identical diagnoses, κ=1), partial (*e.g.* non-specific interstitial pneumonia (NSIP) *vs*. NSIP/usual interstitial pneumonia (UIP), κ=0.5), or no agreement (κ=0). Results were visualized via Alluvial step-by-step diagrams.
Results. Among 82 patients (22 IIM, 32 SSc, 28 RA) who underwent lung transplant, RA patients were older, more often smokers, and less frequently female than IIM/SSc. IIM patients most commonly required emergency transplantation (50% *vs*. 19% for SSc and 36% for RA). Among the 22 IIM patients, the subtypes included: anti-MDA5-positive dermatomyositis (DM) (n=10), antisynthetase syndrome (n=7), overlap myositis (n=3), and seronegative DM (n=2). Rapidly progressive ILD was the transplant indication in 50% of IIM cases. For the 32 SSc patients, ILD was the primary transplant indication. Concomitant pulmonary hypertension was present in 28 patients (88%). Initial HRCT showed NSIP predominance in IIM (59%) and SSc (81%), while UIP dominated in RA (57%). An organizing pneumonia (OP) pattern was observed in 23% of IIM cases but was rare in RA (4%) and absent in SSc. UIP patterns were identified in 9% of both IIM and SSc patients on HRCT. Immediately prior to transplant, a notable proportion of IIM patients (27%) exhibited an evolution to a diffuse alveolar damage (DAD) pattern on HRCT. In contrast, SSc and RA patients largely maintained HRCT patterns consistent with their initial diagnosis. Explant pathology revealed NSIP as the primary pattern in SSc (62%) and UIP in RA (50%). IIM explants exhibited diverse histopathology without dominance. Anti-MDA5+ DM patients universally developed rapidly progressive ILD, progressing to DAD or end-stage fibrosis despite initial NSIP on HRCT. Using weighted κ analysis, we observed moderate HRCT-histology concordance in RA (κ=0.46, p=0.002), fair but non-significant agreement in SSc (κ=0.31, p=0.06), and no meaningful correlation in IIM (κ=0.07, p=0.6).
Conclusions. SSc-ILD and RA-ILD demonstrated fair-to-moderate HRCT-histology correlation, whereas IIM-ILD shows marked histologic heterogeneity independent of imaging patterns. Anti-MDA5+ disease consistently exhibited aggressive progression, underscoring the limitations of HRCT in predicting IIM-ILD pathology.
Key words: myositis, interstitial lung disease, systemic sclerosis, rheumatoid arthritis, pathology, lung explant, lung transplant, radiology

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OBJECTIVE EVALUATION OF GASTROINTESTINAL INVOLVEMENT IN ANTI-SYNTHETASE SYNDROME

Clara Edo-Fernández[1], Albert Gil-Vila[1,2], Ernesto Trallero-Araguás[3], Carolina Malagelada[2,4], Francisco Felix-Tellez[2,4], Luis G. Alcalá-Gonzalez[2,4], Albert Selva-O'Callaghan[1,2]
[1]Systemic and Autoimmune Diseases Unit, Internal Medicine. Vall d'Hebron University Hospital, Barcelona, Spain, [2]Department of Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain, [3]Rheumatology Department. Vall d'Hebron University Hospital, Barcelona, Spain, [4]Digestive System Research Unit, Vall d'Hebron University Hospital, Barcelona, Spain

Background. Anti-synthetase syndrome (ASyS) is a rare autoimmune disorder characterized by the presence of anti–aminoacyl-tRNA synthetase (anti-ARS) antibodies along with myositis, interstitial lung disease (ILD) or arthritis. Although gastrointestinal (GI) involvement has been sporadically reported, its motor manifestations remain poorly characterized. The aim of this study was to describe gastrointestinal motor dysfunction in patients with ASyS using advanced motility techniques and correlate objective findings with disease characteristics and digestive symptoms.
Methods. We analyzed four consecutive patients with definite ASyS referred to our tertiary motility center for a thorough GI motility evaluation between 2018 and 2024. All patients underwent high-resolution esophageal manometry, 4-hour gastric emptying scintigraphy, and 5 hour high-resolution jejunal manometry, 3 hours fasting and 2 hours during continuous nutrient infusion directly in the jejunum. Clinical and immunological data was collected from a prospectively maintained database.
Results. Four ASyS patients were include in this study (75% women; median age 53 years, range 41–64). The median disease duration was 9 years (range 4-30). All patients presented anti-ARS antibodies (3 anti-Jo1 and 1 anti-EJ) and anti-Ro52. ILD was present in 4/4, and 3/4 had muscular involvement with CK elevation (2637 UI/L, range 1019-5703). Arthritis was reported in 2 patients. Focusing on GI involvement, all patients presented postprandial heaviness and abdominal distension. Two patients reported heartburn and acid regurgitation, and three patients described diarrhea, of whom two showed alternating episodes of constipation.
Regarding GI motility evaluation, 3/4 patients had abnormalities in one or more GI motility tests: Esophageal evaluation revealed aperistalsis of the esophageal body (n=3) and hypotensive lower esophageal sphincter (n=3). Gastric motility testing demonstrated delayed gastric emptying in 2 patients. Small bowel high-resolution manometry showed abnormal motility during fasting in all patients: absent peristaltic contractions (n=2), disorganized neuropathic activity (n=1). Three patients had abnormal motor response to nutrients; hypomotility (n=1) and minute-rhythm neuropathic pattern (n=2). One patient developed small bowel dilation and pseudo-obstructive crisis, compatible with intestinal pseudo-obstruction. A full-thickness biopsy of the jejunum was performed, which showed marked atrophy of the inner circular muscle layer and mild inflammatory infiltrate in the myenteric plexus. In the 3 patients with objective GI involvement, muscular involvement coexisted, though this potential relationship remains uncertain and merits further study.
Conclusions. Gastrointestinal motor dysfunction in ASyS may affect the entire digestive tract. These findings support a significant underlying GI dysmotility in ASyS with digestive symptoms and highlight the need for systematic motility assessment in symptomatic patients.
Key words: inflammatory myopathies, anti-synthetase syndrome, intestinal manometry, intestinal pseudo-obstruction, small bowel motility

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PROGNOSTIC SIGNIFICANCE OF 1-YEAR PULMONARY FUNCTION CHANGES IN MYOSITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

Shiri Keret[1], Silvia Martinez Laverde[2], Irada Choudhuri[3], Raisa Lomanto Silva[4], Eugenia Gkiaouraki[2], Tanya Chandra[2], Nantakarn Pongtarakulpanit[2], Niladri Bhowmick[5], Vaidehi Kothari[2], Kaushik Sreerama Reddy[2], Eaman AlHassan[2], Anushka Aggarwal[6], Maha Almackenzie[7], Daniel Sullivan[8], Koichi Yamaguchi[8], Daniel Kass[8], Kevin Gibson[8], Dana P. Ascherman[2], Siamak Moghadam-Kia[2], Chester V. Oddis[2], Rohit Aggarwal[2]
[1]Bnai Zion Medical Center, Haifa, Israel, [2]Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, USA, [3]Internal medicine, University of Pittsburgh Medical Center, Pittsburgh, USA, [4]Department of Rheumatology, Allergy & Immunology, Massachusetts General Hospital, Boston, USA, [5]Department of Clinical Immunology and Rheumatology, Yashoda Hospital, Malakpet Hyderabad, Hyderabad, India, [6]Department of Rheumatology, Indraprastha Apollo Hospital, New Delhi, India, [7]Division of Rheumatology, Medical Cities of the Ministry of the Interior, Riyadh, Saudi Arabia, [8]Division of Pulmonary, Allergy, Critical Care, and Sleep Medicine, University of Pittsburgh Medical Center, Pittsburgh, USA

Background. Lung involvement is the most frequent and severe extramuscular complication of Idiopathic Inflammatory Myopathies (IIM). Despite its clinical importance, the utility of pulmonary function test (PFT) monitoring for predicting long-term outcomes in IIM-associated interstitial lung disease (IIM-ILD), as well as its role in assessing treatment efficacy in clinical trials, remains unclear.
Objectives: We aimed to evaluate the association between one-year changes

in PFTs and long-term outcomes, including 10-year mortality and lung transplantation, in patients with IIM- ILD.
Methods. A prospective cohort of adult IIM-ILD patients was analyzed retrospectively. ILD was defined by high-resolution chest CT (HRCT), and myositis was classified according to either myositis-specific autoantibodies and/or the 2017 EULAR/ACR IIM classification criteria. Baseline was defined as the first rheumatology visit. Inclusion criteria required baseline and follow-up PFTs 6-18 months apart. Changes in forced vital capacity (FVC)% and diffusing capacity (DLCO)% were calculated as annualized values: [ΔFVC or ΔDLCO ÷ interval in months] × 12. Cox regression identified associations between PFT trends and outcomes, adjusting for age, sex, smoking, baseline FVC%, and interval from baseline to the first PFT. Kaplan-Meier analysis compared survival by FVC% trends, HRCT patterns, and IIM subsets.
Results. The study included 149 patients (mean age 50.5 ± 12.9 years, 63% female, 85% White). Based on serology, ASyS was the most frequent IIM subset (73.2%), followed by dermatomyositis (10.7%) and polymyositis (8.7%). Over a mean 6.3-year follow-up, 41 (27.5%) died and 6 (4.0%) underwent transplantation. Mean baseline FVC was 67.5 ± 19.3%, and DLCO was 54.2 ± 19.4%.
In univariate analyses, absolute and relative FVC declines of ≥5% over one year were significantly associated with increased 10-year mortality (HR=2.03, p=0.03 and HR=2.01, p=0.03) and reduced transplant-free survival (HR=1.90, p=0.048; HR=1.87, p=0.050). Larger FVC declines (≥10%/≥15%) showed stronger mortality associations, whereas stable or improved FVC predicted better outcomes (HR=0.49, p=0.03). Baseline DLCO, but not its decline, was significantly associated with transplant-free survival (HR 0.96, p<0.001). Multivariate analysis revealed similar results. Kaplan-Meier analysis demonstrated worse survival with FVC decline ≥5% (p = 0.028) and ≥10% (p=0.001), with curves diverging early during follow-up. Survival did not differ by autoantibody subtype or HRCT pattern.
Conclusions. FVC decline, even at a threshold as low as 5%, is a significant predictor of long-term mortality and lung transplant in IIM-ILD. Routine FVC monitoring may support risk stratification, guide transplant referral, and serve as a trial endpoint.
Key words: idiopathic inflammatory myopathies, anti-synthetase syndrome, polymyositis, dermatomyositis, interstitial lung disease, outcome measures, prognostic factors, pulmonary function tests

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PULMONARY FINDINGS IN HIGH RESOLUTION COMPUTED TOMOGRAPHY ACCORDING TO THE DIAGNOSIS AND MYOSITIS AUTOANTIBODIES. RESULTS FROM THE MYOTRECSZ COHORT

Samuel Govea-Peláez[1], Nancy R. Mejía-Domínguez[2], Yatzil Reyna-Juárez[1], Beatriz Alcalá-Carmona[1], Jennifer T. Balderas-Miranda[1], Carlos Nuñez-Álvarez[1], Martha E. Baños-Laredo, Berta Riveros-Gilardi[3], Diana Gómez-Martín[1], Jiram Torres-Ruiz
[1]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico City, [2]Red de apoyo a la Investigación, Cordinación de Investigación Cientfica, Universidad Nacional Autónoma de México, Mexico City, Mexico City, [3]Department of Radiology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico City

Background. Interstitial lung disease (ILD) is observed in approximately 41% (33–50%) of patients with idiopathic inflammatory myopathies (IIM), precluding an excess mortality of 40%, and implying bad prognosis. High resolution computed tomography (HRCT) of the lung is the gold standard for the diagnosis of ILD, and the aim of this study was to describe the pulmonary tomographic findings of a cohort of well characterized IIM.
Methods. This cross-sectional study included 98 patients and was nested in the myositis translational research cohort Salvador Zubirán (MYOTReCSZ), a prospective study of patients classified as IIM according to ACR/EULAR classification criteria or the Connors' criteria for anti-synthetase syndrome (AS). We assessed the disease activity and damage accrual. Within six months of this evaluation, a HRCT of the lung was obtained and interpreted by an expert radiologist (BRG), who calculated the Warrick score. Myositis specific (MSA) and associated antibodies (MAA) were assessed by Lineblot (EUROIMMUNE).
Results. Eighty-eight participants (89.7%) were women. The most frequent diagnosis was dermatomyositis (DM) (75.5%). The most frequent MSA and MAA were the Mi2 (23.4%) and the Ro52 (28.5%) respectively. Thirty-five patients (35.7%) had ILD, being the most frequent type of ILD the non-specific interstitial pneumonia (42.8%). The more frequent tomographic findings were interstitial thickening (82.8%), ground glass opacities (65.7%), and irregular pleural margins (57.1%). Anti-MDA5+ patients were at great risk of having ILD (OR 6.61 (95% CI 1.22-123.11), p<0.05), whilst patients with anti Mi2 were protected (0.16 (0.05-0.44), p<0.05). A higher amount of monocytes was observed in patients with ILD (595 (477-705) *vs*. 510 (380-620), p=0.035). The Warrick score showed a gradient among the different diagnosis as following: Warrick severity: AS (8 (4-11)), immune mediated necrotizing myopathy (IMNM) (3 (3-3)), and DM (1 (0-3.75)); Warrick extension AS (5 (4-7)), IMNM (2 (1-4)), and DM (1 (0-2)); and total Warrick score AS (12 (8-18)), IMNM (5 (4-7)), and DM (2 (0-5.75)). The totalpWarrick score was higher among patients with anti Jo1+ (11.0 (5.5-18.0) *vs*. 2.0 (0.0-6.5), p<0.05), MDA5+ (6.0 (4.5-10.5) *vs*. 2.0 (0.0-7.0), p<0.05), whilst patients with anti TIF1-γ+ (0.0 (0.0-0.0) *vs*. 4.0 (0.0-9.25), p<0.05), and Mi2+ (0.0 (0.0-3.0) *vs*. 5.0 (0.0-10.0), p<0.05) showed less severity.
Conclusions. Pulmonary findings in HRCT vary according to the different IIM clinical phenotypes and the positivity for MSA.
Key words: ILD, IIM, HRCT, MSA, MAA

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DISSEMINATED ENTEROVIRUS INFECTION ASSOCIATED WITH SEVERE IMMUNE MEDIATED MYOSITIS IN A PATIENT PRESENTING WITH ANASARCA AND PROXIMAL MYOPATHY

Anna Brusch[1,2,3,4], Elizabeth Klinken[1,2], Gabrielle Rule[1,2], Jason Dyke[1], Michael Taggart[2]
[1]PathWest - QEII Medical Centre, Perth, Australia, [2]Sir Charles Gairdner Hospital, Perth, Australia, [3]University of Western Australia, Perth, Australia, [4]Perron Institute for Neurological and Translational Research, Perth, Australia

Background. A 40-year-old female presented with progressive lower limb oedema over several months. Subsequently she developed widespread myalgias, weakness and daily high fevers with worsening widespread oedema. Her past medical history was significant for multiple sclerosis treated with Ocrelizumab every 6 months for several years and no other medications. Owing to progressive symptoms and immobility, she was admitted to a tertiary hospital for diagnostic evaluation where she was found to be febrile, with massive leg swelling and proximal myopathy (3/5 hip flexion, 4/5 abduction).
Methods. The patient's diagnostic evaluation and treatment are summarised. A review of the literature is presented.
Results. Blood tests were notable for elevated CK (peak 342U/L), high CRP (78mg/L), hypogammaglobulinemia (IgG 3.2g/L) and absent B-cells. Liver function tests (LFTs) showed a mixed cholestatic and hepatitic pattern with hypalbuminaemia. Myositis antibodies including HMGCR antibodies were negative. MRI of lower limbs identified extensive anasarca and diffuse muscle oedema without atrophy. Muscle biopsy of vastus lateralis identified features of a severe, active, chronic immune mediated myositis with a predilection for perifascicular fibres. PCR analysis of the muscle biopsy specimen was positive for enterovirus RNA. Additionally, enterovirus RNA was detected in peripheral blood.
The patient was diagnosed with disseminated enterovirus infection causing myositis, hepatitis and anasarca. This was attributed to hypogammaglobulinemia in the context of chronic B-cell depletion.
Intravenous immunoglobulin 2g/kg over 4 days was administered. The patient experienced immediate resolution of fever. Objective improvement of oedema was noted within days. At two weeks, LFTs showed significant improvement, albumin was normal and she was able to walk short distances independently. Further monthly infusions of IVIG 2g/kg were planned until complete resolution of oedema and recovery of muscle strength.
Enterovirus infections in healthy individuals are generally mild and self-limiting, but in immunocompromised hosts they can be severe and chronic, particularly in those with humoral immune defects. Muscle manifestations of disseminated enterovirus infection resembling polymyositis, dermatomyositis and necrotising immune myositis have been reported rarely in the literature; a review of reported cases and summary of associated findings will be presented.

Conclusions. Disseminated enterovirus infection is a rare cause of myositis. Clinicians should remain alert to the possibility of infective causes of myositis in patients receiving immunosuppression. Muscle biopsy and extensive microbiological testing were instrumental in reaching diagnosis in a patient who did not have myositis autoantibodies.
Acknowledgements. Thanks to the patient for agreeing to present their case.
Key words: enterovirus, anasarca, myositis, hypogammaglobulinemia, ocrelizumab

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CUTANEOUS CLUES: DISTINGUISHING ANTI-SYNTHETASE SYNDROME FROM DERMATOMYOSITIS

Edoardo Conticini[1], Silvia Grazzini[1], Elena Marras[1], Laura Calabrese[1], Alessandra Cartocci[1], Luca Cantarini[1], Pietro Rubegni[1], Bruno Frediani[1]
[1]University of Siena, Siena, Italia

Background. Skin involvement may vary in terms of severity, extension, features and response to treatment among different idiopathic inflammatory myopathies (IIM).
Aim of this study is therefore to provide a pictorial essay of skin manifestation in ASyS, through a direct comparison with DM also in terms to extra-cutaneous manifestations and response to treatment.
Methods. We retrospectively included all patients followed up in our "Myositis clinic" between 2020 and 2024, affected by ASyS and DM and displaying an unequivocal cutaneous involvement.
Exclusion criteria were a diagnosis of immune-mediated necrotizing myopathy, juvenile DM, polymyositis and overlap myositis, as well as a follow-up period shorter than 12 months.
Patients who were referred to our center and, despite a positive history, had skin domain in remission were excluded, too
Baseline visit (T0) was considered the first one in our center.
Patients were treated as per internal procedures and a number of core set measurements as per IMACS guidelines were recorded for any visit.
Results. A total of 21 ASyS and 41 DM were retrospectively included. Seventeen (80,9%) ASyS had MH, while the remaining features were reported in no more than 3 patients, each. On the opposite, among DM, MH were found in 5/41 (12,1%) of patients, while Gottron's papules, heliotrope rash and V-sign in 78%, 63,4% and 46,3%, each.
Directly comparing the single lesions, MH were strongly significant for ASyS (T 3.59, p=0.0001), while Gottron's papules, heliotrope rash, V-sign, shawl sign, malar rash, holster sign, periungual erythema and hair loss strongly correlated with DM.
Focusing on ASyS only, the presence of any skin sign, including MH, did not correlate with disease severity or damage neither with any kind of extra-cutaneous involvement rate or MSA positivity.
Specifically focusing on skin, disease activity at baseline was quite low (MDAAT skin 2.52, CDASI activity 1.87, CDASI damage 0) and rapidly dropped near to 0 (MDAAT 0.3, CDASI activity 0.07, CDASI damage 0) after 12 months, with no correlation with extra-cutaneous disease activity scores.
On the opposite, for DM, CDASI and MDAAT skin were significantly higher at baseline ($p<0.05$) and during all timepoints ($p<0.01$), proving an overall poorer response to first-line immunosuppression.
Discussion. Skin involvement in ASyS deeply differ from DM in terms of features, severity and response to treatment, being usually more smoldering, better responding to the treatment, less burdened by damage and generally restricted to MH.
Currently available scores may underestimate cutaneous features of ASyS and, therefore, specific ones should be warranted.
Key words: skin

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ACUTE KIDNEY INJURY IN HOSPITALIZED PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Dante Dahabreh[1,2], Yun-Yi Hung[3], Siamack Nemazie[4], Ali Mehr[5], Nirmala Ramalingam[6], Jeffrey Klingman[7], Sara Khorasani[7], Jafar Kafaie[8], Amir Sabouri[7]
[1]Department of Internal Medicine New York Presbyterian- Weill Cornell, New York City, United Sates, [2]Department of Internal Medicine, Kaiser Permanente Oakland Medical Group, Oakland, USA, [3]Division of Research, Kaiser Permanente Northern California, Pleasanton, USA, [4]Department of Nephrology, The Permanente Medical Group, Santa Rosa, USA, [5]Department of Nephrology, The Permanente Medical Group, San Francisco, USA, [6]Graduate Medical Education, Kaiser Permanente Oakland Medical Center, Oakland, USA, [7]Department of Neurology, The Permanente Medical Group, Walnut Creek, USA, [8]Department of Neurology, St. Louis University, St. Louis, USA

Background. Elevated creatine kinase (CK) is common in idiopathic inflammatory myopathies (IIM), but the relationship between CK elevation and acute kidney injury (AKI) remains unclear. Clarifying this risk could reduce unnecessary hospitalizations and guide evidence-based decision making (1).
Methods. We conducted a retrospective study of 469 adults with IIM in Kaiser Permanente Northern California based on dermatomyositis, polymyositis, immune-mediated necrotizing myopathy, inclusion body myositis, anti-synthetase syndrome, or overlap myositis diagnosis (2010–2021). Baseline estimated glomerular filtration rate (eGFR) was estimated using the CKD-EPI equation (2), with chronic kidney disease (CKD) defined as eGFR<60 mL/min/1.73 m^2. Baseline and follow-up CK levels were used to identify those with peak CK >500 and those with a hospitalization/emergency department (ED) visit within 30 days of peak CK. Diagnosis of AKI during the hospitalization/ED visit was confirmed using Kidney Disease Improving Global Outcomes (KDIGO) criteria. Chart review was conducted to determine the temporal and clinical relationship between CK elevation and AKI.
Results. Among 469 patients with IIM (mean age 56.5 years, 63.3% female), 365 (77.8%) had peak CK >500 IU/L, of whom 95 (20.3%) had a hospitalization/ED visit within 30 days of peak CK. Of these, 11 had AKI from any cause and 5 (5.6%) had AKI temporally associated with CK elevation (CK-AKI). All CK-AKI patients had hypertension, 60% had diabetes, and 40% had CKD at baseline, whereas only 8.9% of the remaining 90 hospitalized/ED IIM patients had CKD at baseline. Over 40% of CK-AKI patients had baseline CK ≥40,000 IU/L versus none in other hospitalized/ED IIM patients and ≤1% in the remaining IIM cohort. Those with CK-AKI were older (age 71 *vs*. 56 years) and had greater comorbidity burden. Median peak CK trended higher for CK-AKI (11,030 [interquartile range 10,820–46,731] IU/L *vs*. 7674 [3197-14330]).
Conclusions. In a large cohort of adults with IIM and CK >500 IU/L, hospitalized AKI attributable to CK elevation was very uncommon (5.6%). Elevated CK alone is insufficient to predict AKI risk in IIM and may prompt avoidable hospitalizations; instead, AKI risk is driven by the combination of CK elevation with older age and higher comorbidity burden. These findings may inform efforts to optimize resource allocation for patients with IIM without compromising patient safety.
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Key words: idiopathic inflammatory myopathy

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INTERSTITIAL LUNG DISEASE IN MIXED CONNECTIVE TISSUE DISEASE: A DISTINCT CLINICAL PATTERN COMPARED TO SYSTEMIC SCLEROSIS AND MYOSITIS?

Filipa Costa[1,2], Inês Sopa[1,2], Khea Hasmucrai[2], Manuel Silvério-António[3], Ana Teresa Melo[4], Joana Martinho[1,2], Bianca Paulo Correia[1,2], Nikita Khmelinskii[1,2], Catarina Resende[1,2], Raquel Campanilho-Marques[1,2], Gonçalo Boleto[1,2]
[1]Serviço de Reumatologia, Unidade Local de Saúde Santa Maria, Centro Académico de Medicina de Lisboa, Lisboa, Portugal, [2]Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa, Lisboa, Portugal, [3]CUF, Clínica do Barreiro, Barreiro, Portugal, [4]Unidade de Reumatologia, Unidade Local de Saúde de São José, Lisboa, Portugal

Introduction. Mixed connective tissue disease (MCTD) has overlap features with systemic sclerosis (SSc) and inflammatory idiopathic myopathies (IIM) with a proportion of patients presenting with lung involvement. Data directly comparing lung involvement between these diseases remains limited.
Objectives. To assess whether MCTD-associated interstitial lung disease (MCTD-ILD) has a higher proportion of yearly relative FVC decline during follow-up when compared to SSc-ILD and IIM-ILD.
Methods. We included 45 patients diagnosed with MCTD, SSc, IIM and ILD, established through chest tomography (CT) scans with a follow-up of 4 years (±12 months).
Each group had 15 patients that were matched in a 1:1:1 ratio based on age and disease duration. ILD progression was defined as an annual ≥10% relative decline in FVC or ≥15% relative decline in DLCO. The proportion of patients with at least one-year severe progression was compared across the 3 groups. Secondary analyses included intermediary assessments of FVC and DLCO decline at 1, 2, and 3 years, as well as mortality.
Results. 45 patients were included, with 33 (84.6%) being female. Mean age at ILD diagnosis was 47.6 ± 2.6 years and median time for ILD diagnosis was 12 months. Extension of lung involvement on CT scan was not significantly different across groups. Most patients (n=34, 75.6%) exhibited a non-specific interstitial pneumonia (NSIP). However, SSc patients presented significantly more frequently with usual interstitial pneumonia (UIP) when compared to the MCTD subgroup (n=4, 26.7% in SSc *vs*. n=0, 0% in MCTD p<0.007).
During the follow-up period, patients with IIM were more likely to experience a relative decline in FVC of >10% (p=0.035) within the first year of follow-up when compared with MCTD.
After 3 years (±12 months), the average relative decline in DLCO was significantly greater in SSc-ILD compared to the MCTD-ILD (average decrease of 24.9%, p<0.001). We found no other associations when comparing average decrease of absolute/relative FVC and absolute DLCO at yearly follow-up. There was no significant difference in the number of yearly periods of decrease of relative/absolute FVC greater than 10% and 5% and DLCO greater than 15%. No deaths were recorded
Conclusions. MCTD-ILD may have a more favorable prognosis regarding progression of lung disease compared to those with SSc-ILD or IIM- ILD. Patients with IIM-ILD and SSc-ILD demonstrated a more rapid decline in FVC and DLCO particularly in the first years of follow-up. These findings highlight the differences in the progression of ILD and underscore the importance of disease-specific monitoring of lung function.
Key words: lung, myositis, MCTD, systemic sclerosis

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CHARACTERISTICS AND OUTCOMES IN PATIENTS WITH ANTI-SYNTHETASE SYNDROME (ASYS) RELATED INTERSTITIAL LUNG DISEASE (ILD): ANALYSIS FROM THE "CLASSIFICATION CRITERIA FOR ANTI-SYNTHETASE SYNDROME (CLASS)" PROJECT DATABASE

Francisca Bozan[1], Sharon Bae[2], Daphne Rivero-Gallegos[3], Giovanni Zanframundo[4,5], Sara Faghihi-Kashani[6], Iazsmin Bauer Ventura[7], Eduardo Dourado[8,9,10], Darosa Lim[11], Aravithan Loganathan[12,13,14], Gianluca Sambataro[15], Akira Yoshida[16], Laure Gallay[17], Francesco Bonella[18], Tamera Corte[19], Tracey J Doyle[20], David Fiorentino[21], Miguel A. Gonzalez-Gay[22], Marie Hudson[23], Masataka Kuwana[16], Antonella Natarnicola[24], Andrew L Mammen[25], Neil McHugh[13], Fredrick W. Miller[26], Carlomaurizio Montecucco[27], Chester V. Oddis[6], Jorge Rojas-Serrano[3], Jens Schmidt[28], Carlo Scire[29], Ana Villar[30], Victoria Werth[11], Rohit Aggarwal[6], Lorenzo Cavagna[4,5]
[1]Section of Rheumatology, Department of Medicine, Hospital Clínico Universidad De Chile, Santiago, Chile, [2]Division of Rheumatology, Department of Medicine, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, USA, [3]Rheumatology service, National Institute of Respiratory Diseases, Ismael Cosío Villegas, Mexico City, Mexico, [4]Department of Internal Medicine and Therapeutics, University of Pavia, Pavia, Italy, [5]Rheumatology Division, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [6]Division of Rheumatology and Clinical Immunology, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, USA, [7]Section of Rheumatology, Department of Medicine, University of Chicago, Chicago, USA, [8]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal, [9]Aveiro Rheumatology Research Centre, Egas Moniz Health Alliance, Aveiro, Portugal, [10]Rheumatology Research Unit, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa, Lisbon, Portugal, [11]Department of Dermatology, Perelman School of Medicine & Corporal Michael J. Crescenz Department of Veterans Affairs Medical Center, Philadelphia, USA, [12]Royal National Hospital for Rheumatic Diseases, Bath, UK, [13]Department of Life Sciences, University of Bath, Bath, UK, [14]Arthritis Australia, Broadway, Glebe, Australia, [15]Regional Referral Center for Rare Lung Disease, Policlinico "G. Rodolico-San Marco", University of Catania, Catania, Italy, [16]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Tokyo, Japan, [17]Department of Clinical Immunology, Hôpital Édouard Herriot, Lyon, France, [18]Center for interstitial and rare lung diseases, Ruhrlandklinik, University of Duisburg-Essen, Essen, Germany, [19]Royal Prince Alfred Hospital, University of Sydney, Sydney, Australia, [20]Brigham and Women's Hospital, Boston, USA, [21]Stanford University, Department of Dermatology, Redwood City, USA, [22]Division of Rheumatology, IIS-Fundación Jiménez Díaz, Madrid, Spain, [23]Division of Rheumatology, McGill University, Quebec, Canada, [24]Division of Rheumatology, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden, [25]National Institute of Arthritis and Musculoskeletal and Skin Disorders, National Institutes of Health, Bethesda, USA, [26]Environmental Autoimmunity Group, Clinical Research Branch, National Institute of Environmental Health Sciences, National Institutes of Health, Durham, USA, [27]Rheumatology Division, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [28]Department of Neurology, Neuromuscular Center, University Medical Center Göttingen, Göttingen, Germany, [29]Rheumatology Unit, IRCCS San Gerardo dei Tintori Foundation, Monza, Italy, [30]Systemic Autoimmune Diseases Unit, Internal Medicine Department, Vall d'Hebron University Hospital, Universitat Autònoma of Barcelona, Barcelona, Spain

Background. ASyS is a systemic autoimmune rheumatic disorder with significant heterogeneity. ILD is the most common cause of mortality and an important prognostic factor associated with poor survival.
Objective. We aimed to analyze the characteristics of patients with ASyS-related ILD (ASyS-ILD) and their clinical outcomes using the CLASS project database
Methods. The CLASS database contains data entered by local physicians from 103 centers across 30 countries. The database includes comprehensive clinical, serological, radiographic, and physiological data. We compared clinical characteristics between 'active progressive ILD' and 'chronic stable ILD' per the local physician's discretion at the last follow-up, performed logistic regression to assess associations between baseline predictor variables and clinical ILD status at last follow-up, and analyzed all-cause mortality using Cox regression models.
Results. 812 patients with ASyS-ILD who had follow-up data were included in the analysis. Patients with active progressive ILD were older at ILD onset and, more frequently, smokers. Nonspecific interstitial pneumonia (NSIP) was the most common radiological pattern in both groups. Patients with active progressive ILD had higher rates of usual interstitial pneumonia (UIP) pattern at baseline, and initial forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO) were significantly lower. Follow-up data showed that patients with active progressive ILD had a significantly greater number of deaths, the majority due to ILD progression. Older age at ILD onset, smoking, New York Heart Association (NYHA) class III/IV, UIP pattern, and lower initial FVC and DLCO were associated with active progressive ILD status. Multivariable analysis confirmed that NYHA class III/IV and lower initial DLCO remained as independent predictors of ILD progression. Multivariable Cox regression showed that older age at ILD onset and lower initial FVC and DLCO were associated with increased mortality risk.
Conclusions. Older age at ILD onset, an initial NYHA class III/IV status, a reduced baseline DLCO and FVC are predictors of poor outcomes, underscoring the importance of a comprehensive risk assessment in ASyS-ILD patients.
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Key words: anti-synthetase syndrome, outcomes, interstitial lung disease

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GASTROINTESTINAL INVOLVEMENT IN IDIOPATHIC INFLAMMATORY MYOPATHIES: A COMMON CLINICAL OBSERVATION

Albert Gil-Vila[1,2], Clara Edo-Fernández[1], Ernesto Trallero-Araguás[3], Carolina Malagelada[2,4], Francisco Félix-Tellez[2,4], Luis G. Alcalá-González[2,4], Albert Selva-O'Callaghan[2,4]
[1]Systemic and Autoimmune Diseases Unit, Internal Medicine. Vall d'Hebron University Hospital, Barcelona, Spain, [2]Department of Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain, [3]Rheumatology department. Vall Hebron University Hospital, Barcelona, Spain, [4]Digestive System Research Unit, Vall d'Hebron University Hospital, Barcelona, Spain

Background. Gastrointestinal (GI) involvement is an underrecognized manifestation of idiopathic inflammatory myopathies (IIM). Even though skeletal muscle weakness and skin lesions are the hallmark of these disorders, smooth muscle and autonomic dysfunction can also contribute to a broad

spectrum of manifestations. Oropharyngeal dysphagia has been the main symptom described, nonetheless, other clinically relevant GI symptoms remain poorly characterized. This study aimed to assess the prevalence of self-reported GI symptoms in patients with IIM.

Methods. We developed a comprehensive self-reported electronic survey to assess GI symptom prevalence and severity in patients with IIM. All patients met the 2017 ACR/EULAR classification criteria for definite IIM. Between October 2024 and September 2025, 60 consecutive patients were enrolled. Clinical and immunological data were collected. GI symptoms were categorized as absent, mild, moderate, severe, or disabling depending on their impact on quality of life (QoL). We considered moderate or higher as clinically significant. Upper GI symptoms include heartburn, oropharyngeal and esophageal dysphagia, regurgitation, nausea, vomiting, epigastric burning and early satiety. Lower GI symptoms include postprandial fullness, bloating, mid-abdominal pain, infraumbilical abdominal pain and fecal incontinence to liquid or solid stool.

Results. A total of sixty patients were enrolled in the study, with 48 completing the e-survey in full. Sixty-one percent were female with median age of 65 years (IQR 52-71). Fifteen patients were classified as DM (6 MI2, 4 MDA5, 2 SAE, 2 TIF1γ, 1 negative), 15 as IMNM (4 SRP, 11 HMGCR), 13 as ASyS (6 Jo1, 3 PL7, 2 PL12, 2 EJ) and 4 as scleromyositis (PM-Scl).

GI symptoms were heterogeneous but overall 83% of patients reported at least one moderate symptom. Upper GI manifestations predominated, particularly bloating (38%) and postprandial fullness (34%). Of note, 19% of patients reported fecal incontinence (Fig. 1). Evaluating specific subgroups, DM patients (mean score 23.9, SD 6.9) most frequently reported postprandial fullness (33%) and bloating (40%); IMNM patients (mean score 25.6, SD 8.1) experienced postprandial fullness (46%) and bloating (33%); and ASyS patients were the most affected (mean score 28.1, SD 14.6), with regurgitation (31%), epigastric burning (31%), bloating (38%), early satiety (31%) and fecal incontinence (23%).

Conclusions. Our data shows that GI symptoms with a negative impact on QoL are highly prevalent in patients with IIM. GI involvement seems to be heterogeneous along the GI tract organs. Incorporating a structured GI evaluation into clinical practice may help identify patients who could benefit from objective GI motility investigations.

Key words: idiopathic inflammatory myopathies, myositis, gastrointestinal involvement, quality of life

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PREDICTORS FOR INTERSTITIAL LUNG DISEASE IN ANTI-MDA5/ANTI-SYNTHETASE ANTIBODY NEGATIVE IIM PATIENTS: INSIGHTS FROM THE HONG KONG MYOSITIS REGISTRY

Iris Yan Ki Tang[1], Ka Ki Yam[2], Lucas Tsz Ho Luk[2], Dennis Tin Ho Chan[3], Roy Ho[4], Billy Lai[5], Vivian Hoi San Tang[6], Virginia Lao[2], Ho So[7]

[1]The University of Hong Kong, Hong Kong, China, [2]Kwong Wah Hospital, Hong Kong, China, [3]Alice Ho Miu Ling Nethersole Hospital, Hong Kong, China, [4]Queen Elizabeth Hospital, Hong Kong, China, [5]Tseung Kwan O Hospital, Hong Kong, China, [6]North District Hospital, Hong Kong, China, [7]The Chinese University of Hong Kong, Hong Kong, China

Background. Patients with idiopathic inflammatory myopathy (IIM) is at risk of developing interstitial lung disease (ILD). While ILD screening is widely accepted in IIM patients with anti-MDA5 or anti-synthetase antibody (ASA) positivity, screening strategies for those negative for anti-MDA5 or ASA are less well-established. This study aims to explore the risk factors for ILD development in IIM patients who are negative for anti-MDA5 or ASA, using data from the Hong Kong myositis registry (MyoHK).

Methods. MyoHK is a multicentre observational cohort that collected longitudinal data from IIM patients across seven rheumatology centres in Hong Kong. Patients with at least 6 months of follow-up (FU) data were included in the analysis. Patients with anti-MDA5 or ASA positivity (anti-Jo1/PL7/PL12/EJ/OJ), or unknown myositis specific/ associated antibody (MSA/MAA) were excluded. Demographic, clinical, laboratory and radiological data were reviewed up to February 2025. ILD was defined based on compatible CT thorax or histology findings. MSA/MAA testing was performed using commercial line immunoassays. Multivariable logistic regression was performed to determine independent risk factors for ILD.

Results. Data from 361 patients (female 67.3%, mean age 56.8±15 years) were analysed after excluding 304 patients for positive anti-MDA5/ASA, and 68 patients for unknown MSA/MAA. After a median FU of 78 months (Interquartile range: 30–145), 96 (26.6%) patients developed ILD. Notably, 70% of ILD was detected within three months of IIM diagnosis. Patients with ILD more frequently presented with arthritis (50% *vs*. 17.7%, p<0.001), mechanic's hands (12.5% *vs*. 3%, p<0.001), raynaud's phenomenon (20.8% *vs*. 7.2%, p<0.001), vasculitic rash (11.5% *vs*. 4.9%, p=0.027) and unexplained fever (24% *vs*. 9.8%, p<0.001). Anti-Ro52 positivity was more common in ILD patients (53.1% *vs*. 26.8%, p<0.001), while there was no significant difference in anti-Ku or anti-PMScl positivity. 21.9% of ILD patients had both negative MSA and MAA. No significant differences were observed in baseline levels of creatine kinase, lactate dehydrogenase, erythrocyte sedimentation rates, C reactive protein or neutrophil-to-lymphocyte ratio (all p>0.05). Additionally, 59.4% of ILD patients reported respiratory symptoms at baseline. Multivariable analysis identified arthritis (OR 3.03, 95%CI 1.72–5.3), anti-Ro52 positivity (OR2.47, 95%CI 1.47–4.17) and unexplained fever (OR 2.29, 95% CI 1.17–4.51) as independent risk factors for ILD.

Conclusions. Arthritis or anti-Ro52 positivity are consistent risk factors for ILD even in IIM patients negative for anti-MDA5 or ASA. Additionally, careful clinical evaluation for respiratory symptoms or unexplained fever might aid in early detection of ILD.

Key words: interstitial lung disease, risk factors

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DOES COVID-19 INFECTION IMPACT CARDIOVASCULAR RISK IN IDIOPATHIC INFLAMMATORY MYOPATHY? FINDINGS FROM WHOLE-POPULATION DATA IN ENGLAND

Max Lyon[1], Eva Henning[2], Alexander Oldroyd[1,3], Fiona Pearce[5], Jennifer Hannah[6], Patrick Gordon[6], Hector Chinoy[1,4], on behalf of the CVD-COVID-UK/COVID-IMPACT Consortium[7]

[1]Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK, [2]Division of Population Health, Health Services Research & Primary Care, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK, Manchester, UK, [3]National Institute for Health Research Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, University of Manchester, UK, [4]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [5]Lifespan and Population Health, School of Medicine, University of Nottingham, Nottingham, UK, [6]Department of Rheumatology, King's College Hospital NHS Foundation Trust, London, UK, [7]British Heart Foundation Data Science Centre, Health Data Research, London, UK

Background. Evidence indicates that individuals with idiopathic inflammatory myopathy (IIM) and COVID-19 infection independently have an increased risk of cardiovascular and thromboembolic events, potentially due to chronic inflammation (1, 2). However, the overall prevalence and risk of cardiovascular events in IIM remain poorly defined (2). Additionally, the impact of COVID-19 infection on cardiovascular outcomes in this population has yet to be fully investigated. This study aims to:

1. Assess the impact of COVID-19 infection on major cardiovascular and thromboembolic events in individuals with IIM;
2. Compare all-cause and cardiovascular-related mortality in this population with that of the general population.

Methods. A population-based matched cohort study was conducted in England, using linked primary care (GPES Data for Pandemic Planning and Research, GDPPR) and secondary care (Hospital Episode Statistics, HES) data. 2,886 adult patients diagnosed with IIM between 2019 and 2023 were identified and matched 1:1 with healthy controls by age, gender and ethnicity. Information on baseline demographics and comorbidities, including traditional cardiovascular risk factors, alongside COVID-19 data, was extracted. Incidence rates (IRs) and 95% confidence intervals (CIs) were calculated for cardiovascular, thromboembolic and mortality outcomes. Unadjusted and adjusted hazard ratios (HRs) were estimated using stratified proportional hazards models

Results. COVID-19 infection significantly exacerbated cardiovascular risk in IIM (HR:2.84, p<0.001), with 1 in 20 suffering a cardiovascular event per year. Baseline analyses showed IIM patients had higher cardiovascular and thromboembolic risk than healthy controls (IR:52 *vs*. 16.5 per 1000 person-years; adjusted HR:3.65, CI:2.8-4.8), with 52.8% of events occurring within the first year of IIM diagnosis. The greatest cardiovascular risks observed were for deep vein thrombosis (HR:13.59, CI:4.92-37.59), pulmonary embolism (HR:11.34, CI:4.07-31.57), and heart failure (HR:4.46, CI:2.49-7.98). All-cause mortality was elevated in IIM patients (IR:49 *vs*. 6.0 per

1,000 person-years; HR:10.56, CI:6.50-17.16). Post-cardiovascular event mortality was threefold higher (HR:3.14, CI:1.64-6.00), with 30% of deaths within 30 days.
Conclusions. Preliminary findings indicate that COVID-19 significantly amplifies cardiovascular and thromboembolic risk in adults with IIM, compounding an already elevated baseline risk. These findings underscore the importance of early cardiovascular surveillance and risk management in IIM. Future studies should evaluate whether targeted cardiovascular screening and COVID-19 vaccination can reduce the excess burden and mortality in this high-risk population.
Key words: cardiovascular risk, COVID-19, mortality, thromboembolism

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RISK FACTORS FOR PROGRESSIVE PULMONARY FIBROSIS AND MORTALITY IN THE ANTISYNTHETASE SYNDROME-ASSOCIATED ILD: A COHORT STUDY

Daphne Rivero Gallegos[1], Rubi Navez Medina[1], Juan Ricardo Posada García[1], Montserrat Ixchel González Pérez[1], Ivette Buendia Roldan[2], Héctor I. Rocha González[4], Mayra Edith Mejía Ávila[3], Espiridion Ramos Martínez[5], Jorge Rojas Serrano[1]
[1]Rheumatology Clinic, Instituto Nacional De Enfermedades Respiratorias Ismael Cosío Villegas, Mexico City, Mexico, [2]Research Unit, Instituto Nacional de Enfermedades Respiratorias Ismael Cosío Villegas, Mexico City, Mexico, [3]Diffuse Interstitial Lung Disease Clinic, Instituto Nacional De Enfermedades Respiratorias Ismael Cosío Villegas, Mexico City, Mexico, [4]Sección de Estudios de Posgrado E Investigación, Escuela Superior de Medicina, Instituto Politécnico Nacional, Mexico City, Mexico, [5]Facultad de Medicina, Unidad de Investigación en Medicina Experimental, Universidad Nacional Autónoma de México, Mexico City, Mexico City

Background. Interstitial lung disease (ILD) is the main cause of death in antisynthetase syndrome (ASyS). Although most patients stabilize lung function within 6 months on immunosuppressive therapy, around 25% develop progressive pulmonary fibrosis (PPF), which is associated with mortality. Previous studies have identified non-Jo-1 antibodies and a usual interstitial pneumonia (UIP) pattern as risk factors for mortality; however, predictors of PPF and death in ASyS remain insufficiently characterized. We therefore aimed to identify risk factors for mortality and PPF in ASyS-ILD.
Methods. We conducted a prospective, single-center cohort study (February 15, 2022–August 2025) enrolling consecutive ASyS-ILD patients with a single anti–aminoacyl tRNA synthetase (anti-ARS) antibody (Jo-1, PL-7, PL-12, EJ, or OJ). The primary outcome was overall survival; the secondary outcome was PPF or death (PPF per 2022 ATS/ERS/JRS/ALAT). Survival was estimated with the Kaplan-Meier method. Associations of antibody subtype, extent of fibrosis, and pulmonary function tests with mortality and PPF or death were evaluated using hazard ratios (HRs).
Results. We included 106 patients (median follow-up 23.5 months). Seventy-three (74%) were non–Jo-1. Overall, 31.7% met criteria for PPF; 25 patients died (24%), and 47.6% experienced the composite outcome PPF or death. Mortality was associated with baseline fibrotic Goh index (aHR 1.08; 1.04–1.11), age (aHR 1.06; 1.01–1.11), and non–Jo-1 antibodies (aHR 6.06; 1.37–26.75). A greater fibrotic component by Goh index at baseline increased the risk of PPF or death (aHR 1.03; 1.00–1.06), whereas higher forced vital capacity (FVC)% (aHR 0.98; 0.97–1.00) and anti-Ro52 positivity (aHR 0.47; 0.25–0.90) were associated with lower risk. Survival differed by anti-ARS: the non-Jo-1 subgroup had the poorest survival, particularly anti-OJ (log-rank p=0.001), with a median survival of 9 months.
Conclusions. Baseline fibrotic extent, measured by the Goh index, was associated with PPF and mortality regardless of anti-ARS subtype. Each one-unit increase in the baseline Goh fibrotic index was associated with an 8% higher risk of death. Additionally, male sex, older age, and non–Jo-1 positivity were associated with mortality. These findings suggest that patients with a fibrotic pattern on high-resolution computed tomography at initial assessment might benefit from earlier antifibrotic therapy to improve survival.
Acknowledgements. We thank the patients and the multidisciplinary ILD team for their collaboration.
Key words: antisynthetase syndrome, interstitial lung disease, progressive pulmonary fibrosis

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THE SEVERITY OF INTERSTITIAL LUNG DISEASE IN ANTISYNTHETASE SYNDROME DURING ITS ACUTE PHASE: INCIDENCE OF ACUTE RESPIRATORY DISTRESS SYNDROME

Montserrat Ixchel González Pérez[1], Jennifer Lerma López[3], Daphne Rivero Gallegos[1], Mayra Edith Mejía Ávila[2], Jorge Rojas Serrano[1]
[1]Rheumatology and Internal Medicine Clinic, Instituto Nacional De Enfermedades Respiratorias, Ismael Cosío Villegas, Mexico, city, Mexico, [2]Difuse Interstitial Lung Disease Clinic, Instituto Nacional de Enfermedades Respiratorias, Ismael Cosío Villegas, Mexico, city, Mexico, [3]Hospital Regional del ISSSTE Dr. Manuel Cárdenas de la Vega, Culiacán, Sinaloa, Mexico

Background. Pulmonary manifestations are the leading cause of morbidity and mortality in antisynthetase syndrome (ASyS). To date, the incidence of acute respiratory distress syndrome (ARDS) during the acute phase of the syndrome and the risk factors associated with prognosis remain unknown. Objective:To estimate the incidence of ARDS, evaluate associated risk factors, and determine its prognosis in patients with antisynthetase syndrome.
Methods. Subjects diagnosed with ASyS according to the 2025 ACR (American College of Rheumatology)/EULAR(European Alliance of Associations for Rheumatology) criteria were included. All patients underwent a standardized evaluation. Clinical and tomographic variables were recorded. ARDS was defined according to the 2012 Berlin criteria and classified as mild (PaO_2(Partial Pressure of Arterial Oxygen)/FiO_2(fraction of inspired oxygen) <300), moderate (PaO_2/FiO_2 <200), or severe (PaO_2/FiO_2 <100). The strength of association between clinical, tomographic, and serological variables (antisynthetase antibody type) and ARDS was estimated. Mortality and associated factors were also analyzed. This study is a sub-analysis of protocols approved by the ethics committee under registrations C08-17 and C06-23.
Results. A total of 210 patients with ASyS and baseline arterial blood gas measurements were identified. One hundred seventy-two patients (82%) met ARDS criteria, 118 (56.19%) with mild ARDS, 54 (25.71%) with moderate ARDS, and none with severe ARDS. All patients received prednisone up to 50 mg/day, and 55% were treated with a combined methotrexate-leflunomide regimen. Among ARDS patients, 81% showed improvement, with an absolute increase of 10% or 15% in predicted FVC (Forced vital capacity) or DLCO (Diffusing capacity of the lung for carbon monoxide) on pulmonary function tests at 6 months of follow-up. Nine patients died. No difference in mortality was found between patients with and without ARDS.
Conclusions. ARDS has a high incidence during the acute phase of ASyS. Despite the severity of this diagnosis, most patients show improvement with appropriate treatment. It is essential to consider ASyS as part of the differential diagnosis of ARDS.
Acknowledgements. We thank the patients involved and clinical staff for their collaboration
Key words: antisynthetase syndrome (ASyS), acute respiratory distress syndrome (ARDS), PaO_2 (partial pressure of arterial oxygen)/FiO_2 (fraction of inspired oxygen)

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LONGITUDINAL TRAJECTORIES OF ANTISYNTHETASE SYNDROME-ASSOCIATED INTERSTITIAL LUNG DISEASE

Maxime Billotte[1], Thomas Moulinet[1,2], Alain Meyer[3], Houda Camara[4], Loïs Bolko[5], Kévin Didier[6], Sandra Dury[7], Bernard Bonnotte[8], Hervé Devilliers[9], Philippe Bonniaud[10], Guillaume Beltramo[10], Julien Campagne[11], Nadine Magy-Bertrand[12], Aurore Chaudier[13], Simon Valentin[14], Roland Jaussaud[1,15], Paul Decker[1,2]

[1]Département de Médecine Interne et Immunologie Clinique, CHRU Nancy, Vandœuvre-lès-Nancy, France, [2]UMR 7365 CNRS-Université de Lorraine IMoPA, Université de Lorraine, Vandœuvre-lès-Nancy, France, [3]Département de rhumatologie, Hôpitaux universitaires de Strasbourg, Strasbourg, France, [4]Unité de Méthodologie, Datamanagement et statistiques (UMDS), Département de Recherche Clinique et Innovation, CHRU Nancy, Vandoeuvre-lès-Nancy, France, [5]Département de Rhumatologie, CHU Reims, Reims, France, [6]Département de Médecine Interne, CHU Reims, Reims, France, [7]Service des maladies respiratoires, CHU Reims, Reims, France, [8]Département de Médecine Interne et Immunologie Clinique, CHU Dijon, Dijon, France, [9]Département de Médecine Interne et Maladies Systémiques, CHU Dijon, Dijon, France, [10]Institut Universitaire du Poumon, Centre de Référence Constitutif des Maladies Pulmonaires Rares de l'adultes, Inserm 1231 CTM, Université Bourgogne Europe, Centre Hospitalo-Universitaire Dijon-Bourgogne, Dijon, France, [11]Service de Médecine Interne, UNEOS, Metz, France, [12]Département de médecine interne, CHU Besançon, Besançon, France, [13]Service de Médecine Interne et Rhumatologie, Hôpital Legouest, Metz, France, [14]Département de Pneumologie, CHRU Nancy, Vandoeuvre-lès-Nancy, France, [15]EA 3450 DevAH - Développement, Adaptation et Handicap, Université de Lorraine, Vandoeuvre-lès-Nancy, France

Background. To identify and characterize longitudinal ILD trajectories in patients with antisynthetase syndrome-associated interstitial lung disease (ASyS-ILD) in a multicentric retrospective cohort.

Methods. A total of 92 patients with ASyS, defined according to the 2024 ACR/EULAR ASyS classification criteria, and ILD, diagnosed by CT scan, and with FVC measurement at ILD diagnosis and at least once during follow-up were included. Latent class mixed model (LCMM) and linear mixed-effect models were performed to determine groups of patients with similar FVC trajectories. and to identify risk factors of FVC longitudinal change.

Results. The 3-classes model was the best fitting. Class 1 (n=17) was characterized by worsening FVC over time and poor long-term (ILD relapses, pulmonary hypertension, chronic respiratory failure). Class 2 (n=44) had stable FVC at diagnosis and during follow-up, and patients were younger. Class 3 (n=31) had lower baseline FVC with more rapidly progressive ILD at diagnosis but improved over time. Classes 2 and 3 tended to have a lower risk of chronic respiratory failure during follow-up compared to class 1 (reference). CRP level at diagnosis, NSIP and OP patterns were associated with significant FVC improvement over time, whereas anti-Jo1 antibodies and anti-Ro52 antibodies were associated with FVC decline.

Conclusions. We identified three phenotypes of ILD trajectories in ASyS patients, with one group of patients that experienced FVC decline and poor prognosis. ILD CT pattern and anti-Ro52 antibodies were the most predictive factor of FVC change over time.

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ASSOCIATION OF ANTI-AMINOACYL-TRNA SYNTHETASE ANTIBODY SUBTYPES WITH SEVERITY AND EVOLUTION OF INTERSTITIAL LUNG DISEASE: AN ANALYSIS OF THE CLASS PROJECT DATABASE

Daphne Rivero Gallegos[1], Sharon Bae[2], Francisca Bozan[3], Giovanni Zanframundo[4,5], Akira Yoshida[6], Eduardo Dourado[7], Iazmin Bauer Ventura[8], Gianluca Sambataro[9], Aravi Loganathan[10], Davide Rozza[11], Angela Ceribelli[12], C. Selmi[12], A. Selva O'Callaghan[13], A. Mammen[14], Carlo Scirè[15], C. Montecucco[4,5], C. Oddis[16], D Fiorentino[17], F. Bonella[18], F. Miller[19], I. Lundberg[20], J. Schmidt[21], J. Rojas Serrano[1], M. Hudson, M. Kuwana[6], L. Gupta[23], V. Codullo[4], S. Faghihi-Kashani S.[22], S. Moghadam-Kia[16], F. Iannone[24], I. Cavazzana[25], V Wolff[26], M. Piga[27], H. Gunawardena[28], E. Volkmann[2], P. Gandiga[29], M. Sebastiani[30], L. Cavagna[4,5], R. Aggarwal[16]

[1]Instituto Nacional De Enfermedades Respiratorias Ismael Cosío Villegas, Mexico City, Mexico, [2]University of California, Los Angeles, USA, [3]Hospital Clínico Universidad de Chile, Santiago de Chile, Chile, [4]Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [5]Università Di Pavia, Pavia, Italy, [6]Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [7]Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal, [8]University of Chicago, Chicago, USA, [9]University of Enna "Kore", Enna, Italy, [10]Arthritis Australia, Glebe NSW, Australia, [11]Italian Society of Rheumatology, Milan, Italy, [12]IRCCS Humanitas Research Hospital Rozzano, Milan, Italy, [13]Vall d'Hebron University Hospital, Barcelona, Spain, [14]Johns Hopkins University School of Medicine, Baltimore MD, USA, [15]University of Milano Bicocca, Milan, Italy, [16]University of Pittsburgh School of Medicine, Pittsburgh, USA, [17]Stanford University School of Medicine, Redwood City, USA, [18]University of Duisburg-Essen, Essen, Germany, [19]National Institutes of Health, Durham, USA, [20]Karolinska Institutet, Stockholm, Sweden, [21]University Medical Center Göttingen, Göttingen, Germany, [22]University of California San Francisco, San Francisco, USA, [23]Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, UK, [24]University of Bari, Bari, Italy, [25]ASST Spedali Civili, Brescia, Università di Brescia, Brescia, Italy, [26]Instituto Nacional del Torax, Santiago, Chile, [27]University of Cagliari and AOU Cagliari University Clinic, Cagliari, Italy, Cagliari, Italy, [28]North Bristol NHS Trust, Bristol, UK, [29]Emory University, School of Medicine, Atlanta, USA, [30]AULS Piacenza, Piacenza, Italy

Background. Antisynthetase syndrome (ASyS) is characterized by anti-aminoacyl-tRNA synthetase (anti-ARS) antibodies and a heterogeneous clinical spectrum, including interstitial lung disease (ILD), which is a major cause of morbidity and mortality. Outcomes of ILD vary depending on the anti-ARS subtype: non-Jo-1 antibodies are associated with a higher risk of progressive pulmonary fibrosis (PPF) and worse lung outcomes. We aimed to compare ILD severity and evolution in anti-Jo-1-positive versus non-Jo-1-positive patients using large international data.

Methods. We analyzed the CLASS Project database, including adults with ASyS-ILD from 103 centers in 30 countries. We excluded records without anti-ARS results or with more than one anti-ARS antibody. We compared anti-Jo-1-positive ILD patients with non-Jo-1 subtypes (PL-7, PL-12, EJ, OJ, KS, Zo, and YRS/Ha). Lung variables included baseline and last pulmonary function tests (PFTs: forced vital capacity [FVC] and diffusing capacity for carbon monoxide [DLCO], both as % predicted), high-resolution computed tomography (HRCT) pattern/severity, and ILD status at last follow-up. We used linear regression for the last FVC% and DLCO%, and logistic regression for severe ILD on follow-up HRCT. Multivariable models were adjusted for age, sex, smoking, ethnicity, baseline PFTs, baseline HRCT pattern, diagnostic delay, and treatment.

Results. Among 1,729 ASyS patients, 1,547 (89.5%) had ILD. Anti-Jo-1 was the most frequent subtype (61.8%); non-Jo-1 subtypes were PL-7 (12.8%), PL-12 (14.8%), EJ (6.5%), OJ (2.7%), KS (1.2%), and Zo (0.2%). Non–Jo-1 patients had worse baseline PFTs (median FVC 67% [interquartile range (IQR) 53–82] *vs*. 73% [59–88], p=0.032; DLCO 52% [40–65] *vs*. 60% [47–72], p<0.001), with nonspecific interstitial pneumonia (NSIP) predominating and usual interstitial pneumonia (UIP) <10% in both groups. At last follow-up (FVC n=564; DLCO n=524), non-Jo-1 values remained lower (median FVC 77% [IQR 59–91] *vs*. 81% [67–98]; DLCO 56% [41–71] *vs*. 64% [48–78]). In multivariable models, anti–PL-7 was independently associated with lower last DLCO% and with severe ILD on follow-up HRCT (adjusted odds ratio [aOR] 2.77); baseline UIP pattern also predicted severe ILD (aOR 2.78).

Conclusions. Non-jo–1, especially anti-PL-7, was associated with more severe ILD, lower follow-up DLCO, and greater HRCT severity. These findings support antibody-based risk stratification and closer pulmonary monitoring in this high-risk subgroup.

Acknowledgements. We thank all investigators and patients participating in the CLASS Project.

Key words: antisynthetase syndrome, interstitial lung disease, progressive pulmonary fibrosis

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COMPREHENSIVE MYOSITIS ANTIBODY PANELS IMPROVE RECOGNITION OF IDIOPATHIC INFLAMMATORY MYOPATHY RELATED INTERSTITIAL LUNG DISEASE

Erica Ludtke[1], Andrea Davis[1,2], Deja Wilson[1,3], Justin Hewlett[1], Rosemarie Dudenhofer[1], Erin Wilfong[1]
[1]Vanderbilt University Medical Center, Nashville, USA, [2]University of Colorado Anschutz, Aurora, USA, [3]Vanderbilt University, Nashville, USA

Background. Interstitial lung disease (ILD) is a major cause of morbidity and mortality for idiopathic inflammatory myopathy (IIM) patients. Most work in the myositis community has focused on identifying which IIM patients develop ILD. Equally important, however, is improving the recognition of IIM in patients presenting with ILD. This retrospective cohort study explored (1) how myositis ILD patients present to our center, (2) the sensitivity of antinuclear antibodies (ANA), rheumatoid factor (RF, and anti-cyclic citrullinated peptide antibodies (CCP) in identifying myositis ILD, and (3) the frequency of lung limited IIM-ILD patients presenting to our center.
Methods. Patients consented to participate in the longitudinal Vanderbilt University Medical Center Myositis and Scleroderma Treatment Initiative Center (MYSTIC) Cohort between 9/1/2016-10/15/2022. Patients were recruited from the Pulmonary and Rheumatology clinics as well as the Rheumatology, Pulmonary, and Critical Care inpatient services. All patients had confirmed radiographic ILD and a positive myositis related autoantibody (Jo-1, PL-7, PL-12, EJ, OJ, Pm/Scl, Ku, MDA5). Clinical features, referral diagnoses, and first point of contact at VUMC were determined by chart abstraction using standardized case report forms. Descriptive statistics and Fisher's exact tests were performed using GraphPad Prism.
Results. Ninety-three IIM-ILD cases were identified. Participants were mostly female (68.9%), of European ancestry (56%), and had a median age of 53.2 (IQR 53.2, 59.6) years. Sixty-two participants (67%) initially presented to the pulmonary service, but only 13/62 (21%) were referred with the diagnosis of IIM-ILD. Even for the 28/63 patients previously seen by a rheumatologist, only 9/28 (32%) were diagnosed as having IIM-ILD. Of the 19/28 incorrectly diagnosed patients, 6/19 (32%) were not on either a glucocorticoid or disease modifying agent at the time of tertiary ILD evaluation. Screening for autoimmune ILD with ANA, RF, and CCP autoantibodies failed to identify 26/50 (52%) IIM-ILD cases for whom comprehensive serologic data was available. Similar to prior observations, 15% of participants presented with lung-limited disease.
Conclusions. We found that most patients with IIM-ILD presented to a tertiary pulmonary service. Screening for IIM-ILD with ANA, RF, and CCP is insufficient to identify IIM-ILD, and comprehensive myositis panels can improve recognition of IIM-ILD patients with either subtle manifestations or lung-limited disease. IIM-ILD outcomes will be improved through close cooperation with pulmonary colleagues to optimize rapid diagnosis and minimize therapeutic delays.
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Key words: interstitial lung disease

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LUNG-DOMINANT ANTI-SRP AUTOIMMUNITY: A DISTINCT CLINICAL SUBSET CHARACTERIZED BY ISOLATED INTERSTITIAL LUNG DISEASE WITHOUT MYOPATHY

Illiasul Ibad[1], Ruchika Goel[1], Ashish J. Mathew[1], John Antony Jude Prakash[1], John Mathew[1]
[1]Christian Medical College Vellore, Vellore, India

Background. Anti-signal recognition particle (anti-SRP) antibodies are traditionally linked to immune-mediated necrotizing myopathy (IMNM) – a severe, muscle-predominant disorder marked by proximal weakness, striking creatine kinase (CK) elevations, and necrotic muscle fibers with minimal inflammation. Lung involvement has been reported in nearly one-third of such patients, yet the occurrence of anti-SRP positivity without any muscle disease remains an enigma. These cases are often dismissed as incidental findings, though emerging evidence suggests they may represent a genuine, lung-dominant autoimmune phenotype rather than a mere serological coincidence.
Methods. We reviewed all anti-SRP-positive patients evaluated at our tertiary rheumatology center between January 2019 and December 2024. Anti-SRP antibodies were detected using the EUROIMMUN Euroline myositis immunoblot assay (Lübeck, Germany), where values ≥11 (≥1+) were considered positive. Patients were included if they demonstrated (i) anti-SRP positivity, (ii) interstitial lung disease (ILD) confirmed by high-resolution CT (HRCT), and (iii) no clinical, biochemical, or electrophysiologic evidence of myopathy – defined by normal muscle strength, normal muscle enzymes, and a normal electromyogram. Those with multiple myositis-specific antibodies or borderline results were excluded.
Results. Among 40 anti-SRP–positive individuals, 10 patients (5 men, 5 women) had ILD with no muscle involvement. The mean age was 53.8 ± 17.2 years. Two patients had inflammatory arthritis at presentation. HRCT patterns included nonspecific interstitial pneumonia (NSIP) in six, NSIP–organizing pneumonia overlap in one, diffuse parenchymal lung disease (DPLD) in two, and usual interstitial pneumonia (UIP) in one. The median FVC% was 55.5% (IQR 46–76%). Over a median follow-up of 3 months (IQR 3–24), none developed muscle weakness or enzyme elevation. Pulmonary hypertension was seen in three patients; another three had a prior history of treated pulmonary tuberculosis. During follow-up, ILD worsened in three, two remained stable, and others were lost to follow-up. All received prednisolone (0.5–1 mg/kg/day); four received mycophenolate mofetil, two azathioprine, and the rest continued steroids alone due to infection risk. Two required long-term oxygen therapy.
Conclusions. We identified a lung-dominant form of anti-SRP autoimmunity, expanding its spectrum beyond muscle disease. Previous cohorts report ILD in up to one-third of anti-SRP cases, but our findings reveal patients with isolated ILD and preserved muscle function. This subset may represent an early, or distinct subunit-specific variant of IMNM. Recognition of this entity and vigilant follow-up for evolving IMNM are essential to guide management and future research.
Key words: anti-SRP, interstitial lung disease, IMNM

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JOINT INVOLVEMENT IN ANTI-SYNTHETASE SYNDROME: PRELIMINARY ANALYSIS FROM THE CLASS PROJECT DATABASE

Carolina Vilafanha[1,2], Eduardo Dourado[1,2,3], Giovanni Zanframundo[4,5], Sara Faghihi-Kashani[6], Akira Yoshida[7], Iazsmin Bauer-Ventura[8], Daphne Rivero-Gallegos[9], Francisca Bozán[10], Sangmee Sharon Bae[11], Laure Gallay[12], Lorenzo Cavagna[4,5], Rohit Aggarwal[6]
[1]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal, [2]Aveiro Rheumatology Research Centre, Egas Moniz Health Alliance, Aveiro, Portugal, [3]Rheumatology Research Unit, Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal, [4]Department of Internal Medicine and Therapeutics, Università di Pavia, Pavia, Italy, [5]Division of Rheumatology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy, [6]University of Pittsburgh School of Medicine, Pittsburgh, USA, [7]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [8]Section of Rheumatology, Department of Medicine, University of Chicago, Chicago, USA, [9]Rheumatology Clinic, Instituto Nacional de Enfermedades Respiratorias, Ismael Cosío Villegas, Mexico, [10]Section of Rheumatology, Department of Medicine, Hospital Clínico Universidad de Chile, Santiago de Chile, Chile, [11]Division of Rheumatology, Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, USA, [12]Department of Clinical Immunology, Edouard Herriot Hospital, Hospices Civils de Lyon, Lyon, France

Background. Anti-synthetase syndrome (ASyS) is characterised by anti-synthetase autoantibodies and a clinical triad of myositis, interstitial lung disease, and arthritis. Arthritis is common and can be present before clinical myositis ensues. In some patients, isolated arthritis at disease onset associated with rheumatoid factor (RF) or anti-citrullinated protein antibody (ACPA) positivity can mimic rheumatoid arthritis (RA), contributing to diagnostic delay or misdiagnosis. However, comparative studies of ASyS joint involvement with other systemic autoimmune rheumatic diseases (SARDs) are lacking. We aimed to characterize the joint involvement in ASyS and compare its features with those of mimicking SARDs.

Methods. We analysed data from the Classification Criteria for Anti-Synthetase Syndrome (CLASS) project database, which includes patients with ASyS and mimicking SARDs (controls). Group comparisons were performed using the chi-square, Student's or Welch's t, or Mann-Whitney U-tests.
Results. 3205 patients were included (1801 ASyS, 1404 controls). ASyS patients were predominantly female (70.8%) and had a mean age at disease onset of 50.7 [SD 14.1] years.
Joint involvement was common, with 58.4% ever diagnosed with inflammatory arthropathy (*vs*. 46.0% of controls, p<0.001) and 48.4% presenting with joint symptoms at disease onset (*vs*. 39.5%, p<0.001). Most ASyS patients with joint involvement had symmetric polyarthritis involving the hands (60.2%). Joint deformities (8.0%) and erosions (17.6%) were frequent.
Dermatomyositis was the most frequent control diagnosis (n=539), with lower rates of joint involvement (31.6%, p<0.001) and arthritis at presentation (24.7% *vs*. 48.4%, p<0.001).
Compared with RA patients (n=218), ASyS cases had less frequent joint deformities, erosions, and a longer diagnostic delay (median [IQR] 12.0 [0–24] *vs*. 0.0 [0–12] months, p=0.003).
Among ASyS (and ASyS with joint involvement) patients, 15.2% (18.7%) were RF+, 5.3% (8.0%) ACPA+, and 6.3% (10.8%) and 11.2% (19.2%) fulfilled the 1987 and 2010 ACR RA classification criteria, respectively. RF+ and/or ACPA+ ASyS patients exhibited higher rates of arthritis (61.5% *vs*. 45.8%, p<0.001), isolated arthritis at presentation (4.6% *vs*. 0.9%, p<0.001), symmetric polyarthritis involving the hands (76.1% *vs*. 55.9%, p=0.005), joint deformities (13.1% *vs*. 6.7%, p<0.001), and erosions (28.9% *vs*. 14.1%, p<0.001), and more frequently had a prior diagnosis of RA (42.3% *vs*. 14.0%, p<0.001), compared to RF- and ACPA- ASyS patients.
Conclusions. Arthritis is frequent in ASyS. The presence of RF and/or ACPA identifies a more severe, RA-like subset that may lead to a delayed diagnosis.
Acknowledgement. CLASS project was funded by ACR and EULAR.
Key words: anti-synthetase syndrome, arthritis

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A SERUM BIOMARKER-BASED INDEX FOR PREDICTING PROGRESSIVE PULMONARY FIBROSIS IN PATIENTS WITH ANTI-SYNTHETASE SYNDROME: THE LOCCM INDEX

Longyang Zhu[1,2], Shiyu Wu[1,2], Chen Zong[1,2], Yiran Chen[2,3], Chao Sun[1,2], Yingfang Zhang[1,2], Xinxin Zhang[1,2], Xiaoming Shu[1,2], Xin Lu[1,2], Guochun Wang[1,2], Qinglin Peng[1,2]
[1]Peking University China-Japan Friendship School of Clinical Medicine, Beijing, China, [2]China-Japan Friendship Hospital, Beijing, China, [3]Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China

Background. Interstitial lung disease (ILD) is the most prominent clinical feature of antisynthetase syndrome (ASyS), with a subset of patients developing progressive pulmonary fibrosis (PPF), which is associated with a poor prognosis. However, the prevalence, clinical characteristics, and predictive factors of PPF in patients with ASyS remains unclear.
Methods. This longitudinal cohort study retrospectively enrolled 643 patients with ASyS-associated ILD. Clinical data, outcomes, and serum biomarkers were analyzed in patients with PPF. Receiver operating characteristic curves, least absolute shrinkage and selection operator, and logistic regression were used to identify key biomarkers associated with PPF.
Results. Fibrotic ILD was observed in 51.2% of patients with ASyS, while PPF was observed in 27.6% of patients with ASyS and fibrotic ILD during follow-up (median, 48.9 months). Patients with PPF were more likely to be male (37.5% *vs*. 23.2%, p=0.043), have a smoking history (29.7% *vs*. 14.3%, p=0.012), exhibit higher rates of dysphagia (10.9% *vs*. 2.4%, p=0.017), and have lower diffusing capacity for carbon monoxide (DLCO, 47.30% *vs*. 57.00%, p=0.004) at baseline compared to those without PPF. No association was observed between PPF and anti-aminoacyl transfer RNA synthetase (ARS) antibody specificity (p=0.164). Patients with PPF had significantly worse prognosis than those without PPF (log-rank test, p<0.001). Lactate dehydrogenase (LDH), osteopontin, CA15-3, CYFRA21-1, and matrix metalloproteinase-7 (MMP-7) were identified as key biomarkers associated with PPF and incorporated into a LOCCM index (score range: 0-5). Among patients with LOCCM scores ranging from 0 to 5, the proportions of PPF were 0.0%, 4.5%, 13.3%, 35.1%, 65.0%, and 100.0%, respectively. The LOCCM index demonstrated strong predictive power for PPF in patients with ASyS and fibrotic ILD (AUC: 0.865, p<0.001). Internal validations further confirmed its excellent discriminative performance and good calibration. Longitudinal assessment revealed that LOCCM index scores increased in patients with PPF and decreased in those without PPF.
Conclusions. Approximately half of patients with ASyS-ILD presented with fibrotic ILD, among whom approximately one-quarter developed PPF. The LOCCM index is a promising tool for identifying patients with ASyS at risk for PPF development.
Key words: fibrotic interstitial lung disease, progressive pulmonary fibrosis, serum biomarker, anti-synthetase syndrome

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DO ANTI-MDA5 AUTOANTIBODY TITERS CORRELATE WITH DISEASE SEVERITY AND POOR OUTCOMES IN IDIOPATHIC INFLAMMATORY MYOPATHIES?

Filipa Canhão André[1], Maria João Cadório[1], João Oliveira[1], Sara Alves Costa[1], Fabiana Gouveia[1], André Saraiva[1,2], Mariana Luís[1,2], Tânia Santiago[1,2]
[1]Unidade Local De Saúde De Coimbra, Coimbra, Portugal, [2]Faculty of Medicine, University of Coimbra, Coimbra, Portugal

Background. Anti-MDA5-positive idiopathic inflammatory myopathies (IIM) are associated with poor outcomes, particularly rapidly progressive interstitial lung disease (RP-ILD). The prognostic value of anti-MDA5 antibody titers, however, remains unclear. We aimed to assess whether MDA5 titers correlate with disease severity and clinical outcomes.
Methods. We included all patients with anti-MDA5 antibody positivity, identified using a line immunoblot assay, between January 2015 and October 2025 at ULS Coimbra, a tertiary care centre. Demographic, clinical, and laboratory data were collected longitudinally, along with key outcomes such as hospitalization, need for oxygen therapy, and mortality.
Results. Sera from 25 patients tested positive for anti-MDA5 antibodies. The median age at diagnosis was 43 years (IQR 21.5–64), 76% were female, and 92% were Caucasian. Clinical subtypes included amyopathic dermatomyositis (36%), dermatomyositis (28%), overlap myositis (16%), polymyositis (12%), and juvenile-onset dermatomyositis (8%).
ANA were positive in 83.3% of patients, most frequently with a nucleolar or speckled pattern. Concomitant myositis-specific or -associated antibodies were detected in 79.2% of cases.
MDA5 titers were weakly positive in 52% of the patients, borderline in 20%, strongly positive in 16% and moderately positive in 12%.
At diagnosis, the most frequent findings were muscle weakness (64%), ILD (59%), Gottron's papules (52%), Raynaud's phenomenon (50%), and arthritis (42%). Cutaneous features such as heliotrope rash (30%), V-neck rash (16%), and calcinosis (23%) were also observed, while other manifestations, including dysphagia, livedo reticularis, oral ulcers, and myocarditis, were less common (<15%).
Over a mean 5.4 ± 3.3 years of follow-up: 2 patients developed RP-ILD, 4 required oxygen therapy and 5 died. Three deaths were directly related to myositis, all occurring in those with strong anti-MDA5 positivity. Despite the limited number of events, there was a trend toward higher mortality among patients with moderate-to-strong anti-MDA5 positivity (42.9% *vs*. 12.5%; p=0.142).
Similarly, patients with moderate-to-high anti-MDA5 titers had a higher number of hospitalizations compared to those with low titers (mean rank 13.6 *vs*. 9.7), although the difference did not reach statistical significance (p=0.14).
Conclusions. Although the limited sample size reduced statistical power, this study underscores the heterogeneous course of anti-MDA5-positive IIM. It highlights the potential prognostic value of anti-MDA5 antibody titers, suggesting that baseline levels may serve as useful biomarkers to improve risk stratification, guide therapeutic decisions, and predict clinical outcomes.
Key words: anti-MDA5 antibodies, idiopathic inflammatory myopathies, prognosis

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PREDICTORS OF INTERSTITIAL LUNG DISEASE PROGRESSION IN ANTISYNTHETASE SYNDROME

Marthe Mæhlen[1], Emily Langballe[1], Kastriot Kastrati[1,2], Helena Andersson[1], Anna-Maria Hoffman-Vold[1]
[1]Oslo University Hospital, Oslo, Norway, [2]Medical University of Vienna, Vienna, Austria

Background. Antisynthetase syndrome-associated interstitial lung disease (ASyS-ILD) is a major determinant of morbidity and mortality, especially in patients with progressive disease. Identifying risk factors for lung function decline is essential to guide monitoring and treatment strategies. Our objective was to determine clinical and serological predictors of change in lung function in ASyS-ILD over 24 months.
Methods. We included all patients with ASyS-ILD followed from a nationwide expert referral center who had clinical ASyS, antisynthetase antibodies, and ILD diagnosed by expert radiologists on high-resolution CT. Lung function was assessed prospectively including forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO). We calculated change in relative FVC and DLCO from baseline to 12 and 24 months. At 12 months ILD progression was defined as ≥5% relative FVC decline, improvement as ≥5% FVC increase and stable disease as <+/-5% change. At 24 months progression was defined as FVC decline of ≥10%. For DLCO, progression was defined as ≥8% relative DLCO decline at 12 months and ≥16% at 24 months. Predictors for ILD progression was assessed using logistic regression (progression *vs*. no progression), including antibody subtype, sex, esophageal dysmotility and smoking status.
Results. 189 patients were included with 66% being anti-Jo1 positive, 13.7% anti-PL12, 15.6% anti-PL7, and 4.9% other antisynthetase antibodies. Mean age at ILD diagnosis was 53.9 years, 69% female, 46% were 'ever-smokers' and 39% had esophageal dysmotility. Nearly all patients were treated with immunosuppressants including prednisolone in combination with DMARD/biologics during follow-up. Two-year follow-up data was available for at least 135 patients. At baseline mean FVC was 72.2% (SD 20.1), and DLCO 55.9% (SD 17.2). Mean change from baseline to 12 and 24 months was 10.2% and 10.5% for FVC, and 8.8 % and 10.0% for DLCO. At 12 months, 60.7% improved, 23.0% were stable and 16.3% worsened in FVC, while at 24 months, 10.4 % worsened. Only esophageal dysmotility, and not sex, gender or smoking, was independently associated with FVC progression at 24 months (OR 2,96, 95% CI 1.2–7.3, p=0.02), even after adjustment for sex and antibody subtype. DLCO progression occurred in 13.9% at 12 months and 4.9% at 24 months and was not associated with dysmotility, sex, smoking, or antibody status.
Conclusions. Despite many patients with ASyS-ILD experienced improvement or stability in lung function over 24 months a substantial number of patients declined despite standard of care therapy. Esophageal dysmotility predicted FVC decline and may represent a clinically meaningful marker of progressive disease.
Key words: interstitial lung disease, dysmotilty, progression

Genetic & Environmental Risk Factors

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THE INTERPLAY BETWEEN INFECTIONS AND IMMUNOGENETICS IN THE PATHOGENESIS OF IDIOPATHIC INFLAMMATORY MYOPATHIES

Dorota Lebiedz-Odrobina[1], Tayler Fearn[2], Ramkiran Gouripeddi[1], Pablo J. Maldonado-Catala[1], Naomi Schlesinger[1], Julio C. Facelli[1]
[1]University Of Utah, Salt Lake City, USA, [2]Utah Valley University, Orem, USA

Background. Idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of diseases associated with genetic and environmental factors, yet the etiology remains unclear.
Objective. Explore approaches to understanding IIM etiology: molecular mimicry and temporal analysis of previous infections in electronic medical records.
Methods. We identified homologous epitope sequences between known infectious agents and IIM-related antigens. We assessed their binding affinity to MHC molecules using the Immune Epitope Database (IEDB). For the best empirically found candidates, we performed docking calculations to assess binding using Boltz-2. We used TriNetX to select a cohort of patients with ICD-10 codes associated with IIMs and c-SPADE sequential pattern mining to find sequences of infections before the onset of IIMs.
Results. Among all possible 79,400 epitope pairs between 10 myositis-associated epitopes and the human pathogen epitopes in IEDB, we found nine epitope pairs that exhibiting sequence homology and empirical binding affinity to be considered candidates for molecular mimicry. Docking shows that sequence homology and empirical binding are effective to evaluate candidates when large-scale docking is not feasible. The infectious epitopes found correspond to Mycobacterium tuberculosis, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), and Alpha papillomavirus 7 (AP7). Sequential mining yielded 110 frequent infection patterns found across a cohort of 2,444 patients with confirmed IIM. These patterns occurred in five or more patients. The most common ICD-10 codes found in the c-SPADE patterns were: Unspecified infectious disease (B999); Human immunodeficiency virus disease (B20), Influenza due to unidentified influenza virus (J111), Sepsis, unspecified organism (A419), Acute nasopharyngitis [common cold] (J00), and Viral infection, unspecified (B349).
Conclusions. Molecular mimicry-epitope homology was found for nine epitopes from Mycobacterium tuberculosis, SARS-CoV-2, and AP7.The relatively small number of IIM-related epitopes in IEDB may influence these findings.
The lack of specific infectious agent identification in the clinical record, which in many cases is represented by the generic B999 ICD code, makes it difficult to correlate clinical findings with molecular mimicry.
To further our understanding of the etiology of IIM, it will be necessary to identify a larger set of epitopes associated with IIMs and to develop curated clinical data sets in which infectious pathogens are characterized.
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Key words: idiopathic inflammatory myositis, environmental and generic factors, infections, molecular mimicry-epitope homology

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BEYOND STATINS: ALTERNATIVE TRIGGERS IN ANTI-HMGCR IMNM CASE SERIES AND REVIEW OF THE LITERATURE

Mariana Emília Santos[1,2], Antonella Notarnicola[3,4,5], Rui da Silva Rodrigues[6], Inger Nennesmo[7], Ingrid E. Lundberg[3,4,5], Maryam Dastmalchi[3,4,5], Angeles S. Galindo-Feria[3,4,5]
[1]Rheumatology Department, ULS Lisboa Ocidental, Hospital Egas Moniz, Lisboa, Portugal, [2]NOVA Medical School, Universidade NOVA de Lisboa, Lisboa, Portugal, [3]Division of Rheumatology, Department of Medicine, Karolinska Institutet, Solna, Stockholm, Sweden, [4]Center for Molecular Medicine, Stockholm, Sweden, [5]Department of Gastro, Dermatology and Rheumatology, Theme Inflammation and Aging, Karolinska University Hospital, Stockholm, Sweden, [6]Department of Clinical Immunology and Transfusion Medicine, Karolinska University Hospital, Stockholm, Sweden, [7]Department of Oncology-Pathology, Karolinska Institutet, Stockholm, Sweden

Background. Immune-mediated necrotizing myopathy (IMNM) is an idiopathic inflammatory myopathy. Anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) antibodies are highly specific for this entity and frequently associated with prior statin exposure (1). Statin-naive cases suggest alternative triggers (2). Experimental evidence supports that natural substances, including flavonoids, found in multivitamin supplements, have documented HMGCR-inhibitory effects, plausibly reproducing the same pathogenic effects as statins (3). Supraphysiological doses of apparently harmless components, such as vitamin B12, may trigger inflammatory responses through mitochondrial stress and immune activation (4). Recognition of these hidden exposures is crucial for accurate diagnosis, management, and prevention of relapse.
Methods. We conducted a case-based review of anti-HMGCR IMNM cases followed at Karolinska University Hospital (2020–2025). Disease data were retrieved from electronic medical records. Drug and supplement history was obtained. Literature review of natural compounds with documented HMGCR-inhibitory activity was conducted.
Cases presentation. Case 1 describes a 49-year-old woman with progressive proximal weakness, elevated creatine kinase, and high-titer anti-HMGCR

antibodies without statin exposure. Muscle biopsy confirmed IMNM. A detailed anamnesis revealed recent intake of a multivitamin containing flavonoids. Discontinuation of the supplement and treatment with intravenous immunoglobulin (IVIg) and methotrexate led to clinical and biochemical response.
Case 2 involves a 58-year-old man with prior statin-associated anti-HMGCR IMNM who experienced two relapses during follow-up. The second flare coincided with the initiation of a multivitamin supplement containing high-dose vitamin B12 (20-fold RDA). Discontinuation of the supplement, without major immunosuppressive escalation besides an additional cycle of IVIg, resulted in clinical and biochemical improvement.
Conclusions. These cases highlight multivitamin supplements as potential overlooked triggers of anti-HMGCR IMNM, either at disease onset in statin-naive individuals or as relapse precipitants in established disease. While causality cannot be proven, the temporal relationship and clinical reversibility following supplement withdrawal support a biologically plausible link. Clinicians should routinely screen for alternative triggers with potentially HMGCR-inhibitory, proinflammatory or myotoxic effects, especially in those with unexplained onset or relapse. Heightened awareness may prevent misdiagnosis, avoid unnecessary immunosuppressive intensification, and improve disease outcomes.
Key words: immune-mediated necrotizing myopathy, anti-HMGCR, statin mimickers, multivitamins, nutritional supplements

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PRIORITIZING DRUG TARGETS FOR IDIOPATHIC INFLAMMATORY MYOPATHIES VIA QTL-BASED MENDELIAN RANDOMIZATION AND COLOCALIZATION

Gang Chen[1], Hector Chinoy[2,3,4], Sizheng Zhao[2,3], Andrew Morris[2,3], Janine Lamb[1], International Myositis Assessment & Clinical Studies Group
[1]Epidemiology and Public Health Group, School of Health Sciences, The University of Manchester, Manchester, UK, [2]Centre for Musculoskeletal Research, Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK, [3]NIHR Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK, [4]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK

Background. Idiopathic inflammatory myopathies (IIM) are rare autoimmune disorders with incompletely defined genetic mechanisms. Identifying causal genes and proteins may accelerate therapeutic target discovery.
Methods. We performed two-sample Mendelian randomization (MR) with molecular quantitative trait loci (QTLs) and colocalization to evaluate the causal effects of 1,064 proteins and 8,415 genes on overall IIM and clinical subtypes, including polymyositis (PM), dermatomyositis (DM), juvenile DM and anti-Jo-1. cis-protein QTLs (pQTLs) from Fenland serum protein study and cis-expression QTLs (eQTLs) from GTEx skeletal muscle and eQTLGen whole blood were used in two-sample MR. Bonferroni correction accounted for multiple testing. Significant MR signals after correction were assessed by colocalization to confirm shared causal variants (PP4>0.8). Drug target tractability was assessed via the Open Targets Platform
Results. Four targets emerged after MR significance correction and colocalization. pQTL-based MR implicated TLR1 (OR=0.21, 95% CI: 0.10–0.44, p=3.17×10–5) and NFKB1 (OR=3.19, CI: 1.96–5.21, p=3.37×10–6), with concordant eQTL-based MR in whole blood. eQTL-based MR additionally identified DCAKD (skeletal muscle; IIM: OR=0.57, CI: 0.46–0.70, p=1.22×10–7) and PTPN22 (whole blood; PM: OR=3.43, CI: 2.14–5.48, p=2.63×10–7). No significant signals were observed for DM, juvenile DM, or anti-Jo-1. Colocalization confirmed shared causal variants for: (i) IIM with serum levels of TLR1 and NFKB1, and expression levels in skeletal muscle of DCAKD; and (ii) PM with expression levels in whole blood of PTPN22. Drug target assessment indicated tractability for TLR1, NFKB1, and PTPN22 with varying clinical readiness, while DCAKD emerged as a novel target with limited tractability.
Conclusions. Integrating QTL-based MR with colocalization highlights TLR1, NFKB1, DCAKD, and PTPN22 as candidate regulators in IIM and PM, implicating innate immune sensing, NF-κB signaling, and proteostasis pathways. These findings nominate tractable therapeutic targets and demonstrate a scalable framework for causal drug target prioritization in rare autoimmune disease.
Key words: idiopathic inflammatory myopathies, Mendelian randomization, colocalization, candidate targets

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SMOKING HABITS IN UK PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHY – INSIGHTS FROM THE UK MYOPROSP COHORT

Aleksandra Opinc-Rosiak[1], Olga Brzezińska[1], Joanna Makowska[1], Janine Lamb[2], Patrick Gordon[3], Sarah Tansley[4], Harsha Gunawardena[5], James Lilleker[6], Neil McHugh[4], Athiveeraramapandian Prabu[7], Alexander Oldroyd[8,9], Hector Chinoy[8,9]
[1]Department of Rheumatology, Medical University of Lodz, Lodz, Poland, [2]Division of Population Health, Health Services Research and Primary Care, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK, [3]Centre for Rheumatic Diseases, King's College London, 3rd floor Weston Education Centre, London, UK, [4]Department of Life Sciences, University of Bath, Bath, UK, [5]Department of Rheumatology, North Bristol NHS Trust, Bristol, UK, [6]Muscle Disease Unit, Manchester Centre for Clinical Neuroscience, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK, [7]Department of Rheumatology, University of Birmingham, Birmingham, UK, [8]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [9]Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK

Background. Tobacco smoking is a recognized risk factor for many diseases, including systemic connective tissue diseases. In idiopathic inflammatory myopathy (IIM), smoking has been associated with polymyositis, interstitial lung disease (ILD) and antisynthetase antibodies in a dose-dependent manner (1). We aimed to characterise smoking patterns and explore associations with ILD and autoantibody profiles in the MYOPROSP cohort.
Methods. We retrospectively analysed data from adult participants of the MYOPROSP database. Data on smoking history (status, duration, intensity and pack-years) were extracted. Patients were categorised as ever-smokers (current or past) or never-smokers. Prevalence of ILD (as defined by local clinical practice) and autoantibody distribution were compared according to smoking status. Statistical analyses included Shapiro Wilk, two-sided Fisher, student's t- and Mann-Whitney U-tests as appropriate.
Results. Data of 199 participants (70% female; mean age at diagnosis 53 years) was analysed. Overall, 83 patients (42%) were ever-smokers, though only 9 (4.52%) were current smokers at the time of data collection. Among ever-smokers, mean smoking duration was 20 years (± 14) and mean exposure 17 pack-years (±20); 55 patients (70.51%) smoked for >10 years and 45.2% exceeded 10 pack-years. Most patients ceased smoking before IIM diagnosis (n=59, 73.8%). Prevalence of ILD did not significantly differ between ever- and never-smokers and showed no clear association with duration or intensity of smoking. By contrast, anti-TIF1γ antibodies were more frequent among ever-smokers than never-smokers (n=9 *vs*. n=1, p=0.002). Long-term (>10 years) and heavy (>10 pack-years) smokers were less likely to be seronegative (p=0.045 and p=0.026, respectively).
Conclusions. Significant proportion of IIM patients had a history of smoking. Smoking may be associated with the occurrence of anti-TIF1γ antibodies in IIM, however studies on larger groups are needed to verify this observation
Key words: smoking, tobacco, interstitial lung disease, database

Reference

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ENVIRONMENTAL AND LIFESTYLE EXPOSURES ASSOCIATED WITH INTERSTITIAL LUNG DISEASE AND CARDIAC INVOLVEMENT IN IDIOPATHIC INFLAMMATORY MYOPATHY: ANALYSIS FROM THE UK MYONET COHORT

Aleksandra Opinc-Rosiak[1], Olga Brzezińska[1], Joanna Makowska[1], Janine Lamb[2], Patrick Gordon[3], Sarah Tansley[4], Harsha Gunawardena[5], James Lilleker[6], Neil McHugh[4], David Isenberg[7], William Ollier[8], Alexander Oldroyd[9,10], Hector Chinoy[9,10]

[1]Department of Rheumatology, Medical University of Lodz, Lodz, Poland, [2]Division of Population Health, Health Services Research and Primary Care, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK, [3]Centre for Rheumatic Diseases, King's College London, 3rd floor Weston Education Centre, London, UK, [4]Department of Life Sciences, University of Bath, Bath, UK, [5]Department of Rheumatology, North Bristol NHS Trust, Bristol, UK, [6]Muscle Disease Unit, Manchester Centre for Clinical Neuroscience, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, UK, [7]Department of Ageing, Rheumatology and Regenerative Medicine, Division of Medicine, University College London, London, UK, [8]Faculty of Science and Engineering, Manchester Metropolitan University, Manchester, UK, [9]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [10]Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK

Background. Lifestyle factors and environmental exposures are identified as key players of autoimmunity in many connective tissue diseases, but their role in idiopathic inflammatory myopathy (IIM) is poorly understood. Interstitial lung disease (ILD) and cardiac involvement are crucial and potentially life-threatening complications of IIM. We aimed to examine environmental and lifestyle exposures in a UK IIM cohort and explore their associations with ILD and cardiac involvement

Methods. Data from the UK MYONET study, a UK-wide cross-sectional study of participants with IIM, was analysed. Demographic, clinical and serological data as well as self-reported environmental and lifestyle exposures were extracted. ILD and cardiac involvement were reported by physician; diagnosis of ILD was based on x-ray, HRCT or pulmonary function tests. Associations were assessed using chi-square test, Kruskall-Wallis, ANOVA, and logistic regression models.

Results. Data of 1926 participants was analysed. The mean age was 56 years (±15), 1581 (83%) of patients had European ancestry and the mean duration of the disease was 6 years (±6). Most patients were overweight or obese (n=624, 64%), and 450 (33%) were ever-smokers. Exposure to occupational or environmental toxins was reported in 511 (9.3%) participants, most frequently asbestos (n=91, 4.8%) and solvents/chemicals (n=66, 3.5%) and less to fiberglass (n=38, 2%), other dusts (n=38, 2%) and silica (n=18,0.9%). ILD was diagnosed in 444 patients (23.3%) of the cohort. Asbestos and fiberglass exposure were associated with higher odds of ILD (asbestos OR 2.1, 95%CI 1.3-3.5, p=0.003; fiberglass OR 3.1, 95%CI 1.6-6.0, p=0.0012). Additional statistically significant factors associated with ILD included antisynthetase syndrome, overlap myositis, African/Afro-Caribbean ethnicity, and clinical features such as Raynaud's phenomenon, periungual erythema, mechanic's hands and arthritis. Diagnosis of cardiac involvement was reported in 65 patients (3.41%) of the analysed cohort but it was more frequent in patients with overlap myositis, mechanic's hands, Raynaud's phenomenon, arthritis, dysphagia and ILD. Reported toxin exposure was also associated with increased odds of cardiac involvement (OR 3.8, 95% CI 1.4-10.5; p=0.0054).

Conclusions. In this large UK IIM population, occupational and environmental exposures were common and showed associations with both ILD and cardiac involvement. While causality cannot be inferred, these findings highlight the need to consider environmental history in IIM assessment as a possible risk factor for vital organ involvement and to further investigate exposure-related risk using prospective, standardised approaches.

Key words: environmental, exposure, interstitial lung disease, cardiac, database

Inclusion Body Myositis

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MYOFIBER NECROSIS AND COMPLEMENT (C5b-9) DEPOSITION IN INCLUSION BODY MYOSITIS: FREQUENCY AND PATHOLOGIC ASSOCIATIONS

Mustafa Ekici[1,2,3], James B. Lilleker[4], Federico Roncaroli[5], Hector Chinoy[2,3,4]

[1]Hacettepe University Faculty of Medicine, Department of Rheumatology, Ankara, Turkey, [2]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [3]Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK, [4]Manchester Centre for Clinical Neurosciences, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Salford, UK, [5]Geoffrey Jefferson Brain Research Centre, Division of Neuroscience and Experimental Psychology, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK

Background. Inclusion body myositis (IBM) is a slowly progressive inflammatory myopathy characterized by combined immune and degenerative features; however, the clinical relevance of myofiber necrosis and complement deposition within the established pathological framework remains unclear. This study aimed to quantify the frequency of myofiber necrosis and complement (C5b-9) deposition in IBM, and assess their associations with established histopathological features.

Methods. We conducted a retrospective study at the Adult Neuromuscular Clinic, Salford Royal Hospital, Salford, UK, including all patients with IBM with available muscle biopsy data between 2004 and 2024. Eighty-six patients who met at least one of the ENMC 2013 or 2024 criteria were included in the study, and 50 patients (58.1%) underwent biopsies after 2015. Pathology data were collected from original reports, including details of C5b-9 staining (+/-), myofiber necrosis (present/absent), and co-recorded histopathologic domains: MHC-I/MHC-II positivity, rimmed vacuoles, mitochondrial pathology (*e.g.* COX-deficient fibers), lymphocytic infiltration, protein aggregates (p62/TDP-43). Serological variables (anti-cN1A and anti-Ro antibodies) were included where available. The primary outcome was the frequency of necrosis and complement deposition, and the secondary outcomes evaluated their associations with established histopathologic features.

Results. Eighty-six patients with a mean age of 73.8 ± 7.2 years; 54 (62.8%) were male. All patients fulfilled the ENMC 2013 diagnostic criteria (12 clinically defined, 60 clinico-pathologically defined, 14 probable), and 80 (93.0%) met updated ENMC 2024 criteria. Anti-cN1A antibodies were assessed in 30 patients, of whom eight (26.7%) were positive. Core findings were concordant with a diagnosis of IBM: MHC-I upregulation 76/76 (100%), MHC-II 9/11 (81.8%), rimmed vacuoles 71/82 (86.5%), mitochondrial abnormalities 67/80 (83.8%), lymphocytic infiltration 80/82 (97.5%), and protein aggregates 68/82 (82.9%). Myofiber necrosis was observed in 59 (68.6%) patients. Complement deposition was detected in 49 (57.0%) samples; sarcolemmal staining in 21 (42.9%), capillary staining in 21 (42.9%), and both in 7 (14.3%). C5b-9 positivity was associated with rimmed vacuoles (95.7% [45/47] *vs*. 76.2% [16/21], OR 7.03, 95% CI 1.24–39.91; p=0.028). No other histopathological domains, including MHC-I/MHC-II expression, mitochondrial pathology, lymphocytic infiltration, or protein aggregates, were associated with complement deposition or necrosis status.

Discussion: Necrosis and C5b-9 deposition are common in IBM and coexist with the established histopathology of the disease. The association between complement positivity and rimmed vacuoles may indicate that complement activation aligns with degenerative pathology. Our study suggests that C5b-9 could have a role in IBM pathogensis and presence on muscle biopsy is common in patients with IBM.

Key words: inclusion body myositis, complement C5b-9 deposition, myofiber necrosis

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WHEN GOOD B CELLS GO BAD: cN1A-REACTIVITY IN INCLUSION BODY MYOSITIS

Nataliya Slater[1,2], Abha Chopra[1], Merrilee Needham[1,2,3,4], Jerome Coudert[5]
[1]Murdoch University, Murdoch, Australia, [2]Perron Institute for Neurological and Translational Research, Nedlands, Australia, [3]University of Notre Dame, Fremantle, Australia, [4]Fiona Stanley Hospital, Murdoch, Australia, [5]University of Toulouse, Toulouse, France

Background. Inclusion Body Myositis (IBM) is the most common acquired myopathy in individuals over 50, posing major challenges for diagnosis and treatment. Antibodies to cytosolic 5'-nucleotidase 1A (cN1A) are detected in approximately half of IBM patients, ranging from 33% to 80%. Their origin and role in pathogenesis remain unclear. This study aimed to characterise cN1A-reactive B cell receptors (BCR) to elucidate humoral immune mechanisms in IBM and inform the development of B cell-targeted therapies.
Methods. To confirm the presence of circulating cN1A-reactive B cells, peripheral blood mononuclear cells (PBMC) from IBM patients and healthy donors were stimulated with resiquimod (R848). Anti-cN1A produced by memory B cells were measured by ELISA.
cN1A-reactive B cells were isolated from 40–50 mL of venous blood from three IBM patients seropositive for anti-cN1A. IgG+ and IgM+ B cells were isolated individually by fluorescence-activated cell sorting (FACS) using recombinant cN1A. Cells were lysed for RNA extraction and reverse transcribed to cDNA. Single-cell BCR sequencing was performed using Illumina protocols, where individual cell cDNA was barcoded and amplified with BCR-specific primers. Reads were quality-filtered, demultiplexed, pre-processed with MiXCR v. 4.7.0 and analysed in R using the Immunarch package v. 0.9.1.
Results. Following stimulation, IgM+ anti-cN1A were detected in all individuals, including healthy donors. IgG+ antibodies were significantly elevated in IBM, while IgA+ antibodies were low across all samples.
Upon FACS, the proportion of cN1A-reactive B cells ranged from 0.1–1.7% of peripheral CD19+ cells. IgM+ cell frequency correlated strongly with serum IgM (R2=0.99), whereas IgG+ cell frequency correlation with serum IgG was weaker (R2=0.39). A total of 51 complete BCR sequences were obtained: 59% IgG- and 41% IgM-derived. Identical clones were detected within individuals but not between them. Heavy-chain germline gene usage was individually restricted, while light chains showed limited diversity.
Conclusions. cN1A-reactive B cells are part of the natural IgM repertoire but expand and undergo isotype switching in IBM driven by inflammatory mediators and antigen misfolding. Their oligoclonal nature, shortened heavy-chain CDR3, and convergent light-chain usage support an antigen-driven autoimmune response distinct from polyclonal bystander activation.
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Key words: inclusion body myositis, IBM, cytosolic 5'-nucleotidase 1A, B cell receptor sequencing, cN1A, NT5C1A

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GBP6: A HIGHLY SPECIFIC INTERFERON GAMMA-DEPENDENT SERUM AND TISSUE BIOMARKER FOR INCLUSION BODY MYOSITIS

Corinna Preusse[1,2,3*], Felix Kleefeld[4*], Vera Dobelmann[5], Andreas Roos[6], Iago Pinal-Fernandez[7,8], Andrew Mammen[7,8,9], Werner Stenzel[2]
[*]Contributed equally
[1]Charité-Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt Universität zu Berlin, Department of Neurology, Berlin, Germany, Berlin, Germany, [2]Charité-Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health (BIH), Department of Neuropathology, Berlin, Germany, Berlin, Germany, [3]Charité-Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health (BIH), Department of Neuropediatrics, Berlin, Germany, Berlin, Germany, [4]Department of Neurology, Heimer Institute for Muscle Research, University Hospital Bergmannsheil, Ruhr-University Bochum, Bochum, Germany, Bochum, Germany, [5]Department of Neurology, University Hospital Düsseldorf, Düsseldorf, Germany, Düsseldorf, Germany, [6]University Duisburg-Essen, Department of Pediatric Neurology, Centre for Neuromuscular Disorders, Essen, Germany, Essen, Germany, [7]Muscle Disease Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, Maryland, USA, Bethesda, USA, [8]Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, Baltimore, USA, [9]Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA, Baltimore, USA

Background. Inclusion body myositis (IBM) is a common acquired inflammatory myopathy in individuals over age 50. The chronic and slowly progressive disease course, often developing over decades, leads to muscle atrophy and replacement by fat and fibrous tissue. Despite extensive basic and immunological research and insightful data, no effective treatment is available. A prevailing hypothesis that aims to explain this lack of effective treatment response refers to the fact that targeted therapeutic interventions may be initiated too late and that tissue destruction may not be reversible. Identifying early disease markers is therefore crucial for developing strategies to enable timely treatment.
Methods. We explored the role of guanylate-binding protein 6 (GBP6) as a novel biomarker and potential target using histological staining, ELISA-based measurements in serum of patients with early (eIBM) and late-stage IBM (IBM) and non-IBM myositis. Additionally, we performed proteomic and transcriptomic analyses.
Results. We identified a consistent and specific upregulation of GBP6 in IBM compared to other inflammatory myopathies. Serum GBP6 protein levels demonstrated promising discrimination between IBM and other myositis subforms, suggesting its utility as a soluble biomarker. Notably, GBP6 upregulation appears restricted to IBM, with only sporadic expression observed in subsets of anti-synthetase syndrome and dermatomyositis patients. While we identified KLRG1, a prominent marker of immune senescence, being expressed in all myositis subtypes, GBP6 was a more specific biomarker for IBM.
Conclusions. GBP6 emerges as a promising candidate biomarker with strong potential to improve early detection and disease monitoring in IBM. Unlike KLRG1, which is restricted to tissue-level diagnostics, GBP6 offers the advantage of serum-based measurement and could thus become the first blood biomarker for IBM. However, important questions remain regarding its specificity in larger and more diverse patient cohorts, including eIBM. Furthermore, longitudinal data are required to evaluate its relationship with disease onset, progression, and clinical parameters such as IBM-FRS scores, dysphagia, creatine kinase, and anti-cN1A antibodies. Therefore, future studies should validate its specificity, assess longitudinal dynamics, and determine correlations with clinical severity to confirm its role as both a diagnostic and potentially therapeutic marker in IBM. Our current project will be the starting point for this.
Key words: inclusion body myositis, GBP6, biomarker

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DETECTION OF AUTOANTIBODIES AGAINST cN-1A USING A MULTIPARAMETER LINEBLOT FOR AUTO-IMMUNE INFLAMMATORY MYOPATHIES

Julia Janz[1], Anthonina Ott[1], Antje Lindae[1], Tanja Seifert[1], Thomas Scheper[1], Wolfgang Schlumberger[1], Wolfgang Meyer[1]
[1]Institute for Experimental Immunology, affiliated to EUROIMMUN Medizinische Labordiagnostika AG, Lübeck, Germany

Background. Autoantibodies against cN-1A (Mup44) are primarily used as a biomarker for inclusion body myositis (IBM), they also occur with lower prevalence in systemic lupus erythematosus (SLE) and Sjögren's Syndrome (SjS). cN-1A has been included as a parameter on the multiparameter lineblot Autoimmune Inflammatory Myopathies 16 Ag et cN-1A (Euroimmun), allowing the detection of 17 myositis-specific and myositis-associated autoantibodies. The prevalences of anti-cN-1A autoantibodies were determined in different patient collectives and healthy blood donors.
Methods. A lineblot immunoassay containing a highly purified, recombinant cN-1A expressed in E.coli was incubated according to the instructions. Sera of 197 patients with IBM, 48 with collagenosis (systemic sclerosis, undifferentiated collagenosis and mixed tissue collagenosis), 52 with polymyositis/dermatomyositis and 75 with SLE/SjS were screened for cN-1A autoantibodies. Additionally, 151 apparently healthy blood donors as well as a disease control collective comprising sera of 20 patients with thyroiditis, 26 with neuromuscular disorders, 24 with primary biliary cholangitis (PBC), 19 with Wegener's Disease, 17 with Coeliac disease, and 2 with autoimmune liver disease (ALD) were analyzed. Signal intensities were automatically evaluated using the EUROLineScan software (Euroimmun).

Results. Prevalences of cN-1A autoantibodies were 34.5% in IBM, 10.4% in collagenosis, 7.7% in polymyositis/dermatomyositis, 13.3% in SLE/SjS, 2% in the blood donor cohort and 4.6% in the disease control collective.
Conclusions. The addition of cN-1A to a multiparametric lineblot immunoassay now reduces the risk of underdiagnosing IBM in patients with autoimmune inflammatory myopathies and increases the overall diagnostic sensitivity.
Key words: anti-cN-1A, inclusion body myositis, lineblot

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EXPLORING RELATIONSHIPS BETWEEN THE IBMFRS AND TRANSITIONAL AMBULATORY PHASES AND THE IMPACT ON FALL RISK IN PATIENTS WITH INCLUSION BODY MYOSITIS (IBM): INSPIRE-IBM

Stephanie Hunn[1], Namita A. Goyal[2], Anthony Amato[3], Perry Shieh[4], Miriam Freimer[5], Mazen M. Dimachkie[6], Leo H. Wang[7], Matthew Wicklund[8], Stacy Dixon[8], Aziz Shaibani[9], Payam Mohassel[10], Thomas Lloyd[10,11], Colin Quinn[12], Nizar Chahin[13], Olimpia Carbunar[14], Rabi Taweil[15], Emma Ciafaloni[15], Conrad C. Weihl[1], Tahseen Mozaffar[2]
[1]Washington University School Of Medicine, St. Louis, USA, [2]University of California-Irvine, Irvine, USA, [3]The Brigham and Women's Hospital, Boston, USA, [4]University of California - Los Angeles, Los Angeles, USA, [5]Ohio State University, Columbus, USA, [6]University of Kansas, Kansas City, USA, [7]University of Washington, Seattle, USA, [8]University of Colorado, Denver, USA, [9]Nerve and Muscle Center of Texas, Houston, USA, [10]Johns Hopkins University, Baltimore, USA, [11]Baylor College of Medicine, Houston, USA, [12]University of Pennsylvania, Philadelphia, USA, [13]Oregon Health and Science University, Portland, USA, [14]University of Miami, Miami, USA, [15]University of Rochester, Rochester, USA

Background. Inclusion body myositis (IBM) is an inflammatory myopathy characterized by progressive weakness of the knee extensors and finger flexors. While assistive devices may improve gait and minimize fall risk in some patients, challenges remain in clinical decision making as to when certain devices may be appropriate. The IBM Functional Rating Scale (IBMFRS) is a 10-item questionnaire that has been considered standard practice in clinical and research settings for patients with IBM1. The goal of our study is to explore the relationship between the IBMFRS and transitional phases of ambulation, as well as the potential for the IBMFRS to identify and predict patients that are at a fall risk.
Methods. The INSPIRE-IBM study is a 2-year natural history study collecting data related to disease progression in participants across 13 sites. Participants are evaluated every 6 months, performing assessments including the IBMFRS, Timed Up and Go (TUG), and patient-reported outcomes, such as the SIBM Physical Functioning Assessment (sIFA). Participants are instructed to keep a "fall diary" to log the number of falls between visits.
Results/Conclusions. We report a cross-sectional analysis of the 150 participants enrolled, 66 of which were ambulatory without devices and 80 were ambulatory with devices. Participants ambulating with devices had a significantly lower score on the IBMFRS (ambulatory: 30.4 mean ± 4.3; ambulatory with devices: 23.2 mean ± 4.9; $p<0.01$), as well as higher scores on the sIFA (ambulatory: 34.0 ± 17.1; ambulatory with devices: 60.1 ± 20.8; $p<0.001$) compared to those ambulating without devices. Those ambulating with devices who were able to perform the TUG (68.8% of 80 participants), required significantly more time to complete the test (without devices: 10.2 ± 3.0; with devices: 20.6 ± 10.3; $p<0.001$). We found that participants with a score of 21-32 out of 40 on the IBMFRS reported the greatest number of falls. Analysis of the IBMFRS subcategories further indicates that the ability to rise from a chair or climb stairs correlated with earlier loss of independence compared to other functional tasks (median timespan to loss of independence = 10 years for both). With this information, the IBMFRS may be considered a useful tool in identifying patients at high fall risk as well as predicting transitionary phases in ambulation.
Key words: inclusion body myositis, IBMFRS, ambulation

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PATIENT JOURNEY, HEALTHCARE RESOURCE UTILIZATION, AND MORTALITY IN IBM: A US-BASED CLAIMS ANALYSIS

Raymond E. Mankoski[1], Karen Tubridy[1], Jacob Winthrop[2], Chris Koch[2], Elie Naddaf[3]
[1]Abcuro Inc., Newton, USA, [2]Real Chemistry, New York, USA, [3]Department of Neurology, Mayo Clinic, Rochester, USA

Background. Studies evaluating diagnostic journey, associated comorbidities, healthcare resource utilization, and mortality in patients with inclusion body myositis (IBM) consisted mostly of referral centers' cohorts. We sought to evaluate these outcomes in a large United States claims database.
Methods. Patients with ≥2 IBM International Classification of Diseases, Tenth Revision (ICD-10) diagnoses first captured between 1/1/2020 and 7/30/2025 were compared with age- and sex-matched controls. Index date was the IBM Diagnosis date defined as the first time IBM ICD-10 code was used. Demographics, time to diagnosis, IBM-related symptoms, comorbidities, and resource utilization were assessed. Mortality was assessed using Standardized Mortality Ratios (SMR) expressed as (total yearly IBM deaths)/(US population mortality rate). Machine learning (ML) was utilized on an expanded dataset to estimate the number of symptomatic but undiagnosed patients.
Results. The study population included 3659 patients with IBM (60% males and 67% White) and 106,968 controls. Median time from first IBM-related symptom reported to a healthcare practitioner to diagnosis was 2.6 years (± 2.3 years). Forty-one percent of patients were originally diagnosed with an alternative diagnosis, most commonly "myositis" followed by "polymyositis." Immune-mediated disorders more common in the IBM group than in controls (since the initial diagnosis) included Sjögren's syndrome, unspecified (16.1 times (x) more common), ankylosing spondylitis (7.3x), lupus (7.2x), polyneuropathy (3.9x), rheumatoid arthritis (2.6x), multiple sclerosis (2.2x), and psoriatic arthritis (2.1x). Several hematologic malignancies were also more common, including 'other lymphoid leukemia' (52.0x), multiple myeloma (2.4x) and non-Hodgkin lymphoma (2.1x). Solid tumors and neurodegenerative diseases were similar between groups. Compared with controls, in the 12 months after diagnosis, patients had more outpatient office visits (81% *vs*. 74%), emergency room visits (20% *vs*. 17%), inpatient admissions (13% *vs*. 6%), and skilled nursing services (9% *vs*. 2%). All-cause mortality rates were statistically significantly increased (by SMR) in IBM compared with controls for age groups 38–47 (2.4% *vs*. 0.3%), 48–57 (2.8% *vs*. 0.5%), 58–67 (3.3% *vs*. 1.2%), and 68+ years (8.5% *vs*. 4.8%). Male sex and Black race (*vs*. White) had higher death rates. Depending on the specificity used in the ML model, for every diagnosed patient there are 0.8–1.3 patients who have symptoms of IBM but lack a formal diagnosis.
Conclusions. Patients with IBM experience increased healthcare resource utilization and earlier mortality. Earlier recognition of IBM is needed to provide appropriate care.
Key words: inclusion body myositis, mortality, diagnosis, healthcare resource utilization

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COMPARATIVE EVALUATION OF RESPIRATORY ASSESSMENTS IN INCLUSION BODY MYOSITIS FROM INSPIRE-IBM STUDY

Isela Hernandez[1], Marie Wencel[1], Namita Goyal[1], Spencer Matthews[1], Olimpia Carbunar[2], Miriam Freimer[3], Mazen Dimachkie[4], Colin Quinn[5], Thomas Lloyd[6], Payam Mohassel[6], Conrad Weihl[7], Aziz Shaibani[8], Leo Wang[9], Nizar Chahin[10], Anthony A. Amato[11], Matthew Wicklund[12], Stacy Dixon[12], Perry Shieh[13], Laura Herbelin[4], Richard Barohn[14], Rabi Tawil[15], Emma Ciafaloni[15], Tahseen Mozaffar[1], INSPIRE-IBM Study Group
[1]University of California, Irvine, Orange, USA, [2]University of Miami, Miami, USA, [3]Ohio State University, Columbus, USA, [4]University of Kansas Medical Center, Fairway, USA, [5]University of Pennsylvania, Philadelphia, USA, [6]Johns Hopkins University, Baltimore, USA, [7]Washington University, Saint Louis, USA, [8]Nerve and Muscle Center of Texas, Houston, USA, [9]University of Washington, Seattle, USA, [10]Oregon Health & Science University, Portland, USA, [11]Brigham and Women's Hospital, Boston, USA, [12]University of Colorado, Aurora, USA, [13]University of California, Los Angeles, Los Angeles, USA, [14]University of Missouri, Columbia, USA, [15]University of Rochester Medical Center, Rochester, USA

Background. Anti-NT5c1A antibodies have been proposed as a potential biomarker for inclusion body myositis (IBM) and associated with increased disease severity, including respiratory functions. A 2016 study involving a cohort of 25 patients reported that NT5c1A seropositive individuals had significantly lower forced vital capacity (FVC) values (p=0.005), suggesting more severe respiratory involvement. Subsequent literature has been mixed, some supporting the 2016 findings, while others not finding support for this notion. Validation of these findings in a larger cohort of IBM patients in a controlled research setting is needed to clarify these associations. We compared the severity of respiratory dysfunction in NT5c1A seropositive and seronegative IBM patients across multiple timepoints: Baseline, 6-months, 12-months, and 18-months.
Methods. Data was collected from the INSPIRE-IBM Study: A 13-center observational prospective ongoing study involving 150 patients with IBM. Results from the Baseline, 6-month, 12-month, and 18-month visit were analyzed: FVC % predicted (sitting and supine), Maximum inspiratory pressure (MIP), and Maximum expiratory pressure (MEP). We compared the rate of change in pulmonary function (FVC, MIP, and MEP) between seropositive and seronegative IBM patients using a Generalized Estimating Equation (GEE) model with an AR-1 working correlation structure. The model included time, serum status, and their interaction. The primary focus was on the interaction term, which indicates whether the rate of change differs between groups. A significance level of 0.05 was utilized to determine statistical significance.
Results. Among all pulmonary assessments, only FVC (Sitting) Percent Predicted approached statistical significance (p=0.053); all other measures (FVC Supine, MIP, MEP) were not statistically significant. However, a consistent trend was observed: the seropositive group showed lower average rates of change across all time points (Baseline, 6, 12, and 18 months) for each respiratory measure. Additional data has been collected, and further analysis is currently in progress. The results will be presented at the upcoming conference
Conclusions. Based on earlier findings, we anticipate that NT5c1A-seropositive participants will again demonstrate lower pulmonary function test results, providing greater evidence of respiratory involvement in this subgroup.
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Key words: inclusion body myositis, anti-NT5c1A antibodies, pulmonary function tests

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ANABOLIC RESISTANCE IN INCLUSION BODY MYOSITIS VERSUS HEALTHY AGEING: INSIGHTS FROM AN EX VIVO-IN VITRO MODEL

Charlotte Linscott[1], Nathan Hodson[1,2], James B. Lilleker[3,4], Andrew M. Snedden[3,4], Hector Chinoy[1,4,5], Adam Lightfoot[6], Paul T. Morgan[1]
[1]Department of Sport and Exercise Sciences, Manchester Metropolitan University, Institute of Sport, Manchester, UK, [2]School of Sport Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham, UK, [3]Manchester Centre for Clinical Neurosciences, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [4]Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK, [5]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [6]Department of Life Sciences, Manchester Metropolitan University, Manchester, UK

Background. Inclusion body myositis (IBM) is the most common acquired myopathy in adults over the age of 45, characterised by progressive muscle atrophy and asymmetric weakness. The condition remains refractory to pharmacological interventions, with progress limited by an incomplete understanding of disease pathophysiology. Given that IBM predominantly affects older adults, anabolic resistance, a blunted muscle protein synthetic response to anabolic stimuli, may exacerbate muscle wasting in this population.
Anabolic resistance is a hallmark of ageing, underpinned by impaired activation of the mechanistic target of rapamycin (mTOR) signalling pathway. Using an in vitro-ex vivo model, this study aims to determine how IBM affects the muscle anabolic response to amino acids relative to healthy ageing. Evidence of diminished muscle anabolism would suggest that anabolic resistance may contribute to muscle loss in IBM. Elucidating these mechanisms could help guide the development of therapeutic strategies to restore anabolic sensitivity.
Methods. An in vitro-ex vivo model was employed to investigate whether exposure to serum from males with IBM (n=6, 67.3 ± 9.4 years, mean ± 1SD) modulated the anabolic response of human muscle cells to amino acid stimulation. Myogenic cultures (KM155/C25 line) were incubated for 4 hours with 10% serum from individuals with IBM or age-matched, healthy males (n=6 males, 66.3 ± 0.7 years). Following conditioning, cells were stimulated for 1 hour with an amino acid solution containing ~1.6 mM leucine to activate the mTOR pathway. Western blotting was performed to quantify key anabolic signalling proteins (phosphorylated and total mTOR, eEF2, Akt, p70S6K, and 4EBP1). Muscle protein synthesis rates were determined using the SUnSET (surface sensing of translation) technique, which measures puromycin incorporation into newly synthesised protein.
Results. Data collection and analyses are currently underway. It is hypothesised that serum from individuals with IBM will attenuate anabolic signalling and cellular protein synthesis to a greater degree than elderly serum, indicative of exacerbated anabolic resistance. These data will be available by March 2026 and presented at the conference.
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Key words: inclusion body myositis, anabolic resistance, muscle protein synthesis

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ASSESSING IN VIVO BRAIN AMYLOID DEPOSITION IN INCLUSION BODY MYOSITIS USING POSITRON-EMISSION TOMOGRAPHY

Sharfaraz Salam[1], Iwona Skorupinska[1], Michael G. Hanna[1,2], Martin N. Rossor[3], David Lilburn[4], Francesco Fraioli[4], Basil H. Ridha[3], Pedro M. Machado[1,2]
[1]Department of Neuromuscular Diseases, UCL Queen Square Institute of Neurology, University College London, London, UK, [2]NIHR University College London Hospitals Biomedical Research Centre, London, UK, [3]Dementia Research Centre, Department of Neurodegenerative Disease, UCL Queen Square Institute of Neurology, London, UK, [4]Institute of Nuclear Medicine, University College London Hospitals NHS Foundation Trust, London, UK

Background. Inclusion body myositis (IBM) is the most common acquired myopathy in people over 50. IBM is characterised by the accumulation of aberrant multiple-protein aggregates in muscle fibres and shares similar pathological markers to Alzheimer's disease (AD), including beta-amyloid (Abeta) and hyperphosphorylated tau (p-tau) deposition in affected muscles. IBM is not thought to directly influence cognition even though a significant proportion of patients are aged over 75. We previously performed neuropsychological assessments in IBM participants, demonstrating memory and executive function to be similar to normative data (Lu et al, 2022). In this study we sought to determine whether amyloid deposition in the brain was also comparable to that in the healthy population, using amyloid positron emission tomography-computed tomography (PET/CT) brain imaging.
Methods. We recruited IBM patients from an ongoing longitudinal natural history study in the UK. Patients underwent amyloid brain PET/CT with the commercial tracers Florbetaben or Florbetapir. Screening for cognitive impairment was performed using the Mini-Mental State Examination (MMSE). To estimate the expected frequency of amyloid positivity in our cohort, we used published amyloid PET positivity rates by age group and gender in the healthy population. We applied these values, adjusting for age and gender, and calculated the expected prevalence (with 95% Confidence intervals [CIs]) in our cohort. We then derived the expected number of amyloid-positive patients and compared it to the observed cases, including their CIs.
Results. Twenty IBM patients underwent amyloid PET/CT brain scans. Of these participants, only one patient had a positive PET/CT brain scan. According to existing age and gender matched data; the expected prevalence of amyloid positive cases in this sample of 20 individuals would be approximately 4 individuals (95%CI = 3.1 to 5.0). Screening with MMSE excluded any overt evidence of cognitive impairment in any of the patients recruited.
Conclusions. We demonstrated that the frequency of amyloid positivity in IBM patients may be lower compared with the healthy population,

suggesting a reduced risk of AD in this group of patients. These findings could enhance our understanding of the neurobiology of both IBM and AD, potentially opening new therapeutic avenues. Further research is needed to confirm these findings and explore the underlying mechanisms.
Key words: IBM, amyloid, PET/CT

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P-263

QUANTITATIVE MRI OF FOREARM MUSCLES AS A BIOMARKER IN INCLUSION BODY MYOSITIS

Sharfaraz Salam[1], Stephen Wastling[2], Nick Zafeiropoulos[2], Jasper M. Morrow[1], Iwona Skorupinska[1], Sachit Shah[2], Tarek Y. Yousry[2], John S. Thornton[2], Michael G. Hanna[1,3], Pedro M. Machado[1,3]
[1]Department of Neuromuscular Diseases, UCL Queen Square Institute of Neurology, University College London, UK; [2]Neuroradiological Academic Unit, UCL Queen Square Institute of Neurology, University College London, [3]NIHR University College London Hospitals, Biomedical Research Centre, London, UK

Background. Weakness of the finger flexors is a characteristic clinical feature of inclusion body myositis (IBM), particularly affecting flexor digitorum profundus (FDP). Previous MRI studies have demonstrated fatty accumulation within the forearm muscle compartment. Our group has previously demonstrated that quantitative MRI (qMRI) of the lower limb muscles is a valid and responsive outcome measure, suitable to evaluate therapeutic response in clinical trials. Given the heterogeneity of IBM, some individuals exhibit more pronounced forearm involvement than lower limb deficits. Our aim was to characterise MRI changes within the forearm muscles of participants with IBM using qMRI measurements, and to assess the validity and responsiveness of forearm muscle qMRI as a biomarker.
Methods. Twenty-one IBM participants underwent qMRI at baseline and 12 months, including assessments of fat fraction (FF), cross sectional area (CSA), remaining muscle area (RMA), muscle water T2 (T2m) and apparent fat fraction (FFa). These imaging measures were complemented by clinical assessments of upper limb strength and function, including grip myometry, manual muscle testing (MMT), IBM functional rating scale (IBMFRS), and the IBM-PRO Upper Extremity Function Scale. Fourteen age- and sex-matched healthy volunteers underwent baseline qMRI for comparison. Construct validity was assessed using Spearman correlations between baseline clinical and qMRI measurements. Responsiveness was evaluated through standardised response means (SRMs) and correlations between changes in qMRI and clinical measurements over 12 months. When assessing statistical significance of correlations and mean change, two-tailed p-values were utilised.
Results. Baseline FF, RMA, CSA, FFa and T2m for the whole forearm compartment were significantly different in IBM participants compared to healthy controls ($p<0.001$ for all measurements). Baseline FF, RMA, and FFa measurements of the whole forearm and flexor compartment showed high construct validity, particularly in flexor digitorum superficialis (FDS) and FDP, supported by strong correlations with clinical measures of upper limb strength and function. qMRI measurements for the FF, RMA and FFa of the whole forearm demonstrated large responsiveness to disease progression (SRMs>0.9; $p<0.001$] at 12 months, especially in FDP (SRMs≥0.95 for FF, RMA and CSA; $p<0.001$). Longitudinal changes in the flexor compartment FFa and RMA of FDP correlated strongly with changes in MMT sub-scores and grip myometry, respectively ($p<0.05$).
Conclusions. qMRI measurements of the forearm muscles, particularly FDP, revealed progressive fat accumulation and atrophy in IBM, with high construct validity and large responsiveness, emerging as promising biomarkers for monitoring disease progression and evaluating therapeutic response in clinical trials.
Key words: MRI, forearm, IBM

P-264

WEARABLE-BASED MONITORING OF PHYSICAL ACTIVITY AND UPPER LIMB FUNCTION IN INCLUSION BODY MYOSITIS

Ram Kinker Mishra[1], Tejas Parwar[1], Samantha Colgan[2], Claire Hennum[2], Andrew Heim[2], Ilkay Yildiz Potter[1], Hanna Thesken[1], Matthew Varon[2], Ashkan Vaziri[1], Mazen Dimachkie[2]
[1]BioSensics, LLC, Newton, USA, [2]University of Kansas Medical Center, Kansas City, USA

Background. IBM results in physical disability due to progressive muscle weakness.1 Assessment of function is quantified in clinical care and research settings using a combination of clinician-assessed scales for muscle strength and function, as well as the IBM Functional Rating Scale (IBMFRS).2
Methods. This is a 24-month prospective study in 20 IBM patients undergoing assessments at baseline, 6, 12, 18, and 24 months. IBMFRS is assessed during each visit along with strength measures and patient-related outcomes. Participants are given a PAMSysTM pendant and 2 PAMSys ULMTM wrist sensors for at-home monitoring of physical activity, posture and upper limb function for 7 consecutive days after each visit.
Results. Nineteen participants have been enrolled in the study. An interim analysis of the first 19 individuals diagnosed with IBM (mean age 71.0±7.3 years, 11 female) with IBMFRS ranging 14 to 35 show that sensor-derived measures of physical activity collected after the baseline visit have significant correlation with the lower extremity subdomain score of the IBMFRS (items 7–10) with correlations ranging from r = -0.559 to 0.674. Similarly, sensor-derived measures of hand function demonstrated moderate to strong correlations with the upper extremity subdomain score of the IBMFRS (items 2–6), with correlations r = 0.509 to 0.615.
Conclusions. While this study is ongoing, interim analysis of the baseline data indicate that at home wearable-based monitoring has the potential to track physical dysfunction in IBM effectively. Wearable sensors provide objective data, increased convenience, and offer scalability and cost-effectiveness, thereby advancing clinical care and potentially improving future clinical trials in IBM. We plan to present data on all 20 participants at the meeting.
Acknowledgements. Funding for this project was provided by Abcuro, Inc.
Key words: inclusion body myositis, biosensors, IBMFRS

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PREVALENCE OF INCLUSION BODY MYOSITIS IN WESTERN AUSTRALIA: MAPPING CHANGES OVER 25 YEARS

Genevieve Simkovics[1], Georgina Wait, Ian Cooper[1], Althea Doverty[1], Kelly Beer[1], Annik Panicker[1], Nataliya Slater[1], Anna Brusch[2,3], Merrilee Needham[1,4,5]
[1]Murdoch University, Murdoch, Australia, [2]Department of Immunopathology, Pathwest, Perth, Australia, [3]University of Western Australia, Perth, Australia, [4]University of Notre Dame Australia, Fremantle, Australia, [5]Fiona Stanley Hospital, Murdoch, Australia

Background. Reported prevalence of Inclusion Body Myositis (IBM) varies widely between populations and ethnic groups (1). In Western Australia (WA), IBM prevalence was previously calculated at 9.3 per million in 2000 (2) and 14.9 per million in 2008 (3), with 51.3 per million among people aged over 50 years. Using the updated 2024 ENMC diagnostic criteria (4), this study aimed to determine the current prevalence of IBM in WA in 2025.
Methods. Individuals with a diagnosis of IBM were identified from the WA Myositis Registry. The Registry includes all patients attending a statewide Specialist Myositis Clinic. To capture any individuals who were not patients of the clinic, contact with neurologists and rheumatologists was made across WA between March and April 2025. Eligible participants were adults residing in WA who had a documented diagnosis (or suspected diagnosis) of IBM. 2024 ENMC diagnostic criteria for IBM was used to confirm and categorise the diagnosis of IBM. Population data from the Australian Bureau of Statistics was used to calculate prevalence per million population (5).

Results. A total of 105 diagnosed or suspected IBM cases were identified. 67 fulfilled the 2024 ENMC diagnostic criteria for confirmed IBM, and a further 36 were categorised as clinically IBM despite not fully meeting the criteria. Of the combined 103 cases, 56% (n=58) were male. The mean age at symptom onset was 63 years in males and 58.5 years in females, with a mean diagnostic latency of 5.2 years (range <1 year to 21 years). Typical muscle involvement (knee extensors and/or finger flexors) was seen in 74.8% (n=77). Anti-CN1A antibody was tested in 73 participants and detected in 34 cases (47%). Based on combined confirmed cases, the prevalence of IBM in WA is 34 per million (38 per million males, 30 per million females). Among people aged ≥45 years, the age-adjusted prevalence was 86 per million overall (99 per million males, 74 per million females). 2 cases of suspected IBM lacked sufficient data and clinical certainty to confirm diagnosis.
Conclusions. The prevalence of IBM in WA has risen steadily over the 25-year monitoring period, a parallel trend observed in other neurodegenerative and autoimmune diseases (6, 7). Time to diagnosis (5.2 years) remains unchanged from previous prevalence studies, suggesting the reported prevalence figures may be an underestimation
Key words: IBM, prevalence

P-305

ALGORITHM FOR IDENTIFYING US VETERANS WITH INCLUSION BODY MYOSITIS FROM THE CORPORATE DATA WAREHOUSE

Vladimir Liarski[1,2]
[1]VA Pittsburgh Health Care System, Pittsburgh, USA, [2]University of Pittsburgh, Pittsburgh, USA

Background/Objective. We previously published a pilot analysis of U.S. veterans with Inclusion Body Myositis (IBM) (1). However, the predictive values of our algorithm were not established. Although there is only one International Classification of Diseases (ICD) code for IBM across ICD-9 and ICD-10, little is known about its accuracy in identifying IBM cases.
Methods. From 732 Veterans previously identified as having IBM (1), we randomly selected 107 for manual record review. Using the Text Integration Utility (TIU) domain, we performed a keyword search for "Inclusion Body Myositis" or "IBM" via the tvf_TIU_FullTextSearch function in Microsoft SQL Server. Rheumatology and Neurology notes from 1/12011, to 3/1/2024, were reviewed. Text data were tokenized using R packages tidytext and tokenizers. Incomplete records were supplemented with Voogle data.
Results. Of 107 patients, 83 (77.5%) had a definite clinical diagnosis of IBM, and 7 (6.5%) were suspected cases. Four veterans had HIV-associated myopathy indistinguishable from IBM. Other non-IBM diagnoses included HMSN-P, PHKA1 deficiency, suspected muscular dystrophy, myofibrillar myopathy, and Kennedy disease (n=1 each). No other autoimmune disorders were identified. Only 7 individuals were concurrently identified among a separate cohort of 1,136 veterans with a diagnosis of polymyositis.
56 out of 107 veterans underwent muscle biopsy, 6 having repeat procedures. 40 had detailed pathology reports available for review with 30 (75%) being consistent with IBM. Of the 6 patients with repeat biopsies, 5 had unchanged IBM diagnoses, and 1 confirmed PHKA1 deficiency.
Among patients with complete documentation, 30/40 (75%) met ENMC 2024 diagnostic criteria (2) for IBM. Based on ENMC 2011 criteria (3), 2/40 (5%), 12/40 (30%), and 25/40 (62.5%) met clinicopathologic, clinical, and probable IBM definitions, respectively. Using Griggs criteria (4), 2/40 (5%) and 15/40 (37.5%) met definite and probable IBM thresholds.
Sensitivity, specificity, and predictive values are shown in Figure 1. The minimum positive predictive value (PPV) was 74.4% for clinical diagnoses and 88.0% for cases meeting diagnostic criteria, with specificity ≥90% for most groups (70% for ENMC 2011 criteria).
Conclusions. Our algorithm combining billing data and specialty clinic visits demonstrates strong performance and excellent specificity in identifying Veterans with IBM, comparable to algorithms for SLE and other inflammatory myopathies (5, 6).

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P-306

INDUCIBLE NITRIC OXIDE SYNTHASE DEFICIENCY REDUCES B-AMYLOID BURDEN IN SKELETAL MUSCLE AND IMPROVES RUNNING PERFORMANCE IN A MOUSE MODEL OF INCLUSION BODY MYOSITIS

Jana Zschüntzsch[2], Michael Hauke[1], Thorben Ingo Alexy[2], Dörthe Malzahn[4,5], Elisabeth Voigt[2], David Liebetanz[2], Jens Schmidt[1,2,3]
[1]Department of Neurology and Pain Treatment, Immanuel University Hospital Rüdersdorf, Brandenburg Medical School Theodor Fontane, Rüdersdorf / Berlin, Germany, [2]Department of Neurology, University Medical Center Göttingen, Göttingen, Germany, [3]Faculty of Health Sciences Brandenburg, Brandenburg Medical School Theodor Fontane, Rüdersdorf, Germany, [4]Department of Genetic Epidemiology, University Medical Center Göttingen, Göttingen, Germany, [5]mzBiostatistics, Statistical Consultancy, Göttingen, Germany

Background. Inclusion body myositis (IBM) is an acquired inflammatory muscle disorder that mostly occurs beyond age 45 in male > female. The pathological findings include a combination of inflammation consisting of endomysial lymphocytes surrounding non-necrotic muscle fibers, mitochondrial dysfunction and an accumulation of degeneration-associated proteins such as β-amyloid.Inducible nitric oxide synthase (iNOS) was identified as a mediator of inflammatory cellular stress in the skeletal muscle of IBM patients. The influence of iNOS in vivo is, however, still inadequately understood. The myodegenerative changes of IBM could be partially replicated through a double-transgenic mouse model, featuring muscle-specific overexpression of amyloid precursor protein (APP) and presenilin (PS) 1 under the CK promoter. Clinically, these changes manifested as progressive muscle weakness from the age of 12 months onwards. In the present study, the clinical and histopathological parameters of the APP/PS1 mice were studied under in presence or absence of iNOS.
Methods. Double transgenic APP/PS1, iNOS-deficient (iNOSdef.) APP/PS1 mice and age-matched C57/Bl6 wild-type control animals were housed individually in cages equipped with running wheels. Running parameters such as speed and distance were continuously recorded using computerized systems for 21 days until age of 24 months was reached. Following running assessment, mice were sacrificed for collection of blood and limb muscle tissue.
Results. iNOS deficiency led to an improvement of the mean total running distance (APP/PS1: 32,300m; C57/Bl6: 36,169m; APP/PS1 / iNOSdef: 42,782m) and maximum speed (APP/PS1: 0.585m/s; C57/Bl6: 0.615m/s; APP/PS1 / iNOSdef: 0.651m/s) at the age of 24 months. iNOS deficiency was accompanied by amelioration of myopathic changes and reduction of β-amyloid deposits in the leg muscles of mice at 24 months of age.
Conclusions. At an advanced age of 24 months, the results demonstrate impaired motor function in APP/PS1 mice as IBM model, which was ameliorated by iNOS deficiency. The data support the association between inflammatory cell stress and β-amyloid, and their modulation by NO in the mouse model and are, thus, in line with findings in human IBM. Furthermore, the results underscore the utility of investigator-independent and sensitive measurement techniques such as automated voluntary running wheel systems for the functional assessment of mouse models with myopathies.
Key words: IBM, mouse model, pathomechanisms

P-312

PROTEOMIC COMPOSITION OF COX-SDH ABNORMAL FIBRES IN POLYMYOSITIS WITH MITOCHONDRIAL PATHOLOGY

Karsten Krause[1,2], Christopher Nelke[1,2], Tobias Ruck[1,2], Anne-Katrin Güttsches[1,2], Andreas Hentschel[7], Andreas Roos[4,5,6], Felix Kleefeld[1,2,3]
[1]Ruhr University Bochum, BG University Hospital Bergmannsheil, Department of Neurology, Bochum, Germany, [2]BG University Hospital Bergmannsheil, Heimer Institute for Muscle Research, Bochum, Germany, [3]Charité-Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt Universität zu Berlin, and Berlin Institute of Health (BIH), Department of Neurology, Berlin, Germany, [4]Department of Neurology, Medical Faculty and University Hospital, Heinrich Heine University Düsseldorf, Düsseldorf, Germany, [5]Department of Pediatric Neurology, Centre for Neuromuscular Disorders, University Medicine Essen, Duisburg-Essen University, Essen, Germany, [6]Brain and Mind Research Institute, Children's Hospital of Eastern Ontario Research Institute, Ottawa, Canada, [7]Leibniz-Institut Für Analytische Wissenschaften-ISAS-E.V, Dortmund, Germany

Background. Polymyositis with mitochondrial pathology (PM-Mito) is a subtype of inflammatory myopathy first described in 1997. Accumulating evidence has demonstrated a considerable molecular and morphological overlap with inclusion body myositis (IBM). Thus, PM-Mito is now perceived as an early form or precursor of IBM (1, 2). A pathological hallmark in PM-Mito muscle biopsy specimens are cytochrome c oxidase (COX)-negative and succinate dehydrogenase (SDH)-positive fibres, representing the morphological correlate of profound mitochondrial dysfunction. In this study, we performed an in-depth proteomic analysis of the composition of COX-SDH-positive fibres by a combined laser microdissection and mass spectrometry approach.
Methods. COX-SDH-positive fibres were laser-microdissected in skeletal muscle biopsies of 9 patients diagnosed with PM-Mito. Fibres without COX-SDH-abnormalities were microdissected and used as an intraindividual control. Samples were analyzed using an unbiased liquid chromatography/mass spectrometry approach that allowed relative quantification of protein abundances and comparison between COX-SDH abnormal and normal fibres.
Results. In total, 1110 proteins were detected in our samples. 33 were significantly upregulated, while 116 were significantly downregulated. Over-abundant proteins were mainly components of the extracellular matrix (collagens and laminins) and proteins associated with mitochondrial repair processes (*e.g.* parts of the MICOS complex). On the other hand, downregulated proteins were associated with mitochondrial metabolism. Furthermore, DNAJA3, a mediator between mitochondrial damage and IFN-γ response, was upregulated in the COX-SDH abnormal fibres.
Conclusions. Our data suggests a profound dysregulation of mitochondria-associated pathways in COX-SDH-abnormal. Notably, the relative enrichment of extracellular matrix proteins in COX-SDH-abnormal fibres may indicate an early, fibre-intrinsic remodelling response to mitochondrial dysfunction. However, upregulation of ECM proteins may also stem from fibrotic changes within the surrounding myofibre microenvironment. Additionally, our data corroborate earlier findings linking mitochondrial damage and inflammation.
Acknowledgements. We thank Anja Schreiner for support with laser-microdissection.
Key words: PM-Mito, IBM, inflammatory myopathy

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P-340

A CASE OF CHRONIC INFLAMMATORY ANTI-HMGCR MYOPATHY WITH FEATURES OF INCLUSION BODY MYOSITIS

Julia Wanschitz[1], Vera Kleinveld[1], Anna Hotter[1], Corinne Horlings[1], Wolfgang Loescher[1]
[1]Medical Univesity of Innsbruck, Innsbruck, Österreich

Background. Anti-HMGCR myopathy has varied clinical presentations which may cause diagnostic difficulties, particularly in patients with an indolent chronic onset.
Methods. We report clinical and muscle biopsy findings of a patient with overlapping features of anti-HMGCR myopathy and inclusion body myositis.
Results. A 55-year-old male first experienced myalgia and proximal muscle weakness of lower extremities in winter 2020. There was no history of statin exposure. First neurological examination in spring 2021 showed mild bilateral weakness of hip flexion and slight asymmetric atrophy of quadricpes muscles. CK was elevated at 2247 U/l and EMG was myopathic. An MRI of thigh and proximal leg muscles showed fibrosis and fatty degeneration and was interpreted as dystrophic. Screening for late onset Pompe disease was negative and testing for myositis specific antibodies revealed positivity for anti-HMGCR antibodies. Treatment with high-dose steroids, 6 cycles of intravenous immunoglobulins and Rituximab 2 x 1000 mg led to improvement of myalgia und decrease of CK below 250 U/l, however muscle weakness progressed. In July 2023 the patient was referred to our institution for a second opinion. In the meanwhile, the patient presented with marked weakness for hip flexion (MRC 2-3) and mild axial weakness without scapular winging or hyperlordosis, despite oral steroids (25 mg per day). Asymmetric atrophy of quadriceps muscles was evident, but no weakness of finger flexors was noted. Gene panel analysis for myopathies/muscle dystrophies detected no mutations. Anti-HMGCR antibody testing remained positive, while anti-cN1a antibodies were not detectable. Biopsy of left vastus lateralis performed 3 weeks after cessation of steroids, demonstrated marked inflammatory changes with numerous T-lymphocytic infiltrates, MHC-class I upregulation and deposition of the terminal complement complex on the sarcolemma as well as myo-degenerative features with numerous atrophic fibers, rimmed vacuoles, TDP-43 positive inclusions and COX negative fibers.
Conclusions. This case report expands the spectrum of HMGCR myopathy with clinical and histological features of inclusion body myositis and underscores the need of cautious interpretation of antibody results in the clinical context.
Key words: necrotizing immune mediated myopathy, anti-HMGCR antibodies, inclusion body myositis

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NOVEL MOUSE MODEL FOR INCLUSION BODY MYOSITIS: TRANSGENIC UPREGULATION OF LYMPHOTOXIN TOGETHER WITH IMPAIRED AUTOPHAGY INDUCES INFLAMMATION AND PROTEIN ACCUMULATION IN SKELETAL MUSCLE

Juliane Bremer[1], Judith Nagel[2], Jana Zschüntzsch[3], Kamil K. Zajt[1], Tayfun Palaz[1], Thomas Blank[4], Aylin Ikis[1], Laura A. Fischer[3], Anna S.M. Sensmeyer[3], Lara Wiechers[3], Josef J. Reichelt[3], Kai P. Hofmann[5], Monika J. Wolf[6,7], Corinna Leuchtenberger[5], Priyanka Tripathi[1], Claudia Einer[8], Hans Zischka[2,8], Ulrike Rothermel[5], Anna-L. Eck[5], Regina Reimann[6], Veronika Kana[6,9], Elisabeth Rushing[6], Adriano Aguzzi[6], Marco Prinz[4,10], David Liebetanz[3], Francesca Odoardi[11], Chao-Chung Kuo[12], Joachim Weis[1], Florian Kraft[13], Jens Schmidt[3,14], Mathias Heikenwälder[5,15]
[1]Institute of Neuropathology, University Hospital RWTH Aachen, Aachen, Germany, [2]Institute of Toxicology and Environmental Hygiene, Technical University of Munich, School of Medicine and Health, Munich, Germany, [3]Department of Neurology, University Medical Center Göttingen, Göttingen, Germany, [4]Institute of Neuropathology, Faculty of Medicine, University of Freiburg, Freiburg, Germany, [5]Department of Chronic Inflammation and Cancer, DKFZ Heidelberg, Heidelberg, Germany, [6]Institute of Neuropathology, University Hospital Zürich, Zürich, Switzerland, [7]Current address: Roche Pharma Research and Early Development (pRED), Roche Innovation Center Munich, Penzberg, Germany, [8]Institute of Molecular Toxicology and Pharmacology, Helmholtz Munich, Neuherberg, Germany, [9]Department of Neurology, University Hospital Zürich, Zürich, Germany, [10]Signalling Research Centres BIOSS and CIBSS, University of Freiburg, Freiburg, Germany, [11]Institute for Neuroimmunology and Multiple Sclerosis Research, University Medical Center Göttingen, Göttingen, Germany, [12]Genomics Facility, IZKF Aachen, RWTH Aachen University, Aachen, Germany, [13]Center for Human Genetics and Genomic Medicine, University Hospital RWTH Aachen, Aachen, Germany, [14]Department of Neurology and Pain Treatment, Immanuel Klinik Rüdersdorf, University Hospital of the Brandenburg Medical School Theodor Fontane, Rüdersdorf, Germany, [15]The M3 Research Institute, Eberhard-Karls University, Tübingen, Germany

Background. Inclusion body myositis (IBM) is a progressive muscle disorder characterized by inflammation and degeneration with altered proteostasis. To better understand the interrelationship between these two features, we aimed at establishing a novel preclinical IBM model.
Methods/Results. First, we used quantitative PCR to determine expression of pro-inflammatory chemo- and cytokines including lymphotoxin (LT)-signaling pathway components in human skeletal muscle tissue diagnosed with myositis. Based on these results we generated a mouse model that we analyzed at the histological, ultrastructural, transcriptional, biochemical, and behavioural level. Lastly, we subjected this model to anti-inflammatory treatments.
After confirming and extending previous data on activation of lymphotoxin (LT)-signaling in human myositis, we generated a transgenic mouse line co-expressing LTα and -β in skeletal muscle fibers. Transgenic mice displayed chronic myositis accompanied by dysregulated proteostasis, including an altered autophagolysosomal pathway. Related genes were temporarily up- and later downregulated, possibly in a compensatory manner. Therefore, we genetically impaired autophagy in skeletal muscle cells. Autophagy impairment alone induced a pro-inflammatory transcriptional state, but no obvious cellular inflammation.
However, the combination of LT-driven myositis with autophagy impairment induced the full spectrum of characteristic molecular and pathological

features of IBM in skeletal muscle, including protein aggregates with typical ultrastructural morphology and mild mitochondrial pathology. Our attempts to treat the pathology by subjecting these mice to corticosteroids or anti-Thy1.2 antibodies mirrored recent treatment failures in humans, *i.e*. none of these treatments resulted in significant clinical improvement of motor performance or the transcriptional profile of muscle pathology.

Conclusions. In summary, these data provide evidence that inflammation and autophagy disruption play a synergistic role in the development of IBM-like muscular pathology. Furthermore, once established, IBM-like pathology in these mice, as in human IBM patients cannot be reverted or prevented from progression by conventional means of immunosuppression. We expect that this novel mouse model will help to identify future treatment modalities for IBM.

Key words: IBM, mouse model, pathomechanisms

Reference

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P-361

STATIN EXPOSURE MAY AFFECT THE TRAJECTORY OF DISEASE OVER TIME IN INCLUSION BODY MYOSITIS

Mayank Kalra[1], Will Kelly[1], Jemima Albayda[1], Christopher Mecoli[1], Brit Adler[1], Julie Paik[1], Thomas Eugene Lloyd[2], Tim Kaniecki[1], Eleni Tiniakou[3], Lisa Christopher-Stine[1]

[1]Johns Hopkins University, Baltimore, USA, [2]Baylor College of Medicine, Houston, USA, [3]McGovern Medical School, Houston, USA

Background. Inclusion Body Myositis (IBM) is a progressive myopathy leading to functional decline. Statins are known to cause muscle symptoms, but their effect on IBM progression is unknown. This study aims to investigate the association between statin exposure and the trajectory of functional (IBMFRS) and strength (MMT-8) decline in IBM patients.

Methods. We conducted a retrospective cohort study from the Johns Hopkins Myositis Research Registry. Inclusion criteria were an IBM diagnosis for ≥2years and ≥2 IBMFRS scores; All included patients were anti-HMGCR autoantibody negative. Primary outcomes were IBMFRS and MMT-8. We used linear mixed-effects models (LMM) with random intercepts/slopes for time (years since first visit) to assess the interaction of statin over time, adjusting for age, sex, and baseline disease duration.

Results. The primary IBMFRS analysis included 63 unique patients (299 visits with a mean follow-up duration of 3.53 (±1.41) years), composed of 31 statin-exposed and 32 statin-unexposed individuals evaluated between 2019-2025. This cohort was demographically similar in statin-exposed *vs*. unexposed with regard to disease duration at baseline [5.72 (±4.33) *vs*. 7.36 (±5.18) years], p=0.18 and mean baseline age [66.6 (±8.8) *vs*. 65.5(±10.7) years], p=0.65; however there were more females in the statin-unexposed group [77% *vs*. 50% male], p=0.024 . In this model, the IBMFRS in the statin-exposed declined at a rate of 0.33 points/year, the IBMFRS in the statin-unexposed group declined at a rate of 1.12 points/year, and the interaction (difference in slopes) was not statistically significant (β= -0.33, p=0.255; likelihood ratio test p=0.256).

The MMT–8 analysis included 52 unique patients (142 visits), evenly split with 26 statin-exposed and 26 unexposed individuals. In this cohort, the statin exposed group declined at a rate of 4.21 points/year compared to the statin unexposed group which showed a decline in slope of 0.69 points/year. The difference in slopes (3.52 points/year) was statistically significant (p=0.019; likelihood ratio test p=0.021).

Conclusions. In this cohort, statin exposure was not associated with accelerated functional (IBMFRS) decline but was associated with a faster strength (MMT-8) decline. The discrepancy in findings may be due to male predominance in the statin exposed group or selection bias, as the MMT-8 analysis had significant missing data, potentially from an increase in telehealth visits during the COVID-19 pandemic where MMT-8 could not be captured. Limitations include limited follow-up time for IBM, and potential selection bias (*e.g*. less healthy patients receiving statins). Larger, prospective studies are needed to confirm the MMT-8 findings.

Key words: Statin, IBM, IBMFRS, MMT-8

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GALECTIN-3-MEDIATED MACROPHAGE AND FAP INTERACTIONS THAT REGULATE FATTY FIBROSIS IN IBM MUSCLE

Armando Villalta[1], Tahseen Mozaffar[1], Namita Goyal[1], Apoorva Nagendra[1], Isela Hernandez[1], Wei Zhao[1], Qing Nie[1]

[1]University of California Irvine, Irvine, USA

Background. Although the etiological basis of inclusion body myositis (IBM) remains unclear, fatty infiltration and fibrosis (collectively termed fatty fibrosis) are increasingly recognized as key pathogenic processes contributing to muscle dysfunction, reduced quality of life, and disease progression.

Methods and Results. Leveraging advances in single-nucleus transcriptomics, we characterized the cellular composition and molecular landscape of IBM muscle. We identified an elevated population of galectin-3 (gal-3)-expressing macrophages, previously linked to fibrotic and adipogenic activity in murine muscle, in IBM patient samples. Computational inferences of intercellular communication using CellChat revealed several molecular pathways mediating interactions between macrophages and fibroadipogenic progenitors (FAPs), with the galectin pathway emerging as one of the most highly enriched and exclusively mediating macrophage-FAP signaling in IBM muscle.

Preliminary histological assessment of archived IBM biopsies confirmed increased gal-3$^+$ cell abundance, which correlated with enhanced muscle fibrosis. Furthermore, imaging mass cytometry of IBM muscle from the INSPIRE-IBM natural history study demonstrated greater perilipin content in nonambulatory compared to ambulatory patients, suggesting a link between elevated gal-3$^+$ macrophages and intramuscular adipose tissue accumulation.

Conclusions. Given the established pro-fibrotic and pro-adipogenic roles of gal-3 in other disease contexts, these findings highlight gal-3 inhibition as a potential therapeutic strategy to mitigate fatty fibrosis and functional decline in IBM patients.

Key words: inclusion body myositis, fatty infiltration, fibrosis, macrophages

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IMAGING MASS CYTOMETRY IDENTIFIES A POPULATION OF GRANZYME K+ CD8+ T CELLS IN INCLUSION BODY MYOSITIS

Apoorva Nagendra[1], Philip Farahat[1], Vanessa Scarfone[1], Tahseen Mozaffar[1], Armando Villalta[1]

[1]University of California Irvine, Irvine, USA

Background. Inclusion body myositis (IBM) is a rare muscle disease combining inflammatory and degenerative processes that collectively contribute to decline of muscle function in adults over 45.

Methods and Results. Using imaging mass cytometry (IMC) with 30 markers, we characterized CD8+ T cells in IBM muscle biopsies. We identified a CD8+CD45RO+ T cell population marked by granzyme K (GzmK), a cytotoxic effector molecule associated with autoimmunity and complement activation. CD8+CD45RO+GzmK+ T cells were in proximity to galectin 3+ macrophages, and degenerative muscle with myonuclear expression of γH2AX, a marker of DNA double-strand breaks also associated with senescence.

The IMC data indicates that the early phase of muscle damage corresponds to initiation of GzmK+ CD8+ T cell infiltration, the intermediate phase displays their stable presence, and the late phase is characterized by replacement of myofibers with adipocytes. We also notice expression of anaphylatoxin in IBM muscle tissue indication the role of complement activation. We further analyzed KLRG1+CD8+ T cells in IBM patient peripheral blood mononuclear cells (PBMCs) using a 13-marker flow cytometry panel. The proportion of cells expressing GzmK+ and γH2AX, was increased in KLRG1+ CD8+ T cells.

Conclusions. We propose that GzmK+ CD8+ T cells drive complement activation and potentially promote muscle degeneration, marked by DNA stress or damage.

Key words: inclusion body myositis, T cells, granzyme K, complement

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CAREGIVER BURDEN IN INCLUSION BODY MYOSITIS: A CROSS-SECTIONAL STUDY OF 124 IBM CAREGIVERS

Dhruv Nandakumar[1], Marlene Jansen[1], Rodney Jansen[2], Lynn Wilson[1], Manuel Lubinus[1]
[1]Myositis Support and Understanding Association (MSU), Lincoln, Delaware, USA, [2]Myositis Canada

Background. Inclusion body myositis (IBM) is an autoimmune disorder characterized by progressive muscular weakness. The chronic, treatment-resistant nature of IBM leads to ongoing functional decline, resulting in increasing burdens on caregivers. Although previous studies have explored the experiences of IBM caregivers and identified common themes, limited insight exists regarding specific caregiver and dependent factors that significantly influence perceived burden. This study aimed to identify factors associated with caregiver burden in IBM.
Methods. A cross-sectional, anonymous survey was administered to patient advocacy groups and IBM-specific online caregiver communities worldwide between February and April 2025. The survey assessed caregiver demographics, caregiving duration and intensity, functional status, emotional and physical well-being, financial concerns, perceived support, communication, and preparedness. Quantitative data were analyzed using descriptive statistics for frequencies and means, as well as ordinal logistic regression to examine associations between caregiving variables and ordinal outcomes. Qualitative responses were thematically coded and analyzed. Patterns in categorical outcome data were further examined using multinomial logistic regression. Statistical significance was defined as $p<0.05$.
Results. A total of 124 caregivers completed the survey, most of whom were female spouses aged 60 years or older. Caregivers reported limitations in personal time and social engagement, accompanied by feelings of stress, isolation, anger, and being overwhelmed. Although many felt emotionally equipped, financial struggles and concerns related to witnessing their loved one's functional decline were common. Caregivers frequently expressed a desire to consult experts for support and often sought financial advice. Longer disease duration and increased patient disability were significant predictors of feeling overwhelmed by burden. Increased disability and being the sole caregiver predicted a decreased perceived impact of burden on well-being. Older caregiver age and longer caregiving duration were associated with greater comfort in caregiving responsibilities. Single-word descriptors most often reflected emotional strain, anxiety, or effort, though some caregivers reported positive perspectives. Younger or more experienced caregivers were significantly more likely to report a positive descriptor compared to emotion- or effort-based terms.
Conclusions. Caregivers of individuals with IBM experience substantial and multifaceted burdens. Over time, caregivers may develop coping strategies and often underestimate the impact of their responsibilities on their own well-being, likely as a result of witnessing their loved one's decline. Nevertheless, caregivers continue to face persistent emotional, social, and financial challenges. These findings underscore the need for comprehensive, multidisciplinary care models that include caregiver-focused education, psychosocial support, peer networks, and long-term planning resources to improve outcomes for both caregivers and individuals living with IBM.
Key words: IBM, caregiver, burden, patient outcomes

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BIOENGINEERED MUSCLE-ON-A-CHIP AS A MODEL OF INCLUSION BODY MYOSITIS

F. Andújar-Sánchez[1,2], X. Fernández-Garibay[3], L. Valls-Roca[1,2], A. Vilaseca-Capel[1,2], H. Deng[1,2], E. Tobias[1,2], M. Guitart-Mampel[1,2], A. Tejedera-Vilafranca[3], L. Farre-Tarrats[1,2], F. Tort[1,2], A. Manzano-Muñoz[4], C. Rentero[4], A. Bigot[5], V. Mouly[5], A. Selva-O'Callaghan[6], P.J. Moreno-Lozano[1,2], A. Matas[1,2], J. Fernández-Costa[3], J. Ramón-Azcón[3], J.C. Milisenda[1,2], G. Garrabou[1,2]
[1]Inherited Metabolic Diseases and Muscular Disorders Research Group, Cellex-IDIBAPS, Faculty of Medicine and Health Sciences, University of Barcelona, Internal Medicine Department-Hospital Clinic of Barcelona, Barcelona (Spain), [2]Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER), Instituto de Salud Carlos III, Madrid, Spain, [3]Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute of Science and Technology; ICREA-Institució Catalana de Recerca i Estudis Avançats, Barcelona, Spain, [4]Departament de Biomedicina, Unitat de Biologia Cel·lular, Facultat de Medicina i Ciències de la Salut, Universitat de Barcelona, Barcelona, Spain; Fundació de Recerca Clínic Barcelona-Institut d'Investigacions Biomèdiques August Pi i Sunyer (FRCB-IDIBAPS), Barcelona, Spain, [5]Sorbonne Université, Inserm, Institut de Myologie, Centre de Recherche en Myologie, Paris, France, [6]Vall d'Hebrón Systemic Autoimmune Diseases Unit. Internal Medicine Service, Hospital Universitari Vall d'Hebrón (HVH), Universitat Autònoma de Barcelona (UAB), Barcelona, Spain.

Background. Inclusion Body Myositis (IBM) is an inflammatory myopathy affecting 1-180 patients per million, mainly in population over 50 years old. It is clinically characterized by muscle weakness of quadriceps and forearm muscles. Diagnosis is driven by pathological findings on degenerative (different size of fibers, vacuolization), mitochondrial (ragged red and COX-/SDH+ fibers) and immunological (CD8+ cell infiltrates) alterations in patients' muscle biopsies. There are no effective treatments for IBM and current models for drug testing fail to reproduce pathological muscle structure and microenvironment. We aim to overcome this limitation by using patient-derived 3D Muscle-on-a-Chip (MoC) platforms.
Methods. We encapsulated immortalized myoblast control and patient cell lines to construct the bioengineered muscle tissues. We then exposed control tissues to sera from 4 IBM or 4 healthy subjects for 48, 96 and 144 hours. Patient tissues were co-cultured with their own immune cells for 24, 48 and 96 h and compared to co-cultures of these IBM-PBMCs with control tissues. We validated the model by checking skeletal muscle function (Fluo-8 calcium flux). We performed Electric Pulse Stimulation (EPS) on tissues to measure biophysical parameters and performed molecular phenotyping to characterize functional impairment.
Results. Biophysical parameters of MoCs could only be measured in IBM constructs at 24, 48 and 96h (at 144h were all broken), and both at 48 and 96h timepoints, strength and contraction dynamics were abnormal in IBM compared to control sera treated MoCs (reduced 20% in IBM). Calcium dynamics were reduced in IBM tissues co-cultured with their own PBMCs, confirming muscle weaknesses and tissue degeneration. We found a higher lactate secretion and accumulation in PBMC-IBM tissue co-culture (1000% *vs*. 200% at 96h), and decreased COX/CS levels in respect to PBMC-control tissue co-culture (0.095 *vs*. 2.304 AU at 96h), suggestive of mitochondrial dysfunction. Higher levels of CD8+CD25+ cell content in PBMC-IBM co-cultures and abnormal cytokine secretion pattern (showing MCP-2/3 increase in supernatants), confirmed immunological deregulation in PBMC-IBM tissue co-culture.
Conclusions. Our findings indicate tissue degeneration and muscle impairment in IBM-MoCs, that molecularly resemble disease features by abnormal degenerative, mitochondrial and immunological changes. These findings prone MoC technology as a robust platform to study IBM, setting the path to model IBM and foster disease therapeutics.
Key words: 3D model, calcium channel, biophysics, IBM, muscle-on-a-chip

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OBSERVATIONAL STUDY OF INCLUSION BODY MYOSITIS: FUNCTIONAL TRAJECTORIES AND TREATMENT EXPOSURE IN BRAZILIAN AND FRENCH COHORTS

Bruna Moreira de Souza Proença[1], André Macedo Serafim da Silva[1], Eliene Dutra Campos[1], Yves Allenbach[2], Edmar Zanoteli[1], Olivier Benveniste[2]
[1]Department of Neurology, Faculdade de Medicina, Universidade de São Paulo (FMUSP), São Paulo, SP, Brazil, [2]Department of Internal Medicine and Clinical Immunology, Sorbonne Université, INSERM UMR974, Pitié-Salpêtrière University Hospital, Paris, France

Background. Inclusion body myositis (IBM) is a slowly progressive inflammatory myopathy characterized by marked interindividual heterogeneity. Functional decline in IBM varies widely between patients and often occurs before major clinical milestones, limiting the interpretability of cross-sectional analyses. Longitudinal evaluation of functional trajectories may therefore better reflect disease progression and allow exploration of treatment-associated differences. While methotrexate has not demonstrated efficacy in typical IBM, sirolimus has shown signals of functional stabilization in clinical trials.
Methods. We conducted an observational study including 46 patients with IBM (19 from Brazil, 27 from France). Clinical variables included age at symptom onset, disease duration, IBM Functional Rating Scale (IBMFRS), ambulatory status, and time to walking aid and wheelchair use. Patients were categorized according to treatment status into three groups: sirolimus-treated (n=18), methotrexate-treated (n=15), and untreated (n=13). Analyses were performed primarily by treatment group. Untreated patients from both countries served as an internal observational reference reflecting the expected

natural history of IBM. Analyses of IBMFRS trajectories were restricted to ambulatory patients with ≥5 years of disease duration.
Results. Disease duration ranged from 1 to 22 years, and IBMFRS scores ranged from 3 to 39. Treatment patterns differed between national cohorts, with sirolimus predominantly used in France and methotrexate more commonly used in Brazil. Distinct functional trajectories were observed across treatment groups. Estimated annual IBMFRS declines were similar in sirolimus- and methotrexate-treated patients (-0.30 *vs*. -0.27 points/year; p>0.05), with weak correlations between disease duration and IBMFRS in both groups (sirolimus: r = -0.18, ϱ = -0.16; methotrexate: r = -0.24, ϱ = -0.32), reflecting marked interindividual variability. In contrast, untreated patients showed a steeper functional decline, with a stronger association between disease duration and IBMFRS (r = -0.87, ϱ = -0.86) and an estimated decline of -0.55 points/year (p<0.05), consistent with the natural history of IBM. Functional milestones supported these differences, with delayed need for walking aid and wheelchair use in patients treated with sirolimus.
Conclusions. In this observational cohort, patients treated with sirolimus demonstrated a more favorable functional trajectory compared with methotrexate-treated and untreated patients. Although annual IBMFRS decline rates did not differ significantly between treated groups, differences in functional dispersion and delayed loss of ambulation suggest that longitudinal functional assessment and clinical milestones may capture treatment-associated differences not reflected by global scores alone. These exploratory findings are consistent with natural history observations and support longitudinal evaluation of treatment effects in IBM.
Key words: inclusion body myositis, treatment

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EARLY FUNCTIONAL DECLINE IN INCLUSION BODY MYOSITIS DETECTED BY THE MOTOR FUNCTION MEASURE: A LONGITUDINAL OBSERVATIONAL STUDY

Moreira de Souza Proença B.[1], Ribeiro Fernandes T.[1], Macedo Serafim da Silva A.[1], Zanoteli E.[1]
[1]*Department of Neurology, Faculdade de Medicina, Universidade de São Paulo (FMUSP)*

Background. Inclusion body myositis (IBM) is a slowly progressive myopathy characterized by marked functional heterogeneity. Patients frequently report functional worsening despite preserved ambulation and minimal changes in commonly used global clinical scales, complicating disease monitoring and outcome assessment. The Motor Function Measure (MFM) is a standardized, performance-based scale that evaluates motor function across posture, axial/proximal, and distal domains and may offer greater sensitivity to longitudinal functional change in IBM.
Methods. We conducted a longitudinal observational study of patients with IBM followed at a tertiary neuromuscular center. Patients with ≥2 MFM assessments performed at least 6 months apart were included. Annualized changes in MFM total score (%TOTAL) and domain subscores – D1 (posture and transfers), D2 (axial and proximal motor function), and D3 (distal motor function) – were calculated. Clinical status, ambulatory function, and IBM Functional Rating Scale (IBMFRS), when available, were used for contextual comparison.
Results. Five patients met inclusion criteria, with follow-up ranging from 6 to 12 months. Four of five patients (80%) demonstrated measurable decline in MFM %TOTAL, with a median annualized decrease of approximately 2% and substantial interindividual variability. Domain-level analyses revealed that functional decline was most consistently observed in the D1 domain, while changes in D2 and D3 were more heterogeneous over the same interval. Importantly, deterioration in D1 occurred while patients remained ambulatory, without ventilatory support, and with stable or minimally changed IBMFRS scores, indicating early functional impairment preceding overt clinical milestones.
Conclusions. In this longitudinal cohort, the MFM detected short-term functional decline in IBM that was not captured by global clinical scales. The consistent involvement of the D1 domain aligns with the core clinical features of IBM, which are dominated by early impairment in posture and transfers related to quadriceps and axial muscle weakness. Given that D1 can be administered independently of the full MFM and requires minimal time and equipment, it represents a feasible and clinically meaningful endpoint for detecting early disease progression. These findings support the use of MFM – particularly the D1 domain – as a sensitive outcome measure for observational studies and interventional trials in IBM.
Key words: Inclusion body myositis, MFM, outcome measures

Juvenile Myositis

P-15

IDENTIFYING TARGETS FOR INTERVENTIONS TO REDUCE EMOTIONAL DISTRESS AND IMPROVE PHYSICAL ACTIVITY IN JUVENILE DERMATOMYOSITIS AND LUPUS PATIENTS: LONGITUDINAL ANALYSIS OF LUPUS ERYTHEMATOSUS AND DERMATOMYOSITIS STRESS AND CARDIOVASCULAR HEALTH (LEADS-CV) C

Kaveh Ardalan[1], Wenshan Yu[1], Hwanhee Hong[1], Angel Davalos[1], Bryce Reeve[1], Christoph Hornik[1], M. Anthony Moody[1], Donald Lloyd-Jones[2], Rebecca Sadun[1], Jeffrey Dvergsten[1], Lauren Covert[1], Ann Reed[1], Eveline Wu[3], Laura Cannon[3], Leonard Kovalick[3], Caitlan Pinotti[3], Aliese Sarkissian[3], Audrey Ward[4], Simisola Gbadegesin[5], Mark Connelly[6], Laura Schanberg[1]

Background. Emotional distress is prevalent among patients with juvenile dermatomyositis and lupus (JDM/JSLE). We previously showed that JDM/JSLE patients following high emotional distress trajectories tended to have poorer cardiovascular health (CVH), defined as protective factors against cardiovascular disease. Diet and physical activity were suboptimal in >95% of JDM/JSLE patients. To inform intervention development, we evaluated associations of patient-reported resiliency factors, emotional distress, and diet/physical activity.
Methods. The LEADS-CV cohort has been described previously (https://duke.is/y/cx66). Participants with complete data were included (n=76). Emotional distress was assessed using self-report PROMIS Pediatric Psychological Stress Experiences, Depressive Symptoms, and Anxiety (PROMIS-Stress/-Depr/-Anx) measures. Resiliency factors evaluated include PROMIS Positive Affect and Emotional Regulation Questionnaire for Children and Adolescents, which assesses adaptive (cognitive reappraisal, ERQ-CR) and maladaptive (emotion suppression, ERQ-ES) emotion regulation strategies. Self-report measures of diet quality (FLASHE screener) and physical activity (PROMIS Physical Activity) were administered. Longitudinal analyses included: 1. growth mixture models (GMM) to identify latent trajectories of resiliency factors; 2. linear mixed-effects models (LMM) to assess associations among resiliency factors, emotional distress, and diet/physical activity.
Results. GMMs identified latent trajectories for PROMIS Positive Affect and ERQ-ES (good, fair, poor) and for ERQ-CR (good, poor). Poor resiliency trajectories were common (21–50%) and remained stable over time. LMMs showed significant associations of PROMIS Positive Affect and ERQ-ES with all emotional distress measures (β range |0.49–0.96| in expected directions). Female gender was significantly associated with higher emotional distress across most models (β range 4.92–8.49). Higher ERQ-CR was associated with better PROMIS Physical Activity (β range 0.16–0.50), and unexpectedly, higher ERQ-ES was also associated with better PROMIS Physical Activity in most models (β range 0.51–0.61). Minority race/ethnicity was associated with worse PROMIS Physical Activity (β range -5.13 to -6.07), even after adjusting for confounders (*e.g.* diagnosis). Emotional distress and resiliency factors were not significantly associated with diet quality.
Conclusions. Interventions that enhance positive affect and strengthen emotion regulation may help reduce emotional distress in JDM/JSLE patients. The finding that both cognitive reappraisal and emotion suppression were associated with greater physical activity suggests complex, potentially bidirectional relationships where some youth use cognitive reappraisal to facilitate physical activity, while others use physical activity as a coping strategy when other emotion regulation strategies are less developed. Gender and racial/ethnic differences should be considered when developing behavioral interventions for JDM/JSLE patients.
Key words: juvenile myositis, dermatomyositis, lupus, mental health, resiliency, diet, physical activity, cardiovascular disease

P-16

POSITIVE AFFECT AND EMOTION REGULATION PROTECT JUVENILE-ONSET DERMATOMYOSITIS AND LUPUS PATIENTS FROM EMOTIONAL DISTRESS: LONGITUDINAL ANALYSIS OF LUPUS ERYTHEMATOSUS AND DERMATOMYOSITIS STRESS AND CARDIOVASCULAR HEALTH (LEADS-CV) COHORT STUDY PARENT-REPO

Kaveh Ardalan[1], Wenshan Yu[1], Angel Davalos[3], Hwanhee Hong[1], Bryce Reeve[1], Christoph Hornik[1], M. Anthony Moody[1], Donald Lloyd-Jones[2], Rebecca Sadun[1], Jeffrey Dvergsten[1], Lauren Covert[1], Ann Reed[1], Eveline Wu[3], Laura Cannon[3], Leonard Kovalick[3], Caitlan Pinotti[3], Aliese Sarkissian[3], Audrey Ward[4], Simisola Gbadegesin[5], Mark Connelly[6], Laura Schanberg[1]

Background. Patients with juvenile dermatomyositis and lupus (JDM/JSLE) often experience persistent emotional distress and early loss of cardiovascular health (CVH) – the sum of protective factors that reduce cardiovascular disease risk. We previously found that elevated emotional distress trajectories were associated with worse CVH trajectories, especially for diet and physical activity. To inform future intervention targets, we examined parent-reported resiliency factors hypothesized to associate with lower emotional distress and better diet/physical activity.
Methods. The LEADS-CV cohort has been described previously (https://duke.is/y/cx66). We included 58 participants with complete data. Emotional distress was assessed using parent-proxy PROMIS Pediatric Psychological Stress Experiences, Depressive Symptoms, and Anxiety measures (PROMIS-Stress/-Depr/-Anx). Resiliency factors were evaluated for both patients (parent-proxy PROMIS Positive Affect; Emotion Dysregulation Inventory Reactivity & Dysphoria subscales [EDI-R/-D]) and parents (self-reported PROMIS Self Efficacy & Emotional Support). Parent-proxy measures of diet quality (FLASHE screener) and physical activity (PROMIS Physical Activity) were administered. Growth mixture models (GMM) were used to identify latent resiliency trajectories, and linear mixed-effects models (LMM) examined associations among resiliency factors, emotional distress, and diet/physical activity.
Results. GMMs identified good, fair, and poor latent trajectories for parent-proxy PROMIS Positive Affect and EDI-R/EDI-D, and good versus poor trajectories for parent self-report PROMIS Self Efficacy & Emotional Support. Poor resiliency trajectories were common (17–53%) and associated with higher baseline emotional distress. LMMs showed consistent associations of PROMIS Positive Affect, EDI-R, and EDI-D with all emotional distress measures (β range |0.34–0.74| in expected directions). Parent-reported PROMIS Emotional Support was inversely associated with parent-proxy PROMIS-Stress and PROMIS-Depr (β = -0.21 and -0.22 respectively), and parent-reported PROMIS Self Efficacy was inversely associated with PROMIS-Depr and PROMIS-Anx (both β = -0.18). Higher PROMIS-Depr scores were uniquely linked to worse diet quality (β range -0.56 to -0.77), while no other consistent relationships emerged among emotional distress, resiliency factors, diet quality, or physical activity.
Conclusions. Enhancing positive affect and emotion regulation in patients and strengthening emotional support and self-efficacy among caregivers may mitigate emotional distress in patients with JDM/JSLE. Depressive symptoms may uniquely predispose JDM/JSLE patients to worse diet quality and warrant attention in CVH behavior change interventions. Further research incorporating novel assessment tools (*e.g.* wearable devices) and intensive study designs (*e.g.* ecological momentary assessment) is needed to further elucidate the dynamic associations between emotional distress and CVH behaviors.
Key words: juvenile myositis, dermatomyositis, lupus, mental health, resiliency, diet, physical activity, cardiovascular disease

P-24

INTERSTITIAL LUNG DISEASE IN JUVENILE DERMATOMYOSITIS: CLINICAL CORRELATES OF RADIOLOGICAL PATTERNS

Narendra Bagri[1], Pavneet Kaur[1], Stuti Chandola[1], Manisha Jana[1]
[1]All India Institute of Medical Sciences, New Delhi, India

Background. Visceral organ involvement in Juvenile Dermatomyositis (JDM) is poorly described, particularly the extent and severity of pulmonary manifestations, sparing the MDA5 antibody-positive disease.
Objective. This study aimed to review the prevalence, clinical and radiological characteristics of interstitial lung disease (ILD) in children with JDM and systemic sclerosis (SSc) overlap with suspected ILD.
Methods. We retrospectively reviewed the high-resolution computed tomography (HRCT) scans of 52 children with JDM and JDM-systemic sclerosis (SSc) overlap enrolled in the pediatric rheumatology clinic (2016-June 2025). The cohort included 40 patients with JDM and 12 patients with JDM/SSc overlap. Clinical details were retrieved from the pediatric rheumatology clinic records. These were evaluated for features of ILD and categorised into a dominant type of interstitial pneumonitis pattern, wherever possible. The HRCT-based scoring system (Warrick) was also utilised for quantification and severity assessment of the lung involvement. Data was analysed using descriptive statistics.
Results. Eight children (9/52,17.3%), four with JDM and five with JDM/SSc overlap each, showed features of ILD on HRCT in 25 patient-years of follow-up. One child in each group met Solomon's criteria for antisynthetase syndrome. The mean age of disease onset was 7.6 (±3.5) years, with a median 12 (7.5-15.7) months delay in diagnosis of underlying disease.
Children with JDM alone had non-specific interstitial pneumonitis (NSIP) and organising pneumonitis (OP) patterns (NSIP-2, OP-1). Of the overlap patients, three had a usual interstitial pneumonia (UIP) pattern, and one follicular bronchiolitis pattern. Children with MDA5 antibody (n=2/9 MDA5 positive) showed severe lung involvement (score 4 and unclassifiable, respectively). Among the antisynthetase syndrome patients, one had an unclassifiable fibrotic ILD and another organising pneumonia (OP) pattern with the highest score of involvement (9) at index presentation. He subsequently developed rapidly progressive ILD, leading to mortality. Table 1, Figs. 1-3 summarise the management and outcome.
Conclusions. Although severe, the frequency of ILD in JDM is lower in our cohort when compared with adult DM (19.9–42.6%). While the non-fibrotic pattern is the most frequent in JDM, the severe fibrotic pattern is more frequent in the JDM overlap groups.
Key words: JDM, ILD

P-48

THE IMPACT OF FATIGUE IN JUVENILE DERMATOMYOSITIS

Silvia Rosina[1], Ana Isabel Rebollo-Giménez[2], Letizia Tarantola[3], Chiara Campone[3], Valentina Natoli[3], Francesca Bovis[4], Alessandro Consolaro[1,3], Angelo Ravelli[3,5]
[1]UOC Reumatologia e Malattie Autoinfiammatorie, IRCCS Istituto Giannina Gaslini, Genoa, Italy, Genova, Italy, [2]Health Research Institute Gregorio Marañón (IiSGM), Hospital General Universitario Gregorio Marañón, Madrid, Spain, [3]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DINOGMI), University of Genova, Genova, Italy, [4]Department of Health Sciences (DISSAL), University of Genova, Genova, Italy, [5]Direzione Scientifica, IRCCS Istituto Giannina Gaslini, Genova, Italy

Background. Fatigue is a key symptom in juvenile dermatomyositis (JDM). Although it can be very disabling and have a profound impact on quality of life (QoL), its assessment is not included in response criteria and is seldom incorporated in routine practice. Aim of the project was to investigate the relationship between fatigue and clinical measures of disease activity and parent-reported outcomes (PROs).
Methods. The charts of JDM patients followed at study center from October 2016 to March 2025 were reviewed retrospectively. For each patient, the first available visit with complete data was retained. Physician-centered outcomes were retrieved, together with the main PROs. Fatigue was assessed through a 21-points 0-10 numeric rating scale (NRS) (0 = no fatigue; 10 = extreme fatigue). Associations between fatigue scores and demographic and clinical

variables as well as PROs were evaluated using Spearman's rank correlation test. Fatigue scores were also compared among different groups of patients using either U-Mann-Whitney or Kruskal-Wallis test.
Results. 49 patients (59.2% female) with a mean age at visit of 8.9 ± 5.0 years were included. 53.1% were ANA-positive, and 61.7% myositis-specific antibody-positive. Child's fatigue was reported by 69.4% of parents, with a median NRS value of 5 (IQR: 0-8). Moderate to strong correlations were demonstrated between fatigue scores and physician's global assessment of disease activity (r=0.71), parent's global assessment of child's well-being (r=0.77), MMT8 (r=-0.63), hybrid MMT/CMAS (r= -0.65), total DAS (r=0.69), JDMAI1 (r=0.75) and JDMAI2 (r=0.78). Correlations with functional ability and QoL measures were moderate to high (r=0.61-0.79), whilst correlations with skin measures, muscle enzymes and damage index were low (r=-0.16-0.37). Fatigue scores were higher in patients with active disease than in those with remission, as assessed by JDMAI1- and JDMAI2-based criteria and by parent's subjective judgement ($p<0.0001$). Median fatigue scores were also higher in patients with impaired physical function than in those with normal functionality (6.42 *vs*. 0.60, $p<0.0001$), and in patients whose parents were not satisfied with their child's disease outcome than in those who were satisfied (6.25 *vs*. 0.00, $p<0.0001$).
Conclusions. Fatigue is common in children with JDM, and is strongly associated with reduced QoL and impaired physical function, as well as with level of disease activity and parents' satisfaction with illness outcome. Fatigue should be considered for inclusion in composite disease activity scores and response criteria used in JDM. It may also represent a qualified therapeutic goal in the treat-to-target strategy for this disease.
Key words: juvenile dermatomyositis, outcome measures, parent-reported outcomes

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TERTIARY PEDIATRIC RHEUMATOLOGY CENTRE EXPERIENCE WITH FITNESS TESTING IN IDIOPATHIC INFLAMMATORY MYOPATHIES OF CHILDHOOD

Verna Cuthbert[1], Giulia Varnier[1]
[1]Royal Manchester Children's Hospital, Manchester, UK

Background. It is well established that paediatric patients with inflammatory conditions are less fit compared with their peers. Less evidence is available specifically for paediatric idiopathic inflammatory myopathies (PIIM) regarding the best way to evaluate cardiovascular health. It remains unclear whether addressing cardiovascular fitness improves outcome and quality of life measures for PIIM patients. Improving the outcomes for PIIM patients remains crucial and therefore we have introduced fitness testing in our PIIM multidisciplinary (MDT) clinics to explore its feasibility and patient and parents' acceptance. There are several fitness tests available, none have been identified as gold standard in PIIMS. The Kasch Pulse Recovery (KPR) test is a submaximal step test designed to assess cardiorespiratory fitness via heart rate recovery after exercise. Normative data is available for healthy children
The aim of this project was to explore the feasibility and patient and parents' acceptance of KPR fitness testing in a clinical outpatient setting.
Methods. Patients 18 years and below, diagnosed with IIM, under the care of the paediatric and adolescent rheumatology at RMCH were included. Demographic, health data and outcome measures of muscle strength and stamina were collected from June 2024- June 2025.
The KPR test was performed by the senior physiotherapist, and patient and parent feedback was collected after completing the test by a psychology student with a dedicated questionnaire.
Results. Nine patients were included in this study. Seven were girls and mean age at testing was twelve years of age. All patients were able to complete the KPR test without any issue. We observed that patients with high body max index (BMI), clinically active disease (lower MMT8 and CMAS) had high rated perceived exertion (RPE) and low fitness scores. Young people with healthy BMI, good disease control (high MMT8 and CMAS) showed higher fitness scores. We collected feedback from five patients/families which suggested a positive experience of performing the KPR and a genuine interest in improving their physical fitness.
Conclusions. With the limitation of a small sample population, our experience was that the KPR test was easy to perform in clinic and well accepted and tolerated by patients and families. This project helped to stimulate discussion and interest in cardiovascular fitness with our patients.
The study highlights the importance of addressing cardiovascular health from an early age in patients with rare chronic inflammatory diseases such as IMM. Further larger studies are needed to explore cardiovascular health and the role of fitness testing in PIIM.
Key words: paediatric idiopathic inflammatory myopathies, fitness testing, cardiovascular health, outcomes

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BEYOND THE DIAGNOSIS: A QUALITATIVE STUDY EXPLORING PATIENT AND PARENT EXPERIENCES OF LIVING WITH JUVENILE DERMATOMYOSITIS

Katie Roberts[1], Marilena Hadjittofi[1], Jessica Fitzgerald[2], Charalampia Papadopoulou[3], Andrea Murray[4,5], Graham Dinsdale[5], Lauren Huckerby[6], Jenny Ainsworth[2], Andy Vail[4], Klaudia Kupiec[3], Yvonne Glackin[3], Lucy Wedderburn[3,7], Chris Taylor[4], Clare Pain[1], Ariane Herrick[4,5], Liza McCann[1,2], Elizabeth Deja[2]
[1]Alder Hey Children's NHS Foundation Trust, Liverpool, UK, [2]University of Liverpool, Liverpool, UK, [3]Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK, [4]University of Manchester, Manchester, UK, [5]Salford Royal Hospital, Salford, UK, [6]Royal Manchester Children's NHS Foundation Trust, Manchester, UK, [7]University College London, London, UK

Background. Juvenile dermatomyositis (JDM) is a rare and potentially life-threatening idiopathic myopathy that can impose significant physical, psychological, and social burden on those affected. This study aimed to explore patient and parent experiences of living with JDM.
Methods. This is a sub-study of the MYOSCOPE project which investigated the feasibility of using nailfold capillaroscopy to help children and young people with JDM. Semi-structured interviews were conducted with participants of MYOSCOPE. Individuals were included if they were children with JDM, or parents/caregivers of children with JDM, at two specialist paediatric hospitals in the UK and consented to interview. Patient/public involvement informed the interview protocol. Analyses followed an interpretive thematic analysis approach.
Results. Sixteen semi-structured interviews were conducted between March and June 2025 with twenty-four participants (eight patients, sixteen parents). Three main themes were identified: disruption to normal life, psychological effects, and support systems. All participants reported disruption to normal life, with patients' symptoms limiting their ability to participate in hobbies, attend school, and perform daily living tasks. A sibling's ability to attend school was also affected, due to perceived need to isolate to reduce infection risk for the immunosuppressed patient. Frequent hospital visits complicated parents' work and home commitments. One parent chose to become unemployed, and two parents spent less time with their other children. Psychological effects included mental maturation, increased self-awareness, worry, and medication-induced anxiety and depression. One child developed specific phobias of stimuli associated with their medication due to common adverse side effects. Steroid-related weight gain contributed to bullying, eating disorders, and suicidal ideation. Many families sought support through hospital programmes, which sometimes alleviated psychological distress and improved parental disease management. Parents appreciated connecting with other families at the hospital and sharing stories/advice. However, some hospital programmes failed to address specific difficulties and were inaccessible due to travel burden. Alternative support networks were pursued through private therapies and online groups, though the latter was associated with misinformation.
Conclusions. This study highlights various and often interrelated physical, psychological, and social difficulties experienced by JDM patients and their parents. Professionals are encouraged to better understand the impact of JDM on families and address barriers to effective support.
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Key words: juvenile dermatomyositis, patient and parent experiences, biopsychosocial effects

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FIRST STUDY OF BIOENGINEERED MUSCLE FROM A JDM PATIENT REVEALS DISTINCT RESPONSE TO TYPE I INTERFERON

Lauren Covert[1], Sara Kandil[2], Avery Simon[2], Deborah Muoio[3], George Truskey[2]
[1]Duke University School of Medicine, Durham, USA, [2]Duke University Pratt School of Engineering, Durham, USA, [3]Duke Molecular Physiology Institute, Durham, USA

Background. Juvenile dermatomyositis (JDM) research faces challenges due to the disease's rarity and lack of accurate disease models. Myobundles, a human muscle-derived microphysiological system, have been used to study the effects of type I interferons (IFN, including IFNβ) on healthy muscle function (1), development (2), and transcriptomic profile (3) – recapitulating key features of JDM muscle. We aimed to characterize myobundles derived from a JDM patient and compare them to healthy pediatric myobundles.
Methods. A muscle biopsy was obtained from a treatment-naive JDM patient (6 yo F, MSA-, Ro60+, ANA+, CMAS 8/52, PGA 8). Myoblasts were isolated, expanded, and used to create myobundles as previously described (1, 4). Myobundles were treated with IFNβ (0, 0.36, 5, 10, or 20 ng/mL) for 2-10 days (Day 11-21). Contractile force, twitch kinetics, and fatigue were measured in addition to expression of structural sarcomeric-α actinin (SAA) and IFN-stimulated proteins (MHC I, MxA, STAT2) via microscopy and western blot. Mitochondrial stress testing was performed on myotubes after 48h of IFNβ exposure. Outcomes were compared to healthy pediatric myobundles. Statistical analysis included ANOVA and T-test as appropriate.
Results. A 353 mg quadriceps biopsy yielded ~19 million myoblasts (96.3 ± 0.05% purity based on desmin/vimentin co-expression). JDM myobundles demonstrated decreased twitch and tetanus force, slower twitch time to maximum force, and greater fatigue over time. After 48h low-dose IFNβ exposure, JDM myobundles showed robust IFN response with increased MHC I and MxA expression on microscopy, and greater MxA and STAT2 abundance via western blot. JDM myobundle cross-sectional diameter also increased with IFNβ treatment, without change in nuclei density. After 48h high-dose IFNβ exposure, JDM myotubes showed decreased mitochondrial maximal capacity, unlike healthy counterparts. After 7-days high-dose IFNβ, JDM myobundles demonstrated dose-dependent decreases in contractile force, like healthy myobundles treated with IFNβ, but had lower overall forces and no changes in twitch speed or fatigue.
Conclusions. This is the first study of myobundles derived from a child with active, treatment-naive JDM. JDM myobundles were weaker than healthy ones, suggesting key disease traits are preserved in culture. Like healthy myobundles, they responded early and strongly to IFNβ, losing strength with chronic exposure. However, only JDM models showed IFN-induced decreased mitochondrial capacity and resistance to change in kinetics and fatigue – highlighting distinct IFN-driven metabolic and functional responses in JDM.
Acknowledgements. Alec Chaves, Annelise Poss, and Tim Koves from the Duke Molecular Physiology Institute.
Key words: juvenile myositis, bioengineered tissue, interferon

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P-80

SENSITIVITY AND POSITIVE LIKELIHOOD RATIOS OF MYOSITIS-SPECIFIC AUTOANTIBODIES WITH SPECIFIC CLINICAL FEATURES IN JUVENILE DERMATOMYOSITIS IN A LARGE REAL-WORLD MULTI-SITE REGISTRY

Belina Yi[1], Matthew Sherman[2], Kaveh Ardalan[3], Susan Kim[4], Stacey Tarvin[5], Hanna Kim[6], Brian Feldman[7]
[1]Department of Pediatrics, Johns Hopkins University School Of Medicine, Baltimore, USA, [2]National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, USA, [3]Department of Pediatrics, Division of Pediatric Rheumatology, Duke University School of Medicine, Durham, USA, [4]Department of Pediatrics, University of California, San Francisco, USA, [5]Department of Pediatrics, Indiana University School of Medicine, Indianapolis, USA, [6]Juvenile Myositis Pathogenesis and Therapeutics Unit, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, USA, [7]Department of Medicine, University of Toronto, Toronto, Canada

Background. Myositis-specific autoantibodies (MSAs) are associated with distinct clinical features in juvenile dermatomyositis (JDM) and are increasingly being used to tailor treatment. However, pairwise associations of MSAs with specific clinical manifestations in real-world JDM cohorts remain understudied. Therefore, this study was conducted to determine the sensitivity and positive likelihood ratios (LR+) of MSAs with baseline and follow-up clinical features of JDM in a large multi-site registry.
Methods. Patients with JDM enrolled in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry between January 2019 - June 2024 were included. The CARRA Registry is a North America-based international observational inception cohort registry. Sensitivity and LR+ of MSAs for clinical features were calculated for those with more than 2 observations per MSA group, and MSA groups with >5 patients. Significant LR+ was defined as >2 and 95% Confidence Interval (CI) >1.
Results. Out of 303 patients enrolled in the CARRA Registry with JDM diagnosis per enrolling providers and tested for at least 1 MSA, 141 had 1 positive MSA, excluding 16 patients >1 MSA. MSA testing was most performed at Oklahoma Medical Research Foundation in the USA (n=49, 35%). The most common MSA was anti-TIF1γ (n=46, 33%). Overall, the MSAs were poorly sensitive (5-70%) for specific clinical features. Significant LR+ were observed in the following: V-sign with anti-TIF1γ (2.05, 95% CI 1.13-3.69); dysphonia with anti-NXP2 (2.06, 95% CI 1.12-3.82); interstitial lung disease (7.78, 95% CI 4.23-14.30), arthritis (4.52, 95% CI 1.97-10.37), and skin ulcer (2.93, 95% 1.35-6.36) with anti-MDA5. Of note, LR+ for calcinosis with anti-NXP2 (0.95, 95% CI 0.33-2.74) were not significant. Out of 38 JDM patients with calcinosis (9.5%), 11 patients were scored for their calcinosis severity in 0-10 scale. The patient with highest score (5/10) had anti-NXP2, however, the only patient with exoskeleton (severity not scored) had anti-TIF1γ.
Conclusions. Overall, MSAs had low sensitivity for specific disease features, with anti-TIF1γ, anti-NXP2, and anti-MDA5 having significant LR+ for some known associated disease manifestations. Strengths of this study include large sample size and multi-site data source, although insufficient follow-up data to assess progression of features and variability of MSA assays with potential antibody status misclassification remain limitations. Given that MSAs may lack sensitivity to specific disease features, future studies linking MSAs to distinct clusters of disease manifestations in JDM may enhance understanding of their clinical relevance.
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Key words: myositis-specific autoantibody, sensitivity, positive likelihood ratios, juvenile dermatomyositis

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SINGLE-CENTER EXPERIENCE IN JUVENILE DERMATOMYOSITIS: DIAGNOSTIC DELAYS, MYOSITIS-SPECIFIC ANTIBODY PROFILES, AND CALCINOSIS

Mehmet Erkan[1], Erdal Sag[1], Yagmur Bayindir[1], Hulya Ercan Emreol[1], Ozge Basaran[1], Yelda Bilginer[1], Seza Ozen[1]
[1]Hacettepe University, Division of Pediatric Rheumatology, Department of Pediatrics, Ankara, Turkey

Background. Juvenile dermatomyositis (JDM) is a rare idiopathic inflammatory myopathy of childhood, marked by muscle weakness and characteristic skin findings. With an incidence of 1.9–4.1 per million children annually, it presents diagnostic and therapeutic challenges. Delayed diagnosis and diverse myositis-specific antibody (MSA) profiles impact outcomes, especially calcinosis. This study presents a 25-year single-center experience, examining demographic trends, MSA distribution, calcinosis frequency, and the changing use of diagnostic methods.
Methods. We retrospectively analyzed data from 103 children with JDM diagnosed and followed at our tertiary pediatric rheumatology center between 2000 and 2025. Extracted variables included demographics, age at onset, year of diagnosis, time to diagnosis, follow-up duration, MSA profiles, calcinosis status, and diagnostic approaches, including magnetic resonance imaging (MRI), muscle biopsy, and electromyography (EMG). Patients were stratified into two groups: pre-2014 and post-2014, corresponding to the introduction of extended MSA testing in our center.
Results. Among 103 patients (68 females, 35 males; ratio 1.9:1), the mean age at diagnosis was 8.52 years, with a mean diagnostic delay of 9.21 months and a mean follow-up of 72.7 months. Calcinosis was documented in 39 patients (37.8%), who had a younger mean age (7.93 years) and a longer

diagnostic delay (13.89 months) compared with those without calcinosis (9.09 years; 6.39 months). Among patients with calcinosis, anti-NXP2 was the most frequent MSA (20.5%). Dual MSA positivity occurred in 12.8% of all cases, and 41% were MSA-negative. In contrast, MSA profiles were more heterogeneous in patients without calcinosis, with 30.9% MSA-negative and 7.2% dual-positive.
Before 2014 (n=35), the mean diagnostic delay was 7.16 months, whereas after 2014 (n=59), the delay increased to 10.28 months. In the post-2014 cohort, patients with calcinosis had markedly prolonged diagnostic delays (15.31 months) compared to those without (8 months). Muscle biopsy was performed in 52 patients, yielding JDM-compatible findings in 47 (90%). MRI, utilized in 51 patients, demonstrated myositis in 32, while EMG was performed in 38, all upon neurology consultation.
Conclusions. Our findings reaffirm the association between diagnostic delay, anti-NXP2 positivity, and calcinosis in JDM. Despite wider access to non-invasive diagnostic tools and earlier therapeutic interventions, calcinosis prevalence remains unchanged, possibly reflecting persistent delays in recognition or referral bias toward complex cases. Although the reliance on invasive procedures has decreased over time, muscle biopsy continues to play a pivotal role in atypical presentations and remains an indispensable tool in specialized centers
Key words: juvenile dermatomyositis, calcinosis, myositis-specific antibodies, time to diagnosis, muscle biopsy, MRI, EMG

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ENGINEERED HUMAN MUSCLE MODELS THE INTERFERON-DRIVEN TRANSCRIPTOME OF JUVENILE DERMATOMYOSITIS MUSCLE

Lauren Covert[1], Devjanee Swain Lenz[1,2], Sara Kandil[3], Jeffrey Dvergsten[1], Jessica Turnier[4], Jessica Neely[5], Kaveh Ardalan[1], George Truskey[3]
[1]Duke University School of Medicine, Durham, USA, [2]Duke Sequencing and Genomics Technologies Core Facility, Durham, USA, [3]Duke University Pratt School of Engineering, Durham, USA, [4]University of Michigan Medical School, Ann Arbor, USA, [5]University of California, San Francisco School of Medicine, San Francisco, USA

Background. Juvenile dermatomyositis (JDM) mechanistic insights are limited by the lack of accurate disease models. Myobundles, a human muscle-derived microphysiological system, recapitulate JDM features [muscle weakness, myositis antigen expression, type I interferon (IFN) gene signature]. We compared the transcriptomic profile of JDM muscle with IFN-treated myobundles.
Methods. Myobundles generated from myoblasts of healthy pediatric muscle (n=3) were treated with IFNα or IFNβ at 0 (control), 5, 10, and 20 ng/mL for 7 days. Muscle from 12 pediatric controls and 10 treatment-naive JDM patients was obtained from two institutions. RNA was prepared and sequenced at >50M/50 bp paired-end reads/sample. Counts were analyzed separately for muscle and myobundles. Substantial institution-related batch effect in patient data remained despite ComBat-seq correction. Log2-fold-changes were estimated with DESeq2:lfcShrink (apeglm) with adjusted p-values calculated using the Benjamini-Hochberg FDR method. Pathway enrichment was assessed with fgsea for Hallmark gene sets. Differentially expressed genes (DEGs) and normalized enrichment scores (NES) with padj<0.05 and log2FC>2 were compared between JDM muscle and IFN-treated myobundles, with Pearson correlations computed from NES values
Results. JDM patients (mean [SEM] age: 9 [1.2] years) were 60% female and 40% non-Hispanic white. CMAS (35 [6.2]) and PGA (6.4 [0.8]) indicated moderately active disease. Regarding MSAs, three patients were NXP2+; one was Mi-2+. Principal Component Analysis (PCA) separated muscle biopsies by institution and myobundles along PC1 (68%) and PC2 (19%). PC3 (5%) distinguished healthy/untreated from JDM/IFN-treated samples. IFNβ induced greater transcriptomic change than IFNα; IFNβ-treated myobundles had 11,880 DEGs, while IFNα-treated had 5,589 DEGs. JDM muscle had 2,414 DEGs *vs*. control; 72.1% overlapped with IFNβ- and 41.2% with IFNα-treated myobundles. NES correlations were strongly positive (r=0.66, p=2e-7 for IFNα; r=0.74, p=4.8e-10 for IFNβ). All 20 most changed pathways showed concordant directional change between JDM muscle and IFN-treated myobundles, except the unfolded protein response pathway (enriched in JDM and IFNβ, down in IFNα). IFN and inflammatory pathways were most upregulated; apoptosis and epithelial mesenchymal transition were greater in JDM muscle. Oxidative phosphorylation, fatty acid metabolism, and adipogenesis were downregulated in muscle and myobundles, yet more strongly in muscle. Only three of 35 top pathways (DNA repair, apical junction, apical surface) were discordant, being up in JDM but down in IFN-treated myobundles.
Conclusions. Treatment-naive JDM muscle shares meaningful transcriptomic overlap with IFN-treated myobundles, particularly IFNβ-treated ones. Findings support the model's relevance for investigating IFN-driven, muscle-specific pathways in JDM pathogenesis. Future myobundle studies could clarify disease mechanisms, accelerate biomarker discovery, and assess novel therapies preclinically.
Key words: juvenile myositis, bioengineered tissue, interferon, transcriptomics

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METHODOLOGY REPORT: INTERNATIONAL RECOMMENDATIONS FOR THE MANAGEMENT OF JUVENILE IDIOPATHIC INFLAMMATORY MYOPATHIES (JIIM) – AN IMACS-CARRA-PRES CROSS-PARTY INITIATIVE, SUPPORTED BY CURE JM

Belina Yi[1], Ilaria Maccora[2], Raquel Campanilho-Marques[3], Latika Gupta[4], Pedro Machado[5], Polly Livermore[5], Annet Van Royen Kerkof[6], Brian Feldman[7], Adam Huber[8], Susan Kim[9], Liza McCann[10]
[1]Johns Hopkins University School Of Medicine, Baltimore, USA, [2]Meyer Children's Hospital IRCCS, University of Florence, Florence, Italy, [3]Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa, Lisbon, Portugal, [4]University of Birmingham, Francis Crick Institute, London, UK, [5]University College London, London, UK, [6]Wilhelmina Children's Hospital, Utrecht, The Netherlands, [7]University of Toronto, Toronto, Canada, [8]IWK Health Centre, Dalhousie University, Halifax, Canada, [9]University of California San Francisco, San Francisco, USA, [10]Alder Hey Children's Hospital, University of Liverpool, Liverpool, UK

Background. Juvenile idiopathic inflammatory myopathies (JIIM) are rare diseases requiring prompt recognition, diagnosis, and treatment to ensure optimal outcomes. Current guidelines are often country or region-specific, limiting their global applicability. This project aims to develop internationally applicable recommendations for JIIM management through a comprehensive consensus process that meaningfully integrates perspectives from patients, caregivers, physicians, and allied healthcare professionals with the goal of advancing standards of care.
Methods. A systematic literature review with predefined research questions via the Population, Intervention, Comparison, and Outcome (PICO) model covering efficacy and safety of pharmacological and non-pharmacological interventions and diagnostic accuracy on JIIM will inform virtual consensus meetings. These meetings will include diverse stakeholders: adult patients diagnosed with JIIM before age of 18 and/or their caregivers, physicians across relevant subspecialties, and allied health professionals. Artificial intelligent-powered language processing tools will be integrated during the meetings to enable participation from a large number of attendees while enhancing the efficiency of the consensus process. No patient-identifiable information will be included. Ten 1-hour meetings are planned with timing to accommodate international participants
Results. An internationally represented core group consists of early year investigators, senior investigators, methodologists, health professional leads and advisors, patient/parent advisors, a study coordinator, guideline writing group and steering committee members from Childhood Arthritis and Rheumatology Research Alliance (CARRA), Cure JM, International Myositis Assessment and Clinical Studies Group (IMACS), Paediatric Rheumatology European Society (PReS), and other partnerships. Two separate PICOs on pharmacological and non-pharmacological interventional studies identified 4603 articles and a third PICO on diagnostic studies identified 5331 articles. Among interventional studies, 45 studies and case series with 10 or more patients were included for data extraction and risk of bias scoring. Consensus meetings are planned for early 2026.
Conclusions. This novel, inclusive methodology aims to produce recommendations that are: 1. internationally applicable, 2. patient-centered and reflective of lived experience, 3. relevant to healthcare professionals across disciplines, and 4. evidence-based. The resulting recommendations are expected to advance JIIM management and identify priorities for future research. GCOM's international platform will help promote this work to ensure we capture participation across different sub-specialties, medical and allied health, patient/carer organisations and geographic areas.
Acknowledgements. Thanks to Cure JM for funding, Jessica Fitzgerald for administration support, members of steering committee and others involved in this project.
Key words: juvenile dermatomyositis, international guideline, patient, caregiver, PReS, CARRA, IMACS

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PERSISTENT PULMONARY IMPAIRMENT AND ELEVATED IL-18 DEFINE THE INTERSTITIAL LUNG DISEASE PHENOTYPE IN JUVENILE DERMATOMYOSITIS

Charalampia Papadopoulou[1,2], Sirinthip Kittivisuit[2,3], Ying Hong[2], Paul Brogan[1,2], Despina Eleftheriou[1,2], UK Juvenile Dermatomyositis Cohort and Biomarker Study (JDCB)
[1]Paediatric Rheumatology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK, [2]Infection, Immunity and Inflammation Department, UCL Great Ormond Street Institute of Child Health, London, UK, [3]Department of Paediatrics, Prince of Songkla University, Hat Yai, Thailand

Background. Interstitial lung disease (ILD) is a potentially life-threatening complication in juvenile dermatomyositis (JDM) and a major determinant of morbidity. Despite growing recognition of its clinical impact, the underlying mechanisms and reliable biomarkers remain undefined. We investigated clinical and biological features associated with ILD in JDM, longitudinal changes in pulmonary function tests (PFTs), and the predictive value of serum IL-18 in relation to lung outcomes.
Methods. Patients from the UK Juvenile Dermatomyositis Cohort and Biomarker Study (JDCBS) with confirmed JDM and available serum and pulmonary data were included. Clinical, laboratory, and serological characteristics, and PFTs were compared between patients with and without ILD, with serial data assessed up to 12 months. Non-parametric and mixed-effects models were used to evaluate cross-sectional and longitudinal differences, and correlations between biomarkers and PFTs were examined.
Results. Sixty-seven JDM patients were included; 26 (39%) had ILD. ILD patients were younger at presentation (median 8.1 *vs*. 11.1 years) and more frequently had cutaneous ulceration (38% *vs*. 8%, p=0.007) and respiratory symptoms (24% *vs*. 0%, p=0.009). Overlap features and anti-MDA5 positivity were also more common among ILD cases. The use of mycophenolate mofetil was significantly higher in ILD compared with non-ILD (50% *vs*. 20%, p=0.022). At diagnosis, IL-18 was markedly higher in ILD (median 6,839 [IQR 4,158–10,732] *vs*. 2,932 [1,580–4,801] pg/mL; p<0.001) and correlated positively with ferritin (ϱ=0.58), IgG (ϱ=0.45), and LDH (ϱ=0.33), while showing strong inverse correlations with FEV_1%, FVC%, DLCO%, and KCO z-scores (ϱ≈–0.5 to -0.9, p<0.05). CXCL9 trended higher in ILD without reaching statistical significance. Over 12 months, PFTs remained persistently reduced in ILD, with partial recovery despite intensified therapy, whereas non-ILD patients maintained normal PFTs. IL-18 decreased with treatment but remained higher in ILD than in non-ILD throughout follow-up. Exploratory analyses suggested that combining baseline IL-18 with gas-transfer indices improved the identification of patients with subsequent pulmonary improvement versus non-improvement, although larger time-anchored datasets are needed for validation.
Conclusions. JDM-associated ILD presents with a vasculopathic phenotype characterised by early ulceration, higher IL-18, and persistent pulmonary impairment despite treatment intensification. Elevated IL-18 correlates strongly with the severity of restrictive and diffusion defects, supporting its potential role as a biomarker for disease monitoring and prognosis. The combination of IL-18 and PFTs at baseline may help identify patients at risk of poor pulmonary recovery and should be explored in future prospective studies.
Acknowledgements. We thank the clinical team and the UK JDM Cohort and Biomarker Study
Key words: juvenile dermatomyositis, interstitial lung disease, vasculopathy, biomarker

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EOS® IMAGING SYSTEM IS A NOVEL, RAPID, SAFE, AND EFFECTIVE TECHNIQUE TO DETECT AND ASSESS CALCINOSIS IN JDM

Jessica Perfetto[1], Ciara A. Maguire[2], Carli D. Needle[3], Shailee V. Lala[4], Lynne P. Pinkney[4], Vikash S. Oza[2], Philip J. Kahn[1]
[1]Pediatric Rheumatology, Hassenfeld Children's Hospital at NYU Langone, New York, USA, [2]Pediatric Dermatology, Ronald O Perelman Department of Dermatology, NYU Grossman School of Medicine, New York, USA, [3]NYU Grossman School of Medicine, New York, USA, [4]Department of Radiology, NYU Grossman School of Medicine, New York, USA

Background. Calcinosis, detected in up to 47% of children with juvenile dermatomyositis (JDM), causes significant morbidity. Diagnostic delay and active disease duration are associated with increased risk of calcinosis, therefore early identification and treatment are critical. However, there is no standardized approach to assess or quantify calcinosis. Various imaging modalities, including conventional radiographs (x-rays), computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US), are used. However, they have not been directly compared, and they have limitations including 2-dimensional (2D) nature (x-rays), radiation (CT), cost and potential need for sedation (MRI), and limited ability to detect deep lesions (US). EOS® facilitates whole body evaluation via 2D x-rays in ~20 seconds with less radiation than conventional x-rays. It is used for orthopedic conditions but has not been explored for calcinosis. Our objective was to compare EOS® to conventional x-rays in detecting calcinosis in children with JDM.
Methods. Children diagnosed with JDM before age 19 with calcinosis (confirmed with x-rays and/or physical exam) at Hassenfeld Children's Hospital with at least one EOS® scan were included. Socio-demographics, clinical information, imaging modalities, and treatment were collected retrospectively via manual chart review. X-ray and EOS® images were independently assessed by two radiologists blinded to patient information; calcinosis evaluation by each modality was compared. Descriptive statistics were used to summarize each variable. Bivariate analysis was performed using t-test or Chi-squared test, or their non-parametric equivalents (Mann Whitney or Fisher's exact tests).
Results. Seven children with calcinosis and JDM had at least one EOS®. All patients were receiving systemic therapy. Three patients (43%) had clinically active skin and/or muscle disease at the time of EOS®. Calcinosis was initially detected by physical exam in 4 (57%) children; however, EOS® detected additional calcinosis lesions that were missed by either physical exam alone or by physical exam and x-rays in 100% of children. There were no major differences in detection of any given calcinosis lesion by EOS® compared to x-rays
Conclusions. This is the first study to explore EOS® in detecting calcinosis in JDM and to compare EOS® to conventional x-rays. Our single-center retrospective study suggests that EOS® may be comparable to x-rays in detecting a given calcinosis lesion with the advantage of detecting additional lesions due to whole-body imaging, doing so with less radiation than x-rays or ultra-low dose whole-body CT. Future prospective multi-center studies with larger sample sizes comparing other imaging modalities are needed to understand the role of EOS® in detecting and monitoring calcinosis.
Key words: JDM, calcinosis, EOS

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AFRICAN CHILDREN WITH JDM PRESENT WITH SEVERE DISEASE AND HAVE WORSE OUTCOMES OVER TIME COMPARED TO NORTH AMERICAN CHILDREN

Jessica Perfetto[1], Laura B. Lewandowski[2], Ilir Agalliu[3], Dawn M. Wahezi[4], Vanessa Ogega[5], Joan Ahimbisibwe[5], Kate Webb[6], Christiaan Scott[7], Angela Migowa[5]
[1]Pediatric Rheumatology, Hassenfeld Children's Hospital at NYU Langone, New York, USA, [2] Lupus Genomics and Global Health Disparities Unit, Systemic Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH, Bethesda, USA, [3]Albert Einstein College of Medicine, Department of Epidemiology and Population Health, Bronx, USA, [4]Pediatric Rheumatology, The Children's Hospital at Montefiore, Bronx, USA, [5]Aga Khan University Medical College East Africa, Nairobi, Kenya, [6]Red Cross War Memorial Children's Hospital, Cape Town, South Africa, [7]Children's Hospital of Eastern Ontario, Ottawa, Canada

Background. Data on juvenile dermatomyositis (JDM) in low and middle-income countries (LMIC) is limited but suggests higher prevalence of severe manifestations and worse outcomes. Our study aims to compare severity of JDM – defined by weakness severity and prevalence of calcinosis, interstitial lung disease (ILD), and damage – in a cohort of African children with North American children.
Methods. Children diagnosed with JDM before age 19 were included. North American children were from the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry and African children were from 1 center in Nairobi, Kenya and 2 centers in Cape Town, South Africa. Socio-demographics, clinical information, and treatment were collected prospectively from CARRA and retrospectively in the African cohort via manual chart review. Descriptive statistics were used to summarize each variable. Bivariate analysis was performed (t-test or Chi-squared test, or non-parametric equivalents). Logistic regression was performed for the main outcomes (weakness severity, calcinosis, and damage) at two time

points: baseline and 12 month-visit. There was insufficient power to perform multivariable analysis for ILD.
Results. 379 children were included: 349 North American and 30 African (23 South African, 7 Kenyan) children. At baseline, African children were more likely to experience delays greater than 12 months both in diagnosis (30% *vs*. 12%; p=0.04) and seeing a pediatric rheumatologist (37% *vs*. 12%; p=0.001). They were more likely to have moderate/severe weakness (79% *vs*. 39%; p=0.02), though this wasn't seen in multivariable analysis. African children were more likely to have ILD (20% *vs*. 2%; p<0.001); they were more likely to have calcinosis in univariate (23% *vs*. 4%; p=0.001) and multivariable analysis (odds ratio [OR]=6.59, p=0.002). African children trended towards less damage, supported by multivariable analysis (OR=0.36; p=0.09). At 12-months, African children had more damage (50% *vs*. 23%; p=0.047) and were 4.81 times more likely to accrue damage than North American children, adjusting for other variables (p=0.008). Mortality was 7% in the African cohort by the 12-month visit; no North American children died.
Conclusions. This is the first multicenter study of JDM in Africa and the first comparison of JDM between North American and African children. Our study suggests that African children may present with severe disease and delays in care, accrue more damage, and have higher mortality than what's reported in studies from high-income-countries. Future studies with larger sample sizes from more diverse populations over more time are critical to improve the power to detect important differences and understand reasons for these differences.
Key words: JDM, calcinosis, ILD

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ESTIMATING MEANINGFUL SCORE DIFFERENCES IN PATIENT-REPORTED OUTCOMES MEASUREMENT INFORMATION SYSTEM (PROMIS) PEDIATRIC SELF-REPORT AND PARENT-PROXY MEASURE SCORES IN JUVENILE MYOSITIS

Madison Wolfe[1], Amanda Robinson[2], Jin-Shei Lai[3], Theresa Coles[4], Elizabeth Gray[3], Rowland Chang[3], David Cella[3], Kaveh Ardalan[4]
[1]Northwestern University/Ann & Robert H. Lurie Children's Hospital Of Chicago, Chicago, USA, [2]University of Utah, Salt Lake City, USA, [3]Northwestern University Feinberg School of Medicine, Chicago, USA, [4]Duke University School of Medicine, Durham, USA

Background. Juvenile myositis (JM) is an inflammatory myopathy that causes weakness, fatigue, and skin changes, affecting health-related quality of life (HRQoL). We previously found Patient-Reported Outcomes Measurement Information System (PROMIS®) measures are valid and reliable in JM. To enhance interpretability, we present estimates of meaningful score differences (MSDs) for PROMIS fixed short forms in JM.
Methods. JM patients (ages 5-17) and their parents were enrolled. Clinical and demographic data were collected. Patients (≥8 years old) and parents (≥5 years old) completed PROMIS pediatric fixed short forms for Anxiety, Depressive Symptoms, Mobility, Upper Extremity Function, Fatigue and Pain Interference domains. Distribution-based (*i.e*. half the standard deviation) and cross-sectional anchor-based MSD estimates were calculated. Longitudinal anchor-based MSDs (*i.e*. change in PROMIS score associated with change in anchor variable) were estimated for participants with ≥2 study visits. Anchor variables included: Physician's Global Assessment of Disease Activity, muscle enzymes, Disease Activity Score (Muscle, Skin), Childhood Myositis Assessment Scale, PedsQL Generic Core Scales and Rheumatology Modules. Anchor-based MSDs were reported if: 1) Spearman's correlation ≥0.3; 2) n ≥5 per clinically distinct anchor variable category; 3) effect size (*i.e*. Cohen's D) > 0.2. MSDs were reported if greater than mean standard error of measurement (SEM) for each PROMIS domain.
Results. 75 patient-parent dyads were included for analysis, with 42 having ≥2 visits. Participant characteristics mirror published cohorts (*i.e*. 95% juvenile dermatomyositis, 79% White, 79% Female, median [IQR] ages 5.3 [3.6-6.9] at onset and 11.7 [8.1-14.3] at first study visit). Distribution-based MSDs ranged 3.4-6.1 (child) and 4.7-6.3 (parent). Cross-sectional MSDs ranged as follows (child; parent): Anxiety (6.2-12.1; 5.8-14.0), Depression (7.1-12.6; 4.9-12.4), Fatigue (6.0-17.6; 4.0-17.3), Mobility (5.5-11.7; 4.7-13.9), Pain Interference (7.6-16.0; 5.9-13.8), Upper Extremity Function (8.2-12.5; 5.9-14.8). Longitudinal MSDs were estimated (child; parent; note *indicates only a single point estimate could be generated for 1 PROMIS measure-anchor variable pairing): Anxiety (8.3*; 5.9-11.5), Depressive Symptoms (4.9*; 5.5-11.3), Fatigue (7.2-16.0; 4.0-17.3), Mobility (6.1-14.3; 4.6-12.4), Pain Interference (9.3; 6.3-11.2), and Upper Extremity Function (10.8; 5.7-13.1).
Conclusions. MSDs were estimated for PROMIS measures in JM. Empirically derived MSDs enhance clinical interpretability of PROMIS scores and can support power calculations for clinical trials. Future multicenter studies are needed in larger cohorts with wide-ranging disease severity to increase precision and generalizability of MSD estimates.
Key words: juvenile myositis, patient reported outcomes, outcome measures, health-related quality of life, psychometrics

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RECOVERY OF TH1 CELL FREQUENCY IS ASSOCIATED WITH CLINICAL REMISSION OF JUVENILE DERMATOMYOSITIS

Nia M.L. Evans[1,2,3], Lucy R. Marshall[1], Aris E. Syntakas[1,2,3], Elizabeth C. Rosser[3,4], Claire T. Deakin[1,2,3,5], Bethany R. Jebson[1,2,3,4], Vicky Alexiou[1,2,3,4], Coziana Ciurtin[3,4,6], Melissa Kartawinata[1,2,3], Qiong Wu[1], Dario Cancemi[1,2,3], Meredyth G. Ll Wilkinson[1,2,3], Lucy R. Wedderburn[1,2,3], and on behalf of the UK JDM Cohort and Biomarker Study
[1]Infection, Immunity and Inflammation Research and Teaching Department, UCL Great Ormond Street Institute of Child Health, London, UK, [2]NIHR Biomedical Research Centre at Great Ormond Street Hospital, London, UK, [3]Centre for Adolescent Rheumatology at UCL, UCL Hospital and Great Ormond Street Hospital, London, UK, [4]Department of Ageing, Rheumatology and Regenerative Medicine, UCL Division of Medicine, London, UK, [5]School of Population Health, Faculty of Medicine and Health, University of New South Wales, London, UK, [6]NIHR UCLH Biomedical Research Centre, London, UK

Background. Juvenile Dermatomyositis (JDM) is a paediatric autoimmune disorder, characterised by proximal muscle weakness and associated skin disease. T helper cell imbalances in JDM have previously been identified in peripheral blood, however, their contribution to JDM pathology is undefined. We aim to identify whether T helper 1 (Th1) and T helper 17 (Th17) cell dysregulation is present in JDM, and the association of these with clinical disease activity.
Methods. Expression of IFNγ and IL-17 in CD4+ T cells from peripheral blood mononuclear cells (PBMC) of JDM patients was assessed by flow cytometry, following PMA/Ionomycin/Brefeldin A stimulation for 4 hours. Cohort 1 consisted of treatment-naive patients (JDM Pre, n=16), on-treatment patients (JDM On, n=22) (median treatment duration 1.91 years (IQR = 0.98-3.36), and healthy controls (HC, n=34). Findings were validated in a second cohort comprising of JDM Pre patients (n=18), JDM On patients (n=6) (median treatment duration 0.99 years (IQR = 0.78-1.39), and HC (n=17). JDM patients were recruited from the JDCBS, and HC from the Centre for Adolescent Rheumatology at UCL, UCLH and GOSH. Clinically active disease and remission were defined using the Almeida et al amended PRINTO criteria (2015). Clinical disease activity measures were obtained from the JDCBS.
Results. We identified a significant decrease in the frequency of Th1 (CD3+CD4+IFNγ+) cells in cohort 1 JDM Pre (2.48%, p<0.0001) and JDM On (5.74%, p=0.0068) patients compared to HC (9.05%). We also identified a significant decrease in frequency of Th17 (CD3+CD4+IL-17+) cells in JDM Pre patients (0.62%, p=0.0353) compared to HC (1.02%). Decreases in cell frequencies were confirmed in cohort 2, demonstrating consistent reduction in Th1 and Th17 cells in JDM.
After applying the amended PRINTO criteria to cohort 1, we identified a significant increase in Th1 cell frequency in JDM On patients in remission (7.85%) compared to JDM Pre patients with active disease (2.65%) (p=0.0168). No significant difference was observed between HC (9.05%) and JDM On patients in remission, suggesting that a deficit of Th1 cells is associated with more severe clinical disease and recovery of this population is achieved in remission of JDM.
Conclusions. Our findings show reduced Th1 cell frequencies in treatment-naive and on-treatment JDM patients compared to HC. Clinical data indicates that this is associated with increased disease activity, and recovery of this population is seen in remission.
Key words: juvenile dermatomyositis, T cell, IFNγtext of this study, Claude's assessments demonstrated significant consistency with human evaluators. Pearson's correlation coefficients for the "Global assessment" score highlighted a strong positive correlation between the mean MDAAT Global VAS scores provided by Claude 2 and those by expert assessor 1 (r=0.88, *p*<0.001) and 2 (r=0.78, *p*<0.001), while a moderate positive correlation was observed with less experienced assessor 3 (r=0.53, *p*=0.002) (Fig. 1).
Conclusion. Claude 2 has demonstrated excellent consistency with expert human scoring in clinical cases of patients suffering from IIM, with perfor-

mance better than naive assessors. Its potential future uses are broad, ranging from clinical training for MDAAT scoring to the creation of clinical cases for use in trial recruitment, or trial screening of electronic medical records.

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UTILITY OF THE MAWDSLEY CALCINOSIS QUESTIONNAIRE IN PATIENTS WITH JUVENILE DERMATOMYOSITIS ASSOCIATED CALCINOSIS

Gulnara Mamyrova[1], Kelly A. Rouster-Stevens[2], Julie Fuller[3], Hanna Kim[4,1], Vy K. Do[5], Rodolfo V. Curiel[1], Lesley A. Saketkoo[6], Lisa G. Rider[7,1], Adam Schiffenbauer[7]

[1]George Washington University School of Medicine and Health Sciences, Washington, USA, [2]Rheumatology, Department of Pediatrics, Emory University School of Medicine, Atlanta, USA, [3]Rheumatology, Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, USA, [4]Juvenile Myositis Pathogenesis and Therapeutics Unit, NIAMS, NIH, Bethesda, USA, [5]Department of Pediatrics, University of Texas at Austin Dell Medical School, Austin, USA, [6]New Orleans Scleroderma and Sarcoidosis Patient Care and Research Center, Louisiana State University and Tulane University Medical Schools, New Orleans, USA, [7]Environmental Autoimmunity Group, Clinical Research Branch, NIEHS, NIH, Bethesda, USA

Background. Calcinosis is a severe complication of juvenile dermatomyositis (JDM). The Mawdsley Calcinosis Questionnaire (MCQ) is a patient-reported outcome tool developed to assess the severity and impact of adult systemic sclerosis-related calcinosis with 21 items in four domains (Quantity/Frequency, Pain/Sensation, Physical Function, Psychological Impact). The goal of this study was to examine performance of the MCQ for patients with JDM associated calcinosis.

Methods. Thirty patients with probable or definite JDM by Bohan and Peter criteria and their parents completed the MCQ. Calcinosis severity was evaluated using a patient/parent Calcinosis Severity Visual Analog Scale (VAS 0-10cm). Construct validity was assessed using Spearman's correlation. Internal consistency was measured by Cronbach's alpha. Predictive contribution of MCQ items to overall calcinosis severity was determined using multiple linear regression.

Results. The mean age of patients was 13.2±3.4 years, 60% were female. There were no significant differences between patient-reported and parent-reported MCQ items' scores. Calcinosis Severity VAS scores did not differ between the two groups (2.3±1.2 *vs*. 2.3±2.4, respectively). The MCQ demonstrated internal consistency for both patients and parents (Cronbach's alpha 0.92 and 0.89, respectively). There were moderate to strong correlations between several MCQ items and calcinosis severity (VAS) in both the patient and parent groups: Pain/Sensation domain items "experienced pain from calcinosis" (rs 0.67 and rs 0.72, p<0.0001 both), "felt calcinosis getting tighter or having more pressure" (rs 0.57, p=0.0006 and rs 0.72, p<0.0001), "calcinosis been tender to touch" (rs 0.46, p=0.006 and rs 0.56, p=0.0007), "felt calcinosis growing under skin" (rs 0.55, p=0.001 and rs 0.62, p=0.0001); Psychological Impact Domain items "felt the need to protect areas of calcinosis" (rs 0.59, p=0.0004 and rs 0.54, p=0.001), "been fearful of infection" (rs 0.37, p=0.02 and rs 0.43, p=0.009), "interfered ability to enjoy recreational activities" (rs 0.64, p=0.0001 and rs 0.34, p=0.03), and Physical Function domain item "interfered ability to care for self" (rs 0.34, p=0.04 and rs 0.41, p=0.01). Multiple linear regression models for patients with JDM demonstrated that calcinosis severity was best predicted by 10/21 MCQ items (adjusted R2 0.78), and for parents, by 11/21MCQ items (adjusted R2 0.89).

Conclusions. The MCQ demonstrates good internal consistency and construct validity, suggesting its potential for evaluating various aspects of calcinosis severity in patients with JDM.

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Key words: juvenile dermatomyositis, calcinosis, patient reported outcomes

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TYPE I INTERFERON SIGNATURE IS ASSOCIATED WITH DISEASE ACTIVITY AND MUSCLE OUTCOMES IN JUVENILE DERMATOMYOSITIS

Valentina Natoli[1,2], Francesca Bovis[3], Paola Bocca[2], Serena Palmeri[1], Silvia Maria Orsi[1,2], Sabrina Atena Stoian[1], Damiano Lemmi[1], Ana Isabel Rebollo-Giménez[1,4], Chiara Campone[1], Alessandro Consolaro[1,2], Clara Malattia[1,2], Roberta Caorsi[1,2], Riccardo Papa[2], Marco Gattorno[2], Angelo Ravelli[1,5], Stefano Volpi[1,2], Silvia Rosina[2]

[1]Università degli Studi di Genova, Dipartimento di Neuroscienze, Riabilitazione, Oftalmologia, Genetica e Scienze Materno-Infantili (DiNOGMI), Genoa, Italy, [2]IRCCS Istituto Giannina Gaslini, Paediatric Rheumatology and Autoinflammatory Diseases Unit, Genoa, Italy, [3]Department of Health Sciences, University of Genoa, Genoa, Italy, [4]Hospital Universitario Príncipe de Asturias, Madrid, Spain, [5]IRCCS Istituto Giannina Gaslini, Direzione Scientifica, Genoa, Italy

Background. Type I IFN-related gene signatures (IGS) have emerged as potential biomarkers of disease activity, but their association with clinical outcomes in juvenile dermatomyositis (JDM) remains to be fully defined. The study aimed to evaluate associations between IGS and clinical parameters, disease activity states, and remission status in JDM.

Methods. Available IGS measurements made in JDM patients followed at the Gaslini Institute (Genoa, Italy) between 2019 and 2025 were retrieved (n=101). After excluding repeated samples, 43 patients were included, of whom only the first available sample was analyzed. IGS was determined as previously described (1). Correlations of IGS with Juvenile DermatoMyositis Activity Index (JDMAI) 1 and 2 (2), physician global assessment (PhGA), MMT8, hybrid MMT/CMAS (hMC) (3), muscle and skin component of DAS, and 0-10 skin visual analog scale (VAS) were tested using Spearman's rank correlation. IGS were compared across JDMAI1- and JDMAI2-defined disease activity states [4], using the Kruskal-Wallis test and post-hoc comparisons. Mann-Whitney U-test was used to compare IGS by the presence or absence of muscle and skin remission and complete clinical response, and by muscle enzyme status (normal *vs*. elevated).

Results. IGS showed moderate correlation with JDMAI1 (R=0.64, p<0.001), JDMAI2 (R=0.65, p<0.001), PhGA (r=0.61, p<0.001), MMT8 (R= -0.56, p<0.001) and hMC (R= -0.42, p=0.008). No significant correlations were observed with skin VAS and DAS. IGS levels were significantly higher in patients classified as being in the state of high disease activity (HDA) than in those with inactive disease (ID) (median JDMAI1 3.5 *vs*. 0.31, p=0.018; median JDMAI2 3.3 *vs*. 0.3, p=0.0009) and low disease activity (LDA) (median JDMAI1 3.5 *vs*. 0.3, p=0.017). IGS distinguished patients with muscle remission vs those with active muscle disease (p=0.007), with complete clinical response *vs*. no response (p=0.056), and with normal *vs*. elevated muscle enzymes (p=0.020).

Conclusions. IGS levels were associated with higher global and muscle disease activity scores, but not with skin disease activity measures. IGS levels discriminated between HDA and ID/LDA states, as well as between patients who experienced or did not experience muscle remission, complete clinical response, or had or did not have normal muscle enzymes. These observations support the potential role of IGS measurement as a biomarker for disease monitoring and for defining treatment targets in the treat-to-target strategy for JDM.

Key words: juvenile dermatomyositis, type I interferon signature, biomarkers, treat-to-target

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APPLICATION OF ULTRASOUND-GUIDED CRYO-FRACTURE BIOPSY FOR MUSCLE IN PEDIATRIC IDIOPATHIC MYOSITIS

Xinning Wang[1], Yong Zhang[1], Shoudong Pan[1], Ya Ma[1], Jianguo Li[1]
[1]Capital Center for Children's Health, Capital Medical University, Beijing, China

Background. Muscle biopsy is essential for diagnosing idiopathic myositis. Conventional open surgical biopsy, though widely used, requires general anesthesia, results in large incisions, significant tissue trauma, prolonged recovery, and increased infection risk. Traditional minimally invasive puncture biopsy, performed at room temperature, frequently yields fragmented tissue with insufficient volume due to muscle fiber degeneration and inflammatory infiltration, thereby compromising pathological accuracy. There is an urgent need for an improved biopsy technique that balances minimal invasiveness with diagnostic efficacy. This study introduces and evaluates an ultrasound-guided cryo-rotational biopsy technique as a potential solution.
Methods. From March to October 2025, 23 hospitalized children with suspected idiopathic myositis underwent ultrasound-guided cryo-rotational biopsy using a disposable rotary core biopsy needle (BN-10G(3.4×96)-22). Under low-temperature conditions, two muscle tissue specimens (0.3 cm × 1.2 cm) were obtained per patient and promptly sent for pathological examination. Post-procedure, puncture sites were compressed and bandaged, with follow-up ultrasound after 4 hours. Patient demographics, operative time, pathological outcomes, recovery duration, and complications were recorded to assess the safety, accuracy, and efficacy of the technique.
Results. All 23 patients (median age 7 years, range 2–13 years) underwent successful specimen retrieval. The cryo-rotational method yielded 2.4 times more tissue volume compared to conventional warm biopsy. General anesthesia was used in only 4 cases, with the remaining 19 managed under local anesthesia. Two patients developed transient puncture-site hematomas (max diameter 1 cm), which resolved within one week. All puncture sites healed well, with an average healing time of 2 days and maximal scar diameter of 2 mm. No infections were reported. Muscle pathology confirmed diagnosis in 22 cases.
Conclusions. Ultrasound-guided cryo-rotational biopsy is a safe, efficient, and minimally invasive technique for muscle biopsy in children with idiopathic myositis. It reduces physiological and psychological trauma, minimizes the need for general anesthesia, and improves sample quality and diagnostic accuracy compared to traditional warm puncture biopsy. The procedure is associated with less pain, no suturing, shorter recovery, lower infection risk, and reduced hospitalization time and cost. It holds promise for broader application in pediatric patients requiring muscle biopsy.
Key words: idiopathic myositis, muscle biopsy, cryo-rotational biopsy

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SINGLE-CELL SPATIAL TRANSCRIPTOMIC PROFILING REVEALS ABNORMAL INTERFERON AND METABOLIC SIGNATURES IN JUVENILE DERMATOMYOSITIS MUSCLE TISSUE

Aris E. Syntakas[1,2,3], Yara E. Sanchez-Corrales[4], Theodoros Xenakis[4], Huong D. Nguyen[1,2], Charalampia Papadopoulou[2,5], Muthana Al Obaidi[2,5], Clarissa Pilkington[2,5], Olumide Ogunbiyi[6], Ashirwad Merve[6], Lucy R. Wedderburn[1,2,3], Meredyth G. Ll. Wilkinson[1,2,3]
[1]Infection, Immunity and Inflammation Research and Teaching Department, UCL Great Ormond Street Institute of Child Health, University College London, London, UK, [2]NIHR Biomedical Research Centre at Great Ormond Street Hospital, London, UK, [3]Centre for Adolescent Rheumatology Versus Arthritis at UCL, UCL Hospital and Great Ormond Street Hospital, London, UK, [4]Genetics and Genomic Medicine Research and Teaching Department, UCL Great Ormond Street Institute of Child Health, University College London, London, UK, [5]Department of Rheumatology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK, [6]Department of Histopathology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK

Background. Juvenile dermatomyositis (JDM) is a rare paediatric autoimmune disease, characterised by chronic inflammation of muscle and skin tissues, with prominent interferon (IFN) pathway activation. However, the spatial resolution of immune-muscle interactions in affected tissue remains poorly defined. Spatial transcriptomics enables high-resolution mapping of cellular states within preserved architecture. To address this, spatial molecular imaging was applied to muscle biopsies from children with JDM to characterize the transcriptional landscape of resident and infiltrating cell populations
Methods. Muscle biopsies from three patients with JDM were obtained from the UK JDM Cohort and Biomarker Study (JDCBS), and three age-matched control biopsies were obtained through Brain UK. Spatial transcriptomic profiling was performed using the NanoString CosMx Spatial Molecular Imager and the 1000-Plex RNA Human Universal Cell Characterization Panel, yielding 43 fields of view (FOV) from JDM and 23 from controls, totalling approximately 40,000 cells. Cells with low transcript abundance or high negative control probe signal were removed. Data processing, normalization, clustering, and cell type annotation were performed using Seurat v5 and the InSituType packages, guided by canonical cell marker expression. Pseudobulk differential gene expression across cell types was evaluated using DESeq2.
Results. Major muscle tissue and infiltrating immune cell populations were identified, including muscle fibers, fibroblasts, endothelial cells, macrophages, T cells, and B/plasma cells. Pseudobulk differential expression analysis revealed a shared transcriptional pattern in both muscle fibers and macrophage-lineage cells in JDM samples, characterized by increased expression of interferon-stimulated genes and decreased expression of genes associated with oxidative phosphorylation and antioxidant functions. These findings suggest a coordinated inflammatory and metabolic stress response affecting both structural and immune compartments within diseased muscle tissue
Conclusions. CosMx spatial transcriptomic profiling allowed characterization of major muscle and immune cell populations in JDM and control muscle tissue. Early findings indicate shared upregulation of interferon-related transcripts and reduced metabolic gene expression in both structural and immune cell compartments in JDM. Ongoing work will refine cell-state annotations, expand sample numbers, and further evaluate spatial organization of these transcriptional patterns.
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Key words: juvenile dermatomyositis, spatial transcriptomics, interferon

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COMPARISON OF DISEASE SEVERITY AND ACTIVITY BETWEEN JUVENILE- AND ADULT-ONSET DERMATOMYOSITIS: A MULTICENTER COHORT STUDY

Agathe Sinnaeve[1], Brigitte Bader-Meunier[2], Anne Mirguet[3], Thomas Moulinet[1,4], Irène Lemelle[5], Anne-Claire Bursztejn[6], Joëlle Terzic[7], Ariane Zaloszyc[7], Alain Meyer[8], Thierry Martin[9], Claire Ballot-Schmit[10], Julien Campagne[11], Loïs Bolko[12], Bernard Bonnotte[13], Roland Jaussaud[1,14], Olivier Benveniste[15], Paul Decker[1]
[1]Département de Médecine Interne et Immunologie Clinique, CHRU Nancy, Vandœuvre-lès-Nancy, France, [2]Département d'Immunologie, d'Hématologie et Rhumatologie Pédiatrique, Hôpital Necker, APHP, Paris, France, [3]Département de Néphrologie Pédiatrique, Hôpital d'enfants, CHRU Nancy, Vandoeuvre-lès-Nancy, France, [4]UMR 7365 CNRS-Université de Lorraine IMoPA, Université de Lorraine, Vandoeuvre-lès-Nancy, France, [5]Département d'Onco-hématologie Pédiatrique, Hôpital d'enfants, CHRU Nancy, Vandoeuvre-lès-Nancy, France, [6]Service de Dermatologie, CHRU Nancy, Vandoeuvre-lès-Nancy, France, [7]Département de Pédiatrie, Hôpitaux Universitaires de Strasbourg, Strasbourg, France, [8]Département de Rhumatologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, France, [9]Service d'immunologie clinique, Centre de Référence des Maladies Auto-immunes Rares RESO, Hôpitaux Universitaires de Strasbourg, Strasbourg, France, [10]Département de Pédiatrie, CHU Besançon, Besançon, France, [11]Service de Médecine Interne, UNEOS, Metz, France, [12]Département de Rhumatologie, CHU Reims, Reims, France, [13]Département de Médecine Interne, CHU Dijon, Dijon, France, [14]EA 3450 DevAH - Développement, Adaptation et Handicap, Université de Lorraine, Vandoeuvre-lès-Nancy, France, [15]Département de Médecine Interne et Immunologie Clinique, Hôpital de la Pitié Salpêtrière, Sorbonne Université, APHP, Paris, France

Background. To compare the severity at diagnosis and disease activity during follow-up between juvenile and adult-onset dermatomyositis (DM).
Methods. Patients with DM fulfilling the 2017 ACR/EULAR criteria and tested for myositis-specific antibodies were included. Overall severity at diagnosis was defined by at least one of the following: severe muscle impairment, symptomatic interstitial lung disease (ILD), gastro-intestinal vasculitis, myocarditis, severe skin ulceration, or admission to an intensive care unit. Clinically inactive disease and remission were defined according to PRINTO group criteria and IMACS guidelines.

Results. 208 patients were included: 127 with adult DM (≥18 years) and 81 with juvenile DM (<18 years). Anti-NXP2 and anti-Mi2 antibodies (Abs) were more frequent in juvenile DM and adult DM, respectively. Severe disease at diagnosis was present in 45% of cases, with symptomatic ILD more common in adults and gastro-intestinal vasculitis more common in children. No difference was observed in severe muscle disease. In juvenile DM, anti-NXP2 Abs (OR=4.58 [1.55–14.93], p=0.008) and joint involvement (OR=2.70 [1.15–7.74], p=0.04) were associated with severe disease at diagnosis, while in adult DM, anti-Mi2 Abs were associated with a lower likelihood of severe disease (OR=0.14 [0.03–0.48], p=0.005). Clinically inactive disease (90% *vs*. 81%, p=0.09) and remission (31% *vs*. 16%, p=0.01) were more frequent in juvenile DM at last follow-up. Severe infections occurred in 25% of patients.
Conclusions. Severity profiles differ by age of DM onset. Autoantibodies are key indicators of severity at diagnosis in both juvenile DM and adult DM.
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Key words: dermatomyositis, juvenile dermatomyositis, vasculopathy, myositis-specific antibodies

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THROUGH THEIR EYES: ACCEPTABILITY OF NAILFOLD CAPILLAROSCOPY IN CHILDREN WITH JUVENILE DERMATOMYOSITIS. A MIXED-METHODS STUDY

Elizabeth Deja[1], Katie Roberts[2], Marilena Hadjittofi[2], Jessica Fitzgerald[3], Charalampia Papadopoulou[6], Andrea Murray[7,8], Graham Dinsdale[8], Lauren Huckerby[15], Jenny Ainsworth[9], Andy Vail[10], Klaudia Kupiec[6], Yvonne Glackin[6], Lucy Wedderburn[6,11,12,13], Chris Taylor[14], Clare Pain[4], Ariane Herrick[7,8], Liza McCann[4,5]
[1]Public Health, Policy and Systems, University of Liverpool, Liverpool, UK, [2]Clinical Health Psychology, Alder Hey Children's Hospital, Liverpool, UK, [3]Experimental Arthritis Treatment Centre for Children, University of Liverpool, Liverpool, UK, [4]Department of Paediatric Rheumatology, Alder Hey Children's NHS Foundation Trust, Liverpool, UK, [5]Department of Women and Children's Health, University of Liverpool, Liverpool, UK, [6]Department of Paediatric Rheumatology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK, [7]Centre for Musculoskeletal Research, Division of Musculoskeletal and Dermatological Science, University of Manchester, Manchester, UK, [8]Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester, UK, [9]University of Liverpool, Liverpool, UK, [10]Centre for Biostatistics, University of Manchester, Manchester, UK, [11]NIHR Biomedical Research Centre,Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK, [12]Centre for Adolescent Rheumatology Versus Arthritis at UCL, Great Ormond Street Hospital NHS Foundation Trust and University College London Hospitals NHS Foundation Trust, London, UK, [13]Infection Immunity and Inflammation Research and Teaching Department, University College London, Great Ormond Street Institute of Child Health, London, UK, [14]University of Manchester, Manchester, UK, [15]Department of Paediatric Rheumatology, Royal Manchester Children's NHS Foundation Trust, Manchester, UK

Background. The aim of the MYOSCOPE study was to test the feasibility and impact of using handheld nailfold capillaroscopy (NFC) in clinical practice with children with juvenile dermatomyositis (JDM). Participants and parents' perspectives are described here.
Methods. A Mixed-methods design, including questionnaires and interviews, was used. Children with JDM at two tertiary paediatric rheumatology centres were approached to participate in MYOSCOPE and their parent/guardian who attended the clinic were eligible to participate. Questionnaires were given to patients (≥6 years) and parents/guardians at each clinic visit. All participants were invited to take part in patient/family interviews. A thematic analysis approach was used to explore qualitative data. Quantitative data were analysed using descriptive statistics. Data were then synthesised using framework analysis to map findings to the Adapted Theoretical Framework of Acceptability.
Results. Forty patients were recruited to MYOSCOPE. Data were collected (October 2024 - September 2025) from 72 participants. 112 questionnaires were received, linked to all 40 patients (33 patients, 39 parents, three time points). Twenty-four participants, linked to 16 patients, also took part in semi-structured interviews (8 patients,16 parents).
There was strong support for the use of NFC during clinic visits. Findings showed that all eight constructs of acceptability were met. 110/112 (98.2 %) of questionnaire responses felt either 'fantastic', 'really good', or 'okay' about seeing their nailfold capillaries in clinic. Participants felt that NFC increased their understanding of the current condition of their/their child's JDM (94/112, 83.9 %). Participants valued that the process made an 'invisible condition visible' and increased their understanding of why medication was needed 101/112 (90.2 %). 29/38 (76.6%) of participants at second/third visits, felt that seeing NFC helped them/their child take their medication more reliably. A minority (3/16 patients represented in the interviews) described experiencing negative sensory feedback from the placement of olive oil on their fingers for NFC.
Conclusions. Patients and their parents found the use of NFC in JDM clinics acceptable and desirable, increasing understanding of JDM and reinforcing the need to take medication as prescribed. If using NFC in clinical situations accommodations need to be in place to prevent negative sensory feedback.
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Key words: nailfold capillaroscopy, juvenile dermatomyositis, patient perspectives, adherence

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CARDIAC DYSFUNCTION IS ASSOCIATED WITH REDUCED CARDIORESPIRATORY FITNESS IN LONG-TERM JUVENILE DERMATOMYOSITIS

Simon Girmai Berger[1], Birgit Nomeland Witczak[1,2], Kristin Schjander Berntsen[3,4], Elisabeth Edvardsen[5], Thomas Schwartz[1,6], Ivar Sjaastad[1,7], Mathis Korseberg Stokke[1], Helga Sanner[1,8]
[1]Institute for Experimental Medical Research, Oslo University Hospital Ullevål and University of Oslo, Oslo, Norway, [2]The Department of Cardiology, Akershus University Hospital, Lørenskog, Norway, [3]Department of Rheumatology, Oslo University Hospital, Oslo, Norway, [4]Martina Hansens Hospital, Sandvika, Norway, [5]Department of Sports Medicine, Norwegian School of Sport Sciences, Oslo, Norway, [6]Department of Medicine, Diakonhjemmet Hospital, Oslo, Norway, [7]Department of Cardiology, Oslo University Hospital Ullevål, Oslo, Norway, [8]Institute for Clinical Medicine, Medical Faculty, University of Oslo, Oslo, Norway

Background. Juvenile dermatomyositis (JDM) is a rare autoimmune vasculopathy of childhood associated with chronic multisystem involvement. Many patients exhibit reduced cardiorespiratory fitness years after disease onset (1), even during clinical remission (2). While cardiac abnormalities have been described at rest (3), their contribution to long-term exercise limitation remains unclear. Since the ability of the heart to adapt during exercise is a key determinant of cardiorespiratory fitness, impaired cardiac reserve during exercise may be an important – but so far unexplored – mechanism in this population. This study aimed to assess whether cardiac dysfunction is associated with reduced cardiorespiratory fitness in patients with long-term JDM.
Methods. Patients from the nationwide Norwegian JDM (NorJDM) cohort and population-based controls underwent standardized clinical and functional assessments. Cardiorespiratory fitness was determined by cardiopulmonary exercise testing on a treadmill and expressed as maximal oxygen uptake (VO_2max). Cardiac function was assessed by echocardiography at rest and during exercise, including measures of systolic (global longitudinal strain, GLS) and diastolic function. Cardiac dysfunction was defined as systolic or diastolic ventricular impairment according to established reference values. Daily physical activity was measured by accelerometers and expressed as time in moderate-to-vigorous physical activity (MVPA). Disease activity was classified according to updated PRINTO criteria for clinically inactive disease.
Results. Forty-five patients with JDM (62% female, median age 27 years [range 10–58], median disease duration 20 years [2–43]) and 51 controls (61% female, median age 26 years [11–56]) were included. Compared with controls, patients had lower cardiorespiratory fitness (VO_2max 37.6 ± 10.5

vs. 44.7 ± 8.7 ml/kg/min, p<0.001) and spent less time in MVPA (45 ± 25 *vs*. 59 ± 21 min/day, p=0.004). Cardiac dysfunction was present in 24% of patients versus 8% of controls (p=0.03). Patients exhibited reduced systolic and diastolic function at rest, with differences appearing more marked during exercise. Patients with active disease, 17(38%), had lower GLS; also lower GLS was associated with lower VO_2max (both p<0.05).

Conclusions. After a median disease duration of 20 years, patients with JDM demonstrated impaired cardiac function at rest and during exercise. The association between impaired systolic function and lower cardiorespiratory fitness indicates that limited cardiac reserve contributes to long-term exercise limitation, not explained by lower habitual physical activity alone. These findings indicate the need for long-term cardiac follow-up and functional assessment as part of comprehensive JDM management.

Acknowledgements. Stokke and Sanner share senior authorship

Key words: juvenile dermatomyositis, cardiorespiratory fitness, cardiac dysfunction

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COMPARISONS BETWEEN ADULT AND JUVENILE DM PERIPHERAL BLOOD MONONUCLEAR CELL GENE EXPRESSION MAY IDENTIFY CANCER-ASSOCIATED GENE SIGNATURES

Rachael Edwards[1], Nancy Olsen[1], Dajiang Liu[1], Laura Carrel[1], Amanda Nelson[1], Galen Foulke[1]
[1]Penn State College of Medicine, Hershey, USA

Background. Dermatomyositis (DM) is an uncommon autoimmune disease featuring muscle and skin inflammation. Adults with DM are at increased risk for malignancy, most notably of lung, bladder, colon, ovary, and breast. Cancer is often occult, and additional biomarkers beyond myositis specific antibodies are needed to optimize screening. Juvenile DM (JDM) presents with comparable muscle and skin manifestations, yet there is no increased cancer risk in JDM. From a molecular perspective, the primary commonality between these DM subtypes is a striking type I interferon signature; otherwise, these diseases are relatively unique. Understanding gene expression differences between DM and JDM may clarify mechanisms of cancer association in adults.

Methods. We utilized both in-house generated and publicly available peripheral blood mononuclear cell (PBMC) RNA sequencing data from DM (n=10), JDM (n=32), and control (adult: n=5; juvenile: n=12) donors, to identify genes that 1) distinguish DM from JDM; and 2) are indicative of cancer risk in DM patients. Differential gene expression (DGE) between both DM:adult healthy controls and JDM:juvenile healthy controls were utilized as input for Reactome pathway analysis (ReactomePA).

Results. Interestingly, terms related to DDX58/IFIH1 (RIGI/MDA5) signaling were significant only in DM, while interleukin signaling was significant only in JDM (p≤0.05). As expected, type I interferon signaling was significant in both DM subgroups (p≤0.05). DGE performed directly between these DM subgroups highlighted 21 and 14 significantly differentially expressed genes in DM and JDM, respectively (p≤0.05). The top differentially expressed gene in the JDM group was IL6; a finding that supports the implication of overactive IL6/STAT3 signaling in the disease pathogenesis. In the DM group, the genes FAM83A and GUC2YC were of particular interest as literature has indicated a link between their overexpression and lung and colorectal cancer, respectively, wherein gene expression is increased in the local tumor microenvironment, as well as in circulating tumor cells and in circulating mRNA.

Conclusions. Our study defines a list of candidate genes distinguishing JDM from DM in peripheral blood. Continued study will allow us to highlight distinctions between DM and JDM and may lead to more granular discovery of malignancy-associated biomarkers in DM or pathways that are cancer-protective in JDM.

Key words: dermatomyositis, juvenile dermatomyositis, RNAseq

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PULMONARY INVOLVEMENT ACROSS JUVENILE-ONSET CONNECTIVE TISSUE DISEASES: RESULTS FROM A NATIONAL MULTICENTRE COHORT

Carolina Zinterl[1,2,3], Bianca Correia[1,2,3], Constança Durão[4], Sofia Azevedo[5,6], Inês Cunha[5,6], Joana Baptista de Lima[7], Sandra Sousa[8,3], Vanessa Fraga[8], Maria João Cadório[9], João Oliveira[9], Joana Silva-Dinis[10], Helena Sousa[11], Filipa Oliveira-Ramos[1,2,3], Raquel Campanilho-Marques[1,2,3]
[1]Paediatric Rheumatology Unit, Rheumatology and Pediatric Departments, Hospital Santa Maria, ULS Santa Maria, Centro Académico de Medicina de Lisboa (CAML), [2]Rheumatology Department, Unidade Local de Saúde Santa Maria, Centro Académico de Medicina de Lisboa (CAML), [3]Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal, [4]Thoracic Department, Pulmonology Service, Local Health Unit of Santa Maria, Lisbon, Portugal, [5]Rheumatology Department. Unidade Local de Saúde Região de Aveiro, Aveiro, Portugal, [6]Aveiro Rheumatology Research Centre, Egas Moniz Health Alliance, Aveiro, Portugal, [7]Paediatric Rheumatology Unit, Centro Materno Infantil do Norte, Unidade Local de Saúde de Santo António (ULSSA), Oporto, Portugal, [8]Rheumatology Department, ULS Almada Seixal - Hospital Garcia de Orta, [9]Rheumatology Department, Hospital da Universidade de Coimbra, Coimbra, Portugal, [10]Rheumatology Department, Unidade Local de Saúde São José, Lisbon, Portugal, [11]Paediatrics Department, Unidade Local de Saúde Estuário do Tejo

Background. Juvenile-onset connective tissue diseases (jCTDs) are rare autoimmune disorders beginning before age 18 and frequently involving multiple organs. Pulmonary manifestations are well described in adult-onset disease, but paediatric data remain limited. This study characterises the prevalence, incidence, patterns, and clinical associations of pulmonary involvement in jCTDs.

Methods. This national multicentre retrospective cohort study included patients with juvenile systemic lupus erythematosus (jSLE), juvenile mixed connective tissue disease (jMCTD), juvenile systemic sclerosis (jSSc), juvenile idiopathic inflammatory myopathies (jIIM), juvenile Sjögren syndrome (jSS), and overlap syndromes, followed between January 2000 and August 2025. Demographic, clinical, serological, pulmonary, extrapulmonary, and treatment data were collected. Patients with severe asthma, sickle cell disease, or additional inflammatory rheumatic syndromes were excluded. Pulmonary involvement was assessed using high-resolution computed tomography and pulmonary function testing (PFT). Incidence rate of pulmonary involvement was calculated as the number of new events per 100 person-years with 95% CIs and prevalence was calculated as frequencies. Associations between the different variables were tested using Fisher's Exact tests with Bonferroni corrections applied where appropriate.

Results. A total of 222 patients were included, 73.9% female, with median [IQR] age at last visit of 21 [18-27] years and median disease duration of 9 [4.8-14.0] years. Diagnoses included jSLE (n=145, 65.5%), jMCTD (n=8, 3.6%), jSSc (n=12, 5.4%), jIIM (n=32, 14.4%), jSS (n=13, 5.9%), and overlap syndromes (n=10, 4.5%). Pulmonary involvement occurred in 12.6% (n=28) after a median of 3 [0-7] years from disease onset. The highest prevalence was observed in jMCTD (42.9%), followed by jSSc (38.5%) and myositis overlap syndromes (33%). jSLE showed pulmonary disease in 14.3% of cases and jIIM in 3.6%. Interstitial lung disease was the most common manifestation (n=9), predominantly nonspecific interstitial pneumonia, followed by pleural (n=7) and vascular (n=6) involvement. Worst ever PFTs showed a median FVC% of 93 [85.9-104] and a median TLC% of 96.5 [89-104]. Median of DLCO/sb was 6.97 [5.8-8.7] litres and DLCO/VA was 1.72 [1.5-2.0] litres. Most patients (95.5%) received conventional disease-modifying antirheumatic drugs (DMARDs), particularly mycophenolate mofetil (40.5%), and 23% received biologics, mainly rituximab (13.5%). Anti-fibrotic therapy was used in two patients. The incidence rate of pulmonary involvement was 0.94 per 100 person-years (95% CI 0.53–1.55). No statistically significant associations between autoantibody profiles or jCTD subtype and ocurrence of pulmonary disease were found.

Conclusions. Pulmonary involvement in jCTDs, while infrequent, represents a significant complication with variable patterns across disease subtypes. The lack of reliable serological predictors supports systematic pulmonary monitoring in routine follow-up.

Key words: juvenile-onset connective tissue diseases, pulmonary involvement

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NAILFOLD CAPILLAROSCOPY CHANGES ACROSS A DUAL CENTER COHORT OF JUVENILE DERMATOMYOSITIS PATIENTS

Aurora Rynda[1], Zilan Zheng[2], Nick McClellan[1], Li Chen[1], Sophia Matossian[1], Jessica Neely[2], Susan Kim[2], Jessica Turnier[1]
[1]University of Michigan, Department of Pediatrics, Division of Rheumatology, Ann Arbor, USA, [2]University of California, Department of Pediatrics, Division of Rheumatology, San Francisco, USA

Background. Juvenile dermatomyositis (JDM) is a multisystem autoimmune disease characterized by vasculopathy across tissues. Vascular changes can be quantified through use of nailfold video capillaroscopy (NVC), and individual NVC parameters may reflect JDM disease activity and pathophysiology. The objective of this study was to evaluate differences in NVC parameters across disease activity groups and associations with global and organ-specific disease activity in a dual-center JDM cohort.
Methods. Sixty-two JDM patients from the University of Michigan and University of California San Francisco had NVC performed at clinic visits. Sixteen patients had a paired six-month follow-up visit. Clinical disease activity was assessed using the Physician Global Assessment (PGA), Manual Muscle Testing (MMT8), and Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI). JDM disease activity groups were categorized into treatment-naive (TN; n=8), active (PGA>0.5; n=33), and inactive (PGA=0; n=21). Automated NVC image analysis was performed using Capillary.io, and NVC parameters were quantified per millimeter, including normal, enlarged, tortuous, giant, and abnormal (branched + dysmorphic) capillaries. Differences between groups were analyzed using the Kruskal-Wallis test, longitudinal changes were assessed using the Wilcoxon test, and relationships between NVC parameters and disease activity scores were examined using Spearman's correlation ($p<0.05$ significant).
Results. TN JDM exhibited a higher number of giant capillaries and microhemorrhages as compared to inactive JDM, suggesting potential for improvement in these NVC parameters with treatment. Interestingly, TN JDM exhibited less tortuous capillaries compared to both active and inactive JDM, perhaps due to capillary changes in JDM over time. Capillary density, enlarged capillaries, and abnormal capillary morphologies did not differ between disease activity groups. Tortuosity associated with PGA ($r=-0.48$, $p<0.001$), CDASI activity ($r= -0.28$, $p=0.04$), and MMT8 ($r=0.34$, $p=0.02$). Abnormal capillary morphology also correlated with all disease activity measures, including PGA ($r=0.28$, $p=0.03$), CDASI ($r=0.33$, $p=0.01$), and MMT8 ($r= -0.30$, $p=0.03$). Microhemorrhages associated with PGA ($r=0.37$, $p=0.003$), and giant capillaries associated with CDASI activity ($r=0.51$, $p<0.001$). In the longitudinal JDM cohort (n=16), PGA improved from baseline to 6 months, reflecting clinical improvement. Capillary density and abnormal morphology also improved over this period, highlighting that these NVC parameters are changeable in JDM.
Conclusions. Distinct NVC parameters reflect TN, active and inactive disease in JDM, with giant capillaries and microhemorrhages defining TN disease. Tortuosity and abnormal capillary morphology associate with global, muscle and skin disease activity in JDM. Improvement in capillary density and morphology parallels clinical improvement, highlighting NVC as a non-invasive imaging biomarker of JDM disease activity.

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ENDOTHELIAL CELL MEDIATORS REFLECTING ANGIOPOIETIN AND INTERFERON PATHWAY ACTIVATION CHARACTERIZE JUVENILE DERMATOMYOSITIS DISEASE ACTIVITY AND AUTOANTIBODY SUBGROUPS

Kirsten Grant[1], Alyssa Rosek[2], Julie Sturza[3], Sophia Matossian[1], Li Chen[1], Chioma Madubata[4], Daniel Barnett[5], Jessica Neely[4], J. Michelle Kahlenberg[2], Pei-Suen Tsou[2], Jessica Turnier[1]
[1]University of Michigan, Division of Pediatric Rheumatology, Ann Arbor, USA, [2]University of Michigan, Division of Rheumatology, Department of Internal Medicine, Ann Arbor, USA, [3]University of Michigan, Department of Pediatrics Biostatistics and Data Management Unit, Ann Arbor, USA, [4]University of California, San Francisco, Division of Rheumatology, Department of Pediatrics, San Francisco, USA, [5]UPMC Children's Hospital of Pittsburgh, Division of Pediatric Rheumatology, Pittsburgh, USA

Background. Juvenile dermatomyositis (JDM) is a heterogenous multisystem autoimmune disease characterized by vasculopathy. This study aimed to evaluate endothelial cell (EC) mediators in JDM plasma and determine their association with disease activity, myositis-specific autoantibodies (MSA) and nailfold videocapillaroscopy (NVC) features.
Methods. Sixteen EC mediators were measured in JDM (n=52) and control (CTL, n=26) plasma using LEGENDplex™ multiplex immunoassays. Disease activity was assessed using the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI), Manual Muscle Testing (MMT-8), and Provider Global Assessment (PGA). Disease activity subgroups were categorized as treatment-naive (TN; n=13), active (PGA>1; n=24), and low disease activity/inactive (PGA≤1; n=15). Fifteen JDM had paired NVC data. Eight TN JDM had EC mediators measured and Total Improvement Score (TIS) calculated at 6-months post-treatment. Kruskal-Wallis test and Spearman's correlation statistical testing were used ($p<0.05$ significant). Tissue and cell-type specific gene expression were examined in JDM single-nucleus muscle (n=6) and single-cell skin (n=12) transcriptomic datasets.
Results. 9/16 EC mediators were increased in JDM *vs*. CTL, including proteins involved in angiogenesis (Tie-2, Ang-2, HGF, VEGF, Ang-1, Tie-1, sFlt-1), cell adhesion (ICAM-1, E-selectin, VCAM-1, PECAM-1), IFN pathway (CXCL10, Gal-9, IL-18), cell death signaling (sTNF-RII), and matrix remodeling (MMP2). CXCL10 and Ang-2 were increased in NXP2+ relative to TIF1g+ JDM. EC mediators commonly elevated in TN and active JDM included CXCL10, Gal-9, and VCAM-1. TN JDM uniquely displayed elevated Ang-2, Tie-1 and sTNF-RII as compared to active and inactive JDM, suggesting increased vascular permeability and cell death signaling at diagnosis. Tie-2 was increased in inactive and active JDM relative to CTL. HGF was only elevated in active JDM. CXCL10, Gal-9, and VCAM-1 associated with global, muscle and skin disease activity, with CXCL10 ($r=0.76$) and Gal-9 ($r=0.65$) showing strongest correlation with PGA. Higher E-selectin was associated with decreased capillary density. Eight TN JDM showed declines in Tie-2, Ang-2, CXCL10, Gal-9, VCAM-1, sTNF-RII, ICAM-1 and VEGF, but only HGF predicted higher TIS at 6-months. Single-cell and tissue-specific analyses revealed increased VEGF and Ang-1 expression in JDM type I and II muscle cells, while PECAM-1 and Ang-2 were elevated in JDM ECs. ECs from JDM skin displayed increased expression for E-selectin, ICAM-1, Tie-2, CXCL10, sTNF-RII, Gal-9, Tie-1 and sFlt-1.
Conclusions. EC mediators differentiate JDM from CTL and correlate with MSA status, disease activity and NVC features. Our findings provide insight into EC mediators activated at different disease stages, with persistently elevated Tie-2 in inactive JDM suggesting ongoing subclinical vasculopathy.

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DAZUKIBART IS EFFECTIVE IN PATIENTS WITH SEVERE JUVENILE DERMATOMYOSITIS REFRACTORY TO BARACITINIB

Bader-Meunier B.[1], Welfringer A.[1], Reumaux H.[2], Carbasse A.[3], Tiriau S.[4], Gitiaux C.[1], Fournier B.[1]
[1]Hôpital Necker, [2]Hôpital Jeanne de Flandre, [3]Hôpital Lapeyronie, [4]Hôpital Enfants-Adolescents

Background. Janus Kinase (JAKi) inhibitors have emerged as a promising treatment for juvenile dermatomyositis (JDM) refractory to conventional first-line treatment but 10-30% of the patients do not respond to this approach. We aim to evaluate the efficacy and safety of Dazukibart, a humanized immunoglobulin G1 neutralizing monoclonal antibody directed specifically against interferon-beta (IFNβ), in juvenile dermatomyositis (JDM) refractory to JAKi.
Methods. We conducted a single-center study of patients with JDM treated by Dazukibart with a follow-up period of at least 6 months. Muscle strength was assessed using the Childhood Myositis Assessment Scale (CMAS, range 0–52) and skin disease activity using the skin Disease Activity Score tool (skin DAS, range 0–9). The interferon (INF) score was calculated based on the expression of a subset of 24 IFN-stimulated genes.
Results. Six patients with JDM refractory to baricitinib were included. All patients had refractory muscle involvement and skin disease. The median age at diagnosis of JDM was 6 years (range, 5–10.5). The median CMAS and skin DAS values were 45 (range, 0–47) and 7 (range, 0–9) respectively. Five patients had myositis-specific antibodies (anti-NXP2: 2, anti-TIF1γ:3). The median time from diagnosis to dazukibart initiation was 64 months (range,4-84). Prior to the introduction of dazukibart, all patients had received one to seven immunosuppressive drugs, including baricitinib

in 6/6 patients. Anti-IFN β therapy was effective in all patients within six months of dazukibart introduction: complete or partial muscle remission were achieved in 4/6 (mean CMAS >48) and 2/6 patients respectively (increase of CMAS from 0 to 29 and from 10 to 20 respectively); complete skin remission (mean DAS skin :0) occurred in 6/6 patients. All patients could withdraw other immunosuppressive drugs. Calcinosis improved in 5/5 patients. The mean daily steroid dose decreased from 0.25 mg/kg (range; 0.2–0.5 mg/kg/d) to 0.17 mg/Kg/j (range; 0.1–0.2) in the four patients who received corticosteroids at initiation of dazukibart. INF score was elevated in all patients at the time (mean value: 34) of treatment initiation and did not normalize (mean value: 30) at 6 months. Herpes zoster and persistent elevation of liver enzymes developed in one patient each.
Conclusions. This small series emphasises that targeting IFNβ is a promising therapeutic strategy for JDM patients, particularly those with severe JDM that is refractory to baricitinib. Short-term tolerance was good. These results need to be validated in prospective studies
Key words: juvenile dermatomyositis, dazukibart

Other

P-7

CLINICAL MEANINGFULNESS AND IMPROVEMENT THRESHOLDS OF MYOSITIS CORE SET MEASURES: ASSOCIATION WITH PATIENT-REPORTED OUTCOMES

Shiri Keret[1], Raisa Lomanto Silva[2], Irada Choudhuri[3], Eugenia Gkiaouraki[4], Tanya Chandra[4], Nantakarn Pongtarakulpanit[4,5], Shreya Sriram[4], Niladri Bhowmick[4], Vaidehi Kothari[4], Kaushik Sreerama Reddy[4,6], Eaman AlHassan[4], Anushka Aggarwal[7], Maha Almackenzie[8], Siamak Moghadam-Kia[4], Chester Oddis[4], Rohit Aggarwal[4]
[1]Bnai-Zion Medical Center, Haifa, Israel, [2]Massachusetts General Hospital, Boston, USA, [3]University of Pittsburgh Medical Center, Pittsburgh, USA, [4]University of Pittsburgh School of Medicine, Pittsburgh, USA, [5]Faculty of Medicine Ramathibodi Hospital, Bangkok, Thailand, [6]Duke University School of Medicine, Durham, USA, [7]Indraprastha Apollo Hospital, New Delhi, India, [8]Medical Cities of the Ministry of the Interior, Riyadh, Saudi Arabia

Background. The six myositis core set measures (CSMs) are widely utilized to assess disease activity in idiopathic inflammatory myopathies (IIM). However, their association with how the patient feels and functions, and the minimal thresholds for clinically meaningful improvement, remain undefined. This study aimed to evaluate the validity, meaningfulness, and minimal clinical thresholds of change in CSMs in relation to symptoms, function, and quality of life in patients with IIM.
Methods. Adults with IIM were enrolled in a 6-month prospective observational study. Monthly data collected included CSMs (patient global assessments, Health Assessment Questionnaire [HAQ] and creatine kinase [CK]) and patient-reported outcome measures (PROMs) such as pain and fatigue (VAS), Short Form-36 (SF-36), and PROMIS-Physical Function (PROMIS-PF). Physician measures, including MMT-8 (scale 0-80), MDAAT, and physician global assessments, were gathered every three months. Baseline and longitudinal associations were evaluated using Spearman correlation and linear mixed models. Responsiveness, effect sizes, and clinically important differences (CIDs) were assessed using patient- and physician-reported change at 6 months as anchors.
Results. Fifty patients (mean age 51.6 ± 14.9, 60% female) were enrolled, including 48% dermatomyositis, 12% polymyositis, 18% necrotizing myopathy, and 22% anti-synthetase syndrome. Most CSMs demonstrated strong baseline and longitudinal associations with key patient- and clinician-reported outcome measures, including pain, fatigue, physical function, and quality of life. CK correlated weakly at baseline but significantly over time with most outcome measures. Patients who improved in absolute percentage change in the CSMs and TIS over 6 months, showed parallel gains in quality of life (PCS, MCS), fatigue (VAS), pain (VAS), and PROMIS-PF. Specifically, greater improvements in patient and physician global assessments, HAQ-DI, and MMT were associated with incremental gains in quality of life and physical function measures, along with reductions in fatigue and pain. In patients who improved based on the patient global impression of change (PtGIC) and physician global impression of change (PhGIC) anchors, significant improvements were observed in physician global disease activity, MMT, HAQ-DI, CK, and extra-muscular disease activity, with moderate to large effect sizes. PtGIC CIDs were 2.1 (physician global), 1.4 (extra-muscular), 1.7 (patient global), 4.2 (MMT), 0.5 (HAQ), and 1475 IU/L (CK). PhGIC demonstrated similar results.
Conclusions. Myositis CSMs showed strong validity and responsiveness, reflecting meaningful changes in patient symptoms, function, and quality of life, and supporting their utility in IIM clinical trials and practice. CIDs were defined for all CSMs, improving their interpretability and application in clinical and research settings.
Key words: myositis, inflammatory myopathies, core set measures

P-14

SERONEGATIVE DERMATOMYOSITIS: DO THE CLINICAL PHENOTYPE AND DISEASE COURSE DIFFER FROM SEROPOSITIVE DERMATOMYOSITIS?

Eleonora Antonelli[1], Irene Peralta Garcia[2], Karin Lodin[2,3], Maria Giovanna Danieli[4], Gianluca Moroncini[1,4], Fabricio Espinosa-Ortega[2,3]
[1]Internal Medicine Recidency Programme, Marche Polytechnic University, Ancona, Italy, [2]Division of Rheumatology, Department of Medicine, Karolinska Institutet, Stockholm, Sweden, [3]Karolinska University Hospital, Department of Gastroenterology, Dermatology and Rheumatology, Stockholm, Sweden, [4]Clinica Medica, Marche University Hospital, Ancona, Italy

Background. Dermatomyositis (DM) belongs to the spectrum of idiopathic inflammatory myopathies (IIM). Autoantibody profile supports diagnosis and can predict organ involvement. However, 30–40% of IIM patients are seronegative. This often leads to diagnostic uncertainty, misdiagnosis, and suboptimal treatment. This study aims to compare clinical features, disease course, and treatment response in patients with seronegative DM to those with seropositive DM, using data from a longitudinal Swedish electronic registry.
Methods. Patients diagnosed with DM between 2003 and 2023 were identified from the SweMyoNet registry, a myositis-specific section of the electronic Swedish Quality of Care Registry (SRQ). Seronegative status was determined by the absence of both myositis-specific (MSA) and myositis-associated (MAA) autoantibodies at diagnosis, tested by Line immunoblot (Euroimmun 16) and anti-HMGCR autoantibodies (ELISA). Demographics, clinical manifestations, and treatment data were collected. Longitudinal disease activity was evaluated with individual core set measures. Response to treatment was assessed by using the 2016 ACR/EULAR Total Improvement Score $(TIS)_1$. Linear mixed models and logistic regression were used to evaluate predictors of disease trajectory and treatment response.
Results. Of 140 DM patients, 20 (14%) were seronegative for both MSA and MAA; among these seronegative 7 (30%) tested postive for ANA. Clinical features were largely similar between groups, though seronegative patients had a lower frequency of shawl sign (p=0.01) and lower ESR (p=0.03) at index date (date of registry inclusion). No significant differences were observed in the longitudinal course of physician global assessment, extramuscular activity or muscle strength between groups. After 1 year of follow-up, seronegative patients tended to have a higher proportion of non-responders (TIS <20) compared to seropositive patients (p=0.06), but this difference was not observed at 3 or 5 years. Having interstitial lung disease (ILD) was independently associated with being responder at 1 and 5 years vs. not having ILD (OR 2.9 and 5.0, respectively).
Conclusions. Our results indicate that seropositive patients with DM had broader cutaneous involvement and higher ESR than seronegative patients at index date suggesting a more intense inflammatory status. ILD emerged as a predictor of response at both 1 and 5 years. Seronegative DM patients exhibited a clinical and therapeutic trajectory broadly similar to seropositive patients, with ILD emerging as an independent predictor of favorable prognosis.
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BRINGING MYOSITIS RESEARCH TO THE COMMUNITY: INSIGHTS FROM A CO-DESIGNED 'RESEARCH ROAD-TRIP'

Althea Doverty[1,2], Kelly Beer[1,2], Ian Cooper[1,2], Annik Panicker[1,2], Nataliya Slater[1,2], Christine Lowe[3], Will Barger[3], John Armstrong[3], Kim Armstrong-Wood[3], Peter Brown[3], Trish Brown[3], Sandra Chapman[3], Peter Critchley[3], Val Dempsey[3], Scott Griffiths[3], Merrilee Needham[1,2,4,5]
[1]Murdoch University, Murdoch, Australia, [2]Perron Institute for Neurological and Translational Science, Perth, Australia, [3]Myositis Association of Australia, Berry, Australia, [4]University of Notre Dame Australia, Fremantle, Australia, [5]Fiona Stanley Hospital, Murdoch, Australia

Background. For people living with rare diseases such as myositis, accessing specialist care, reliable information, and research opportunities can be challenging. The Myositis Discovery Programme (MDP), based in Perth, Western Australia, represents the country's largest myositis research initiative. Funded by a patient bequest and philanthropic support, the MDP has collaborated closely with the Myositis Association Australia (MAA) since 2017 to expand research and education access nationwide. Before the COVID-19 pandemic, the MAA hosted triennial national patient conferences to share research and strengthen community connections. Post-pandemic, health risks and travel costs restricted large in-person gatherings. Within Western Australia, the MDP continued biennial "Research Update Days", but national outreach was limited. To restore national connection and knowledge of myositis research, the MDP and MAA co-designed an innovative patient engagement opportunity: the "Live & Local" Research Roadtrip. This initiative aimed to deliver research updates, clinical information, and research participation opportunities directly to patients across Australia., whilst reinvigorating the national myositis community.
Methods. Conceived in early 2025, the project involved coordinated planning between the MDP and MAA's national and local networks. Locations were selected to include every mainland capital city plus two regional centres, guided by a feasibility survey assessing community interest and preferred locations.
The MAA managed local venue logistics and catering, while the MDP coordinated travel, presentations, and research materials. Each event featured presentations on current myositis research, exercise and wellbeing. Patients were invited to contribute saliva samples for the MDP biobank and to learn about consumer involvement and patient-led research through the MDP Myositis Research Consumer Panel.
Results. Between 25 August and 1 September 2025, seven research update events were delivered in Adelaide, Brisbane, Melbourne, Sydney, Canberra, Bendigo, and the Central Coast. More than 300 people attended, over 100 biobank samples were collected, and 25 local researchers participated through talks or collaborations. Feedback indicated strong appreciation for accessible, community-centred engagement and enthusiasm for future events. For many of the local community groups, the event has stimulated connection and increased participation in regular local meetings.
Conclusions. The "Live & Local" Research Roadtrip successfully energised national engagement between patients, researchers, and clinicians. For rare diseases like myositis, such initiatives are vital for improving health literacy, fostering collaboration, and sustaining a connected, research-active myositis community across Australia
Acknowledgements. The MDP and MAA thank our benefactors, as well as the myositis community in Australia, for supporting these events.
Key words: patient engagement, education, research

P-34

A HUNGARIAN MULTICENTRIC STUDY OF ANTI-MDA5 POSITIVE MYOSITIS PATIENTS

Sándor Mogyoróssy[1], Zoltán Griger[2], Tünde Tarr[2], Éva Zöld[2], György Pfliegler[3], György Nagy[4], Károly Zsolt Mangel[4], Gábor Kumánovics[5], Rita Bakai[5], László Kovács[6], Adrienn Rideg[6], Edit Nagy[7], Orsolya Farkas[8], Sarah Tansley[9], Hui Lu[9], Gabriella Szűcs[1], Szilvia Szamosi[1], Zoltán Szekanecz[1], Levente Bodoki[1]
[1]Department of Rheumatology, Faculty Of Medicine, University of Debrecen, Debrecen, Hungary, Debrecen, Hungary, [2]Division of Clinical Immunology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary, Debrecen, Hungary, [3]Centre of Rare Diseases, Department of Internal Medicine, University of Debrecen, Debrecen, Hungary, Debrecen, Hungary, [4]Department of Rheumatology and Clinical Immunology, Semmelweis University, Budapest, Hungary, Budapest, Hungary, [5]Department of Rheumatology and Immunology, Faculty of Medicine, University of Pécs, Pécs, Hungary, Pécs, Hungary, [6]Department of Rheumatology and Immunology, Albert Szent-Györgyi Medical School, University of Szeged, Szeged, Hungary, Szeged, Hungary, [7]Department of Radiology, University of Debrecen, Debrecen, Hungary, Debrecen, Hungary, [8]Department of Diagnostic Imaging, University of Pécs, Pécs, Hungary, Pécs, Hungary, [9]Department of Pharmacy and Pharmacology, University of Bath, Bath, UK

Background. Clinical presentation of MDA5 antibody positive myositis includes muscle weakness, skin lesions, interstitial lung disease (ILD), arthritis. For laboratory testing of this antibody commercial tests (*e.g.* immunoblot, IB) and gold standard immunoprecipitation (IP) are available. Our first aim was to evaluate prevalence of anti-MDA5 antibody in four immunology centers in Hungary and its association with clinical characteristics and disease course through a retrospective study. Next, we used a cross-sectional study design where we compared antibody-testing results between IB and IP.
Methods. We included in our study myositis patients treated in four Hungarian tertiary rheumatology centers between 2020 and 2023. Relevant clinical information and antibody profiles were collected retrospectively using medical softwares and through EuMyoNet database. All centers used the EUROLINE Autoimmune Inflammatory Myopathies 16 Ag for detecting anti-MDA5. In the second part, we managed to compare the IB results of 10 patients from one center with IP used in Bath, UK.
Results. Anti-MDA5 positivity was detected by IB in 23 patients out of 742 patients, female:male ratio was 1.875:1. According to the classification tree for subgroups of IIM there were 17 DM (73.91%), three amyopathic DM (13.04%), three PM patients (13.04%). In the overlapping cases, we diagnosed three DM patients with rheumatoid arthritis and one PM case with systemic sclerosis. In addition to skin symptoms, arthritis (73.91%) was the most frequent extra-muscular manifestation. Frequency of myocarditis, dysphagia and ILD was 13.04%, 21.74% and 60.87%, respectively, showing strong correlation between anti-MDA5 and lung fibrosis. The most frequent pattern was organizing pneumonia, but nonspecific interstitial pneumonia and usual interstitial pneumonia were also present. Rapidly-progressive ILD was present in two cases. Two patients died because of respiratory failure. Most frequent myositis-associated antibody (MAA) was anti-Ro52 (47.83%). Methylprednisolone was used by every patient, most frequently used immunosuppressants were methotrexate and azathioprine for myositis, mycophenolate mofetil, cyclophosphamide and rituximab for ILD. Laboratory results between IB and IP were comparable but showed a relative discrepancy: IB showed a higher frequency of anti-MDA5 than IP in the tested 10 patients.
Conclusions. Heterogeneous clinical symptoms, mainly muscle, skin, joint, lung complaints were present in anti-MDA5 positive cases. We also highlight the role of anti-Ro52 MAA antibody: according to our results, it can predict the presence of ILD in patients with anti-MDA5 antibody. IB is a reliable method, the results of which are comparable to the results of IP. Patients with this antibody should be evaluated for ILD at diagnosis, followed by long-term monitoring.
Key words: anti-MDA5, ILD, immunoblot, immunoprecipitation

P-44

MATERNAL-FETAL OUTCOMES AND RISK FACTORS IN IDIOPATHIC INFLAMMATORY MYOPATHIES: A PORTUGUESE MULTICENTER STUDY

Ana Rita Lopes[1,2], Ana Teodósio Chícharo[1,3], Raquel Campanilho-Marques[1,2], Catarina Abreu[4], Sara Dias Rodrigues[8], Inês Santos[5], Filipa Paramés[6], Sofia Barreira[1,2], Maria Pulido-Valente[7], Luísa Pinto[2,7], Ana Rita Cruz-Machado[1,2], Susana Capela[1,2]
[1]Rheumatology Department, ULS Santa Maria, Lisbon Academic Medical Center, Lisbon, Portugal, [2]Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal, [3]Rheumatology Department, ULS Algarve, Faro, Portugal, [4]Rheumatology Department, ULS Almada-Seixal, Setúbal, Portugal, [5]Rheumatology Department, ULS Viseu Dão-Lafões, Viseu, Portugal, [6]Clinical Pathology Department, ULS Santa Maria, Lisbon, Lisbon, Portugal, [7]Obstetrics, Gynaecology, and Reproductive Medicine Department, ULS Santa Maria, Lisbon, Portugal, [8]Rheumatology Department, ULS Lisboa Ocidental, Lisbon, Portugal

Introduction. Idiopathic inflammatory myopathies (IIM) are rare autoimmune diseases that may complicate pregnancy, but evidence remains scarce. Disease activity at conception and during gestation, together with autoantibody profiles, are considered major determinants of adverse pregnancy outcomes (APOs).

Methods. We conducted a retrospective multicenter study of 12 pregnancies in 10 women with IIM followed at four Portuguese tertiary centres (2009–2025). Demographic, clinical, immunological, therapeutic, maternal, and perinatal data were collected from medical records. Disease activity was assessed by clinical features, laboratory data, modified skin Disease Activity Score, and Manual Muscle Testing-8.
Results. Phenotypes included overlap myositis (n=4), antisynthetase syndrome (n=3), dermatomyositis (n=3), immune-mediated necrotising myopathy (n=1), and polymyositis (n=1). Myositis-specific/associated autoantibodies were detected in 91.7% of the cases, most frequently anti-Ro52 and anti-Jo-1. Disease remission at conception was documented in 9 pregnancies (75.0%). Overall, APOs occurred in 6 pregnancies (50.0%): 4 miscarriages, 1 stillbirth, and 1 fetal growth restriction (FGR) with a small-for-gestational-age neonate. All APOs occurred in pregnancies with disease flares, none occurred when disease remained stable. Among pregnancies with known preconception status, APOs were universal when conception occurred under active disease (3/3) and frequent despite remission (3/7). The most severe outcomes (stillbirth, FGR) occurred in one mother with antisynthetase syndrome and markedly elevated anti-Jo-1 titres. No cases of preeclampsia, eclampsia, congenital anomalies, or neonatal lupus were observed.
Discussion. Pregnancy in IIM carries a high risk of APOs, predominantly driven by disease activity. While remission at conception reduces risk, it does not eliminate it. Anti-Jo-1 positivity may help flag higher-risk pregnancies, warrating intensified surveillance. Multidisciplinary care, preconception counselling, and vigilant monitoring remain crucial, and integration of national series into multicenter registries is essential to refine risk stratification and management in this rare but high-risk population.
Key words: idiopathic inflammatory myopathies, pregnancy outcomes, maternal-fetal outcomes, autoantibodies

P-50

SAFETY AND EFFICACY OF STATIN THERAPY IN PATIENTS WITH DYSLIPIDEMIA AND IDIOPATHIC INFLAMMATORY MYOPATHIES

Marina Lamas Figueredo[1], Matheus Alves Amaral de Lima[1], Rafaella do Amaral Barbosa[1], Samuel Katsuyuki Shinjo[1]
[1]Faculdade De Medicina FMUSP, Universidade De Sao Paulo, Sao Paulo, Brazil

Background. Dyslipidemia is a frequent comorbidity in idiopathic inflammatory myopathies (IIM), contributing to increased cardiovascular risk. Although statins are widely used in the general population, evidence regarding their safety in IIM is limited due to potential myotoxicity. This study aimed to evaluate the safety and lipid-lowering efficacy of statin therapy in patients with IIM.
Methods. In this longitudinal cohort study (January 2020 - October 2025), 18 of 240 IIM patients with severe dyslipidemia received lipid-lowering therapy. Demographics, clinical characteristics, comorbidities, immunosuppressive regimens, statin type and dose, and adjunctive therapies were recorded. Disease activity was assessed using the IMACS core set (MMT-8, HAQ, MYOACT, physician and patient global VAS scores, and muscle enzyme levels). Lipid profiles were evaluated at baseline and during follow-up.
Results. The median age was 58.6 years (IQR 48.3-62.0); 83.3% were female and 66.7% White. The median disease duration was 4.9 years (3.4-10.9). Diagnoses included seven dermatomyositis (one with anti-TIF1-γ, two with anti-MDA-5), three clinically amyopathic dermatomyositis (one with anti-MDA-5), and eight anti-synthetase syndrome (all with anti-Jo-1). The median body mass index was 30.4kg/m² (25.4-33.6). Comorbidities included hypertension (n=15), diabetes mellitus (n=5), prior myocardial infarction (n=2), stroke (n=2), and family history of cardiovascular disease (n=4). Fourteen patients received atorvastatin (10-80mg/day), three simvastatin (20mg/day), and one rosuvastatin (20mg/day); three patients received ciprofibrate and two ezetimibe adjunctively. Median statin exposure was 3.0 years (2.4-3.5). Concomitant immunosuppressive therapy included azathioprine (33.3%), methotrexate (16.7%), cyclosporine (11.1%), leflunomide (11.1%), rituximab (22.2%), tofacitinib (5.6%), and prednisone (33.3%; median dose 10mg/day, IQR 10-18). Disease activity remained stable (median MMT-8: 80 [80-80]; HAQ: 0.75 [0.38-1.53]; MYOACT: 0.0 [0.0-2.0]; physician's VAS: 0.0 [0.5–2.2]; patients' VAS: 2.0 [0.3-4.0]). Muscle enzymes were within normal limits (CPK: 103U/L [53-109]; LDH: 240U/L [204-296]; AST: 22U/L [19-25]; ALT: 20U/L [17-22]). Statin therapy significantly improved lipid profiles: total median cholesterol 254(204-304)→184(160-189)mg/dL, HDL 47(35-51)→53(48-61)mg/dL, LDL 176(147-216)→114(104-129)mg/dL, triglycerides 195(165-265)→117(97-178)mg/dL (all p<0.001).
Conclusions. In this cohort, statin therapy was well tolerated and effective in improving lipid profiles without affecting IIM disease activity. These findings support the feasibility of lipid-lowering management in IIM and highlight the need for larger, prospective studies.
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Key words: dyslipidemia, inflammatory myopathies, statins, treatment

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P-52

A LONGITUDINAL COHORT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES WITH A MUSCLE BIOPSY REPOSITORY AND A SERUM BIOBANK

Andrea Kemp[1,2], Myositis Research Group[1,2,3], Maryam Dastmalchi[1,3], Ingrid E. Lundberg[1,2,3]
[1]Department of Medicine, Karolinska Institutet, Stockholm, Sweden, [2]Center for Molecular Medicine, Stockholm, Sweden, [3]Department of Gastro, Dermatology and Rheumatology, Karolinska University Hospital, Stockholm, Sweden

Background. For over 40 years, a collaboration between the Karolinska Institutet and Karolinska University Hospital has enabled systematic collection of muscle biopsies from patients with suspected idiopathic inflammatory myopathies (IIM) for research. This research repository of muscle biopsies is located at the Center for Molecular Medicine, Division of Rheumatology, Karolinska Institutet. The repository has been priceless in establishing a national muscle biopsy cohort, which has become a valuable resource for both clinical and translational research in myositis. The cohort can help us understand different disease subtypes, autoantibody profiles, and longitudinal changes, aiding development of personalized treatment strategies.
Methods. A muscle biopsy registry was built using FileMakerPro-17 Advanced to document muscle biopsies collected at Karolinska University Hospital. Sampling is ongoing, with the earliest research samples dating back to 1982. Data analysis was performed in R to identify patients with confirmed IIM. The diagnosis of IIM was made according to the 2017 ACR/EULAR criteria. Patients were further classified into antisynthetase syndrome (ASyS), immune-mediated necrotizing myopathy (IMNM), dermatomyositis (DM), and inclusion body myositis (IBM). Connors' criteria was used for ASyS, the ENMC criteria for IMNM, the 2018 for DM and the 2011 for IBM. Further data cleaning was performed, including removal of duplicates, samples from patients who withdrew consent, and thawed and/or discarded biopsies.
Results. After exclusions, the cohort includes 840 biopsies from 606 patients with confirmed IIM. Most patients contributed one (68.2%) or two (27.2%) biopsies, while a smaller number of individuals had three biopsies (3.5%). A handful of patients contributed >3 biopsies.
The cohort includes patients with DM (26.9%), PM (20.5%), AsyS (12.9%), IBM (9.1%), and IMNM (7.4%). The remaining 23.3% represent overlaps between these subtypes or other autoimmune diseases.
When the autoantibody status was analyzed, the most common MSAs were anti-Jo-1(17.8%), anti-HMGCR (12.0%), and anti-TIF-1g (9.9%). MAA were found in 17.5% of patients and 14.9% were seronegative. The remaining 27.9% display other combinations of MSAs (with or without MAA and/or MSA) or have unknown serological profile.
Conclusions. This muscle biopsy repository including follow-up biopsies represents a diverse population of IIM patients, with detailed clinical longitudinal data and serum samples, opening the possibilities for further studies of disease mechanisms, biomarkers, and treatment response.
Acknowledgements. All patients for donating their samples and actively taking part in research. We thank Julia Norkko, Lucymary Okechukwu and Christina Ottosson. Myositis Research Group: Alexanderson H, Andreasson K, Argyriou.A, Dani L, Demirdal D, Dihkan A, Ekholm L, Espinosa-Ortega. F, Ferreira B.H, Galesic M, Galindo-Feria A, Peralta I, Gerhardson I, Gheorghe K, Horuluoglu B, Jonsson L, Lindroos E, Lodin K, Luo Y-B, Nakazawa M, Notarnicola A, Rostvall G, Sandlund H, Gompel E.V.

Key words: myositis, muscle biopsy cohort, idiopathic inflammatory myopathies (IIM), autoantibodies, translational research

P-54

COGNITIVE DYSFUNCTION IN MYOSITIS: AN UNDER-RECOGNIZED CLINICAL PHENOTYPE AND ASSOCIATED FACTORS

Mustafa Ekici[1], Mustafa Levent[2], Levent Kılıç[1], Burcu Balam Doğu[2]
[1]Hacettepe University Rheumatology Department, Ankara, Turkey, [2]Hacettepe University Geriatrics Department, Ankara, Turkey

Background. Cognitive dysfunction (CD) is common in autoimmune diseases, particularly SLE, RA, MS, and autoimmune encephalitis, and varies by disease type, duration, and severity (1). Data on cognition in myositis are scarce; therefore, we assessed cognitive function and examined the associated clinical factors.
Methods. This cross-sectional study enrolled adult patients with IIM who were followed up at the Hacettepe University Rheumatology Clinic between July 1, 2024, and January 1, 2025. All participants underwent a comprehensive assessment. Cognitive function was assessed using the Mini-Mental State Examination(MMSE); depressive symptoms using the Geriatric Depression Scale (Yesavage); sarcopenia using handgrip dynamometry, SARC-F, and gait speed tests; functional status using the Katz Index of Independence in Activities of Daily Living and the Lawton-Brody Instrumental Activities of Daily Living scale; nutritional status using the Mini Nutritional Assessment-Short Form (MNA-SF); and urinary incontinence using the International Consultation on Incontinence Questionnaire-Short Form (ICIQ-SF).
Results. Thirty-four patients were included; 25(73.5%) were women, with a mean age of 44.4±17.4 years. CD (MMSE ≤24) was identified in 16 (47.1%). Compared with cognitively intact patients, those with impairment were older, had lower educational attainment, and had more children. They had higher CRP and CK levels, lower Katz ADL independence scores, and more frequent urinary incontinence and falls. Poorer physical performance (slower gait speed and longer chair-stand times) was associated with lower MMSE scores. The use of ACE inhibitors, β-blockers, and aspirin was also more common in the CD group.
Univariate analyses showed significant associations of CD with lower education(OR 0.02, 95% CI 0.002–0.29; p=0.004), higher number of children(OR 2.08, 95% CI 1.14–3.80; p=0.01), elevated CRP(OR 1.38, 95% CI 1.02–1.87; p=0.03), depressive symptoms (OR 18.7, 95% CI 1.56–222.9; p=0.02), history of falls(OR 8.33, 95% CI 1.68–41.28; p=0.009), urinary incontinence(OR 21.9, 95% CI 2.31–206.5; p=0.007), and impaired physical performance – slower gait speed (OR 2.9, 95% CI 0.97–8.52; p=0.05) and longer five-times-sit-to-stand time(OR 1.30, 95% CI 1.02–1.66; p=0.03). In the multivariable analysis, only history of falls remained independently associated (OR 10.5, 95% CI 1.22–89.3; p=0.03).
Conclusions. In this cohort, approximately half of the patients with myositis exhibited cognitive dysfunction. Lower educational attainment, depressive symptoms, history of falls, and impaired physical performance were associated with cognitive involvement. However, in the multivariate analysis, only the history of falls remained an independent risk factor. These findings support the incorporation of routine cognitive assessments into the clinical evaluation of myositis to inform risk stratification and comprehensive care.
Key words: idiopathic inflammatory myopathies, cognitive dysfunction, urinary incontinence

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P-62

A PROSPECTIVE STUDY UNVEILS DAMAGE ACCRUAL AND MYOSITIS SPECIFIC ANTIBODIES AS KEY RISK FACTORS FOR MORTALITY IN MYOSITIS

Agustin Hernández-López[1], Nancy R. Mejía-Domínguez[1,2], Yatzil Reyna-Juárez[1], Jennifer T. Balderas-Miranda[1], Beatriz Alcalá-Carmona[1], María José Ostos-Prado[1], Carlos A. Núñez-Álvarez[1], Marta E. Baños-Laredo[1], Diana Gómez-Martín[1], Jiram Torres-Ruiz[1]
[1]Instituto Nacional De Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [2]Red de Apoyo a la Investigación, Universidad Nacional Autónoma de México, Mexico City, Mexico

Background. Idiopathic inflammatory myopathies (IIM) are a group of autoimmune diseases characterized by muscular inflammation that can affect any organ or system. Reported mortality rates are as high as 23–73% due to delayed diagnosis, cardiac and pulmonary involvement, or severe muscle weakness, as well as associated infections and neoplasia. Leading mortality causes vary globally according to different cohorts.
Methods. We recruited 219 IIM patients according to ACR/EULAR or Connors' criteria. At recruitment (baseline), we assessed clinical features, muscle enzymes, myositis disease activity assessment tool (MDAAT), myositis damage index (MDI), health assessment questionnaire disability index, manual muscle test 8 (MMT8), visual analog scale (VAS) of disease activity by the patient and physician and myositis specific and associated antibodies by Line-blot. All patients were followed up prospectively looking for the primary outcome, which was mortality. To assess independent predictors of mortality, we performed multivariate logistic regression and Cox analyses to calculate odds and hazard ratios with 95% confidence interval.
Results. 164 patients were women (74.8%), the most frequent diagnosis was dermatomyositis (n= 157, 71.6%). After a median follow-up of 62 months, 32 patients (14.6%) died. At baseline, patients who died were older at recruitment (47(39-52) *vs*. 41(31-52), p=0.04), had more frequently positive anti-SRP (12.5% *vs*. 1.6%, p=0.009), anti-MDA5 (28.1% vs. 11.7%, p=0.024), cancer (15.6% *vs*. 3.7%, p=0.018), lower serum albumin levels (2.9(2.5-3.6) vs. 3.9(3.3-4.2), p<0.0001), higher median (min-max) of VAS of gastrointestinal (GI) (0 (0-10) vs. 0 (0-7), p=0.0003) and cardiovascular (CV) (0 (0-10) vs. 0 (0-6), p=0.04) damage. Independent mortalip = 0.038), malignancy (6.5 (1.20-33.43), p=0.006), albumin (0.26 (0.12-0.51), p<0.0001), VAS of GI damage (1.41 (1.12-1.81, p=0.006), and VAS of CV damage (2.01 (1.38-3.43), p=0.0001). After Cox analysis, we found the following risk factors for mortality: SRP+ (hazard ratio 19.8 (95% CI 5.52-71.0), p<0.001), MDA5+ (4.92 (1.89-12.8), p=0.001), age at recruitment (1.05 (1.01-1.09), p=0.011), smoking (3.21 (1.35-7.66), p=0.009), physician's VAS of disease activity (1.27 (1.05-1.53), p=0.015), albumin (0.33 (0.17-0.66), p=0.002), aspartate aminotransferase (1.00 (1.00-1.00), p<0.001), VAS of CV damage (1.76 (1.37-2.24), p<0.001), infectious damage (1.25 (1.09-1.43), p=0.002) and malignancy damage (1.41 (1.17-1.70), p<0.001). Figure 1, graphical representation of the effect of each risk factor of mortality. Figure 2, hazard ratios for mortality in patients with IIM.
Conclusions. Anti SRP and MDA5 antibodies and GI, CV, infectious and malignancy damage accrual are key novel risk factors of mortality in IIM.
Acknowledgements. Myositis Treatment and Cohort Salvador Zubirán
Key words: mortality, idiopathic myopathies, epidemiology

P-65

COMPARING THE EFFICACY OF CONVENTIONAL IMMUNOSUPPRESSION AND RITUXIMAB IN ANTI-SRP MYOSITIS: INSIGHTS FROM A TERTIARY CARE CENTRE EXPERIENCE

Abhilasha Manwatkar[1], John Mathew[2], Illiasul Ibad[2], Ajith Sivadasan[2]
[1]All India Institute of Medical Sciences, Nagpur, India, [2]Christian Medical College, Vellore, India

Background. Immune-mediated necrotising myositis (IMNM) is a subgroup of idiopathic inflammatory myopathies (IIMs) characterised by severe myonecrosis and poor recovery despite standard therapy. Anti-signal recognition particle (anti-SRP) myositis is a distinct IMNM subtype with markedly elevated creatine phosphokinase (CPK) levels and predominant proximal muscle weakness, but minimal skin or systemic features. Evidence comparing treatment modalities remains scarce. Rituximab (RTX) has emerged as a potential

therapeutic option, yet comparative data with conventional immunosuppression (cIS) are limited. This study aimed to: a) identify the clinical profile of anti-SRP myopathy, b) determine prognostic factors, and c) compare the efficacy and safety of RTX *vs*. cIS in these patients.
Methods. This was an observational cohort study conducted at a tertiary care centre in India (January 2019–January 2024). Data were extracted from a prospectively maintained myositis registry. Adult patients (>16 years) fulfilling 2017 EULAR/ACR or Bohan and Peter criteria for myositis with confirmed anti-SRP antibody positivity and ≥4 months follow-up were included. Forty patients met inclusion criteria. Clinical, serological, and treatment details were recorded at baseline, 4 months, and 6 months. Patients were grouped as RTX or cIS (mycophenolate mofetil, methotrexate, or cyclophosphamide). Treatment response was classified as improved, stable, or worsening disease. Continuous variables were compared using t-tests; categorical variables with Chi-square or Fisher's exact test. Kaplan-Meier curves were plotted for time-to-improvement and mortality.
Results. The mean age of onset was 44.2 ± 13.1 years, with female predominance (71.4%). Classic IIM rashes were absent, and interstitial lung disease (ILD) was present in 31.4%. No malignancies were observed. Fifteen patients (42.9%) received RTX – eight were treatment-naive and seven refractory to cIS. Twenty (57.1%) received cIS alone. The median follow-up was 12 months (IQR 6–24). Improvement occurred in 73.3% of RTX and 45% of cIS patients (p=0.46). Mean MMT8 improvement at 6 months and steroid-sparing effect were significantly greater with RTX (p=0.001). Mortality was 6.7% in RTX *vs*. 20% in cIS. Predictors of mortality included cardiac involvement (p=0.02) and severe non-ambulatory weakness (p=0.03).
Conclusions. Both RTX and cIS are effective in anti-SRP myositis; however, RTX offers superior steroid-sparing benefit and greater functional recovery. Cardiac involvement and profound muscle weakness predict poorer survival. Larger multicentric studies are warranted to define optimal RTX regimens in IMNM.

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TREATMENT RESPONSE AND LONG-TERM OUTCOMES OF IDIOPATHIC ORBITAL MYOSITIS: 10 YEAR EXPERIENCE FROM TERTIARY CARE CENTRE

Abhilasha Manwatkar[1], John Mathew[2], Illiasul Ibad[2]
[1]All India Institute of Medical Sciences, Nagpur, Nagpur, India, [2]Christian Medical College, Vellore, India

Background. Idiopathic orbital myositis (IOM) is characterised by non-infectious, non-neoplastic space-occupying lesions in the orbit, which leads to a significant threat to vision if left untreated. Chronic IOM cases pose significant diagnostic challenges, and treatment often fails to ameliorate symptoms due to underlying muscle fibre damage. There is scarcity of data regarding treatment and prognosis, due to its rarity. Our aim is to characterise the clinical phenotypes of IOM and to evaluate the effectiveness and safety of various therapeutic strategies.
Methods. Patients diagnosed with IOM between January 2012 to December 2023 were included after ruling out other causes of orbital inflammation. Clinical features, laboratory parameters, imaging and treatment and its response were collected from electronic medical record. Treatment response defined as Complete Remission (CR), Partial Remission (PR) or No Response (NR) as per defined parameters.
Results. Among 10 patients diagnosed with IOM, majority were women (8/10) with mean age of 38.9 (±14.21) years. Demographic features, treatment details, outcome and comparison with different published cohort were summarised in Table 1. Bilateral orbital involvement was seen in seven patients. Six patients received corticosteroid pulse therapy in view of sight threatening involvement followed by oral steroids. Four patients were on steroids initially not on other Immunosuppressants (IS). Two patients who relapsed while tapering steroids were shifted to rituximab (RTX) and the other to mycophenolate mofetil (MMF). Both were in remission at the end of the follow-up period but developed permanent disability in the form of restricted eye movements. On median follow-up of 37.4 months (IQR 12-60). 6/9 had CR, 1/9 had PR.
Conclusions. IOM has variable presentations and often diagnosis is difficult to make. Treatment response with steroids is often excellent, however needs steroid sparing agent to prevent adverse events, relapses and permanent damage.
Key words: idiopathic orbital myositis, treatment response, immunosuppressive response in myositis

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P-73

THE CLINICAL, SEROLOGICAL AND HISTOLOGICAL FEATURES OF MUSCLE DISEASES IN ABORIGINAL AND TORRES-STRAIT ISLANDER PEOPLES IN SOUTH AUSTRALIA

Thomas Khoo[1,2,3], Sarah Saxon[4], Bernice Gutschmidt[4], Jackie Lamshed[5], Kim Morey[1,6], Odette Pearson[1,6], Vidya Limaye[1,2]
[1]Faculty of Health and Medical Sciences, University of Adelaide, Adelaide, Australia, [2]Rheumatology Unit, Royal Adelaide Hospital, Adelaide, Australia, [3]Rheumatology Unit, Southern Adelaide Local Health Network, Adelaide, Australia, [4]Anatomical Pathology, SA Pathology, Adelaide, Australia, [5]Patient Research Partner, Adelaide, Australia, [6]Aboriginal Health Equity Research and Strategy, South Australia Health and Medical Research Institute, Adelaide, Australia

Background. Case reports suggest that Aboriginal and Torres Strait Islander peoples in Australia have worse outcomes from muscle diseases than Australians of other ethnicities. The reasons underpinning this health disparity have not previously been systematically assessed. We aimed to determine the clinical, serological and histological characteristics of muscle diseases in Aboriginal and Torres Strait Islander peoples in South Australia (SA).
Methods. A database of Aboriginal and/or Torres Strait Islander peoples with muscle diseases was established. Cases from SA were retrospectively (01/2021-02/024 from the SA Pathology database, wherein all muscle biopsies in SA are assessed) and prospectively (02/2024-present, from routine clinical encounters within SA public hospitals) identified. Demographic, clinical, laboratory and histological data were recorded.
Results. Twenty-seven patients (63% female, median 53 years [interquartile range, IQR 43.8-59.2]) were identified; 6/27 were prospectively enrolled. Nine were deceased (from infection [6/9], cardiac event [2/9], muscle weakness [1/9]) as of February 2024. Six patients had an urban residence at diagnosis. Immune-mediated necrotising myopathy (IMNM) was the most common diagnosis (11/27). Only one patient was diagnosed with dermatomyositis and one with inclusion body myositis. Four patients had a non-inflammatory diagnosis (rhabdomyolysis). Weakness was present in 23/27 patients with median bilateral manual muscle testing 8 (MMT-8) score at diagnosis of 140/150 (IQR 122-146). Extra-muscular disease was uncommon (rash: 2/27; interstitial lung disease: 4/27).
Amongst patients with IMNM, 10/11 had diabetes mellitus type 2 (T2DM) and 9/11 were statin-exposed; of seven tested for anti-HMGCR, three were positive. No patients had anti-Jo1 but five had a non-Jo1 anti-synthetase antibody (anti-PL7 [2], PL12 [2], EJ [1]) although only one had an overall diagnosis of anti-synthetase syndrome (ASyS). Histologically, 17/23 muscle biopsies showed polyfocal, polyphasic necrosis. Perifascicular atrophy was present in four patients, all of whom had clinical diagnoses of overlap myositis (SLE [2], MCTD [1]) or ASyS. MHC-I upregulation was present in 17/22 of biopsies and MHC-II in 13/22.
Conclusions. In this cohort of Aboriginal peoples with muscle diseases, unique phenotype-antibody-histology associations were observed: (1) IMNM was the most common muscle disease with highly prevalent comorbid T2DM and statin exposure, (2) non-Jo1 antisynthetase antibodies prevailed over anti-Jo1, and ASyS was rare, and (3) perifascicular atrophy was exclusively seen in patients with overlap myositis/ASyS. Investigation in an expanded cohort will help to further determine distinct clinical, serological and histological characteristics of muscle diseases within Aboriginal peoples.
Acknowledgements. We would like to acknowledge the participants in this research and the overseeing governance group guiding this research.
Key words: Aboriginal health research, Ethnic heterogeneity, Immune-mediated necrotising myopathy

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HEART RATE VARIABILITY REFLECTS SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Daniel Zavada[1,2], Sabina Oreska[1,2], Hana Wunsch[1,2], Aneta Prokopcova[1], Jaroslav Kudlicka[3], Vladimir Tuka[3], Ondrej Mikes[3], Zdislava Krupickova[3], Martin Satny[3], Eva Chytilova[3], Jan Kvasnicka[3], Maja Spiritovic[1], Barbora Vala[3], Petr Cesak[4], Marian Rybar[5], Karel Pavelka[1,2], Ladislav Senolt[1,2], Herman Mann[1,2], Jiri Vencovsky[1,2], Michal Vrablik[3], Michal Tomcik[1,2]
[1]Institute of Rheumatology, Prague, Czechia, [2]Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czechia, [3]3rd Department of Internal Medicine, General University Hospital and 1st Faculty of Medicine, Charles University, Prague, Czechia, [4]Faculty of Physical Education and Sport, Charles University, Prague, Czechia, [5]Faculty of Biomedical Engineering, Czech Technical University in Prague, Kladno, Czechia

Background. Reduced heart rate variability (HRV), a non-invasive marker of autonomic nervous system (ANS) function, has been linked to cardiovascular (CV) morbidity and mortality. Patients with idiopathic inflammatory myopathies (IIM) carry increased CV risk often underestimated by routine risk prediction scores. We investigated the relationship between HRV and CV risk parameters.
Methods. We retrospectively analyzed IIM patients (fulfilling the 2017 ACR/EULAR classification criteria, with no manifested CV disease) previously assessed for CV risk, who had a 10-second ECG available within 14 days of risk assessment. For CV risk assessment, we collected the SCORE, SCORE2, modified SCORE (=SCORE×1.5), pulse wave velocity, ankle-brachial index, and ultrasound [CV risk category, carotid intima-media thickness (CIMT), carotid plaque presence and morphology]. HRV was quantified using the root mean square of successive differences (RMSSD), an index reflecting vagal activity. We also collected clinical and laboratory data and explored their associations with HRV.
Results. 30 IIM patients were included [24 female, 6 male; 11 antisynthetase syndrome (ASyS), 9 dermatomyositis (DM), 7 immune-mediated necrotizing myopathy (IMNM), 3 polymyositis (PM)]. Mean±SD age was 55.2 ± 15.3 years, disease duration 3.0 ± 3.8 years.
Overall, baseline RMSSD in IIM was only numerically lower compared to age- and sex-matched published healthy controls [median (IQR) 19.7 (14.2-25.5) *vs*. 22.5 (18.3-29.2), respectively, p=0.12]. In IIM patients, lower vagal activity was independently associated with higher CIMT [log(RMSSD), β= -0.09, 95% CI -0.17 to -0.007, p=0.036], a marker of subclinical atherosclerosis, after adjustment for major cardiovascular risk factors (age, sex, smoking, diabetes, and mean arterial pressure) and disease subtype.
We observed significant correlations between RMSSD and MYOACT (Pearson's r= -0.41, p=0.02), indicating a relationship of lower vagal activity with higher disease activity. Furthermore, lower vagal activity was associated with decreased levels of apolipoprotein A (Pearson's r=0.41, p=0.02).
Conclusions. These findings suggest that reduced vagal activity may represent a marker and possible contributor to CV risk in IIM, a possibility that warrants prospective investigation to confirm and identify causal relationships and whether autonomic modulation could offer a novel avenue for CV risk mitigation in this population.
Acknowledgements. Supported by MHCR023728.
Key words: heart rate variability, cardiovascular risk, idiopathic inflammatory myopathies

P-88

MUSCULAR INVOLVEMENT IN SYSTEMIC SCLEROSIS: HIGH MORTALITY NOT ASSOCIATED WITH NATURE OF HISTOLOGICAL LESIONS

Noémie Le Gouellec[1], Louai Zaidan[2], Benjamin Chaigne[3], Emeline Cailliau[4], Robin Dhote[5], Sébastien Rivière[6], Yurdagül Uzunhan[7], Christian Agard[8], Bertrand Godeau[9], Pierre Wolkenstein[10], Eric Hachulla[11], Luc Mouthon[3], François-Jérôme Authier[2]
[1]Department of Nephrology and Internal Medicine, Valenciennes Hospital, Valenciennes, France, [2]Department of histopathology, Paris Est, Creteil University, Créteil, France, [3]Department of Internal Medicine, Hopital Cochin ,Paris University, Paris, France, [4]Department of Biostatistics, University of Lille, Lille, France, [5]Department of Internal Medicine, Hopital Avicenne, Paris University, Bobigny, France, [6]Department of Internal Medicine, Hopital Saint Antoine, Paris University, Paris, France, [7]Department of Pneumology, Hopital Avicenne, Paris University, Bobigny, France, [8]Department of Internal Medicine, University of Nantes, Nantes, France, [9]Department of Internal Medicine, Paris Est, Creteil University, Créteil, France, [10]Department of Dermatology, Paris Est, Creteil University, Créteil, France, [11]Department of Internal Medicine, University of Lille, Lille, France

Background. The aim of this study was to determine the association between various histological patterns and prognosis in patients with SSc and histologically proven muscle involvement.
Methods. A multicentre retrospective study was conducted of a cohort of scleroderma patients who had undergone muscle biopsy. The biopsies were reviewed in a coordinated manner to classify patients based on the histological findings. Three different patterns were observed: fibrosing myopathy (FMy), inflammatory myopathy (IMy), and immune-mediated necrotizing myopathy (IMNMy). Rates of survival, muscle relapse, and cardiac and pulmonary events were compared between these three groups.
Results. Among the 71 scleroderma patients with muscle biopsy specimens available for review, 33 (46.5%) were classified in the FMy group, 18 (25.5%) in the IMy group and 20 (28%) in the NMy group. The median follow-up time was 6.4years (interquartile range, 2.2–10.9years), and 21 patients died during follow-up, primarily from heart disease and infections. The 10-year survival rate after the first non-RP symptom was 80%, and the cumulative incidence of muscle relapse was 25%. Neither factor differed significantly between the three groups. The risk of pulmonary events was lowest in the IMy group, significantly lower than in the FMy group (hazard ratio, 0.17; 95% CI, 0.04–0.67) and non-significantly lower than in the IMNMy group (hazard ratio, 0.28; 95% CI, 0.06–1.24). The risk of cardiac events did not differ significantly between the three groups.
Conclusions. The mortality rate in scleroderma patients with muscle involvement was not associated with their histological patterns.
Acknowledgements. This research was supported by a grant from L'Association des Sclerodermiques de France (ASF). The "Groupe Francophone de Recherche sur le Sclerodermie (GFRS)" are being acknowledged for passing on the call for observations.
Key words: systemic sclerosis, muscle biopsy, fibrosing myopathy, inflammatory myopathy, immune-mediated necrotizing myopathy, mortality

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P-89

COMPARISON OF ORGAN DAMAGE DEVELOPMENT AND SURVIVAL IN ANTI-SYNTHETASE SYNDROME AND OTHER IDIOPATHIC INFLAMMATORY MYOPATHIES: A RETROSPECTIVE ANALYSIS DECIPHERING DIFFERENT TRAJECTORIES

Ezgi Sahin, Omer Uludag, Yasemin Yalcinkaya, Bahar Artim Esen, Ahmet Gul, Murat Inanc
[1]Istanbul University, Istanbul Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Fatih, Turkey

Background. Our aim was to compare the prognosis of patients with Antisynthetase Syndrome (ASyS) and other idiopathic inflammatory myopathies (OIIM), as ASyS exhibits distinct clinical characteristics that may lead to a different disease course.
Methods. Data of 122 IIM patients fulfilling the Bohan and Peter and 2017 myositis classification criteria, with available myositis-specific antibody results, followed in our clinic between 1991 and 2024, were retrospectively analyzed. Patients were divided into ASyS (defined by positive anti-synthetase antibodies with relevant clinical features) and OIIM groups, and their clinical, laboratory, damage progression, and survival characteristics were compared
Results. Of 122 patients, 35 (28.7%) were classified as ASyS. Females were more frequent in ASyS than OIIM (85.7% *vs*. 59.8%, p=0.011). Median age at diagnosis was 47 and 46 years, respectively, and mean follow-

up was 84.5±77.9 months. Anti–Jo-1, anti–PL-7, and anti–KS were positive in 88.6%, 8.6%, and 2.8% of ASyS patients. Mechanic's hand, arthritis, and ILD were more common in ASyS (11.4%, 51.4%, 68.6%) than OIIM (1.1%, 21.8%, 21.8%) ($p<0.05$), while dysphagia was more frequent in OIIM (37.9% *vs*. 8.6%, p=0.003). Anti-Ro-52 positivity and baseline CRP, leukocyte, and neutrophil levels were higher in ASyS. Median MDI at 6 months was higher in ASyS (3 *vs*. 2, p=0.046). Compared with TIF-1γ–positive patients, ASyS showed greater 6-month damage progression (MDI 3 *vs*. 1.5, p=0.033); ILD predominated in ASyS (72.7% *vs*. 3%, $p<0.001$), while malignancy was more frequent in TIF-1γ (35.3% *vs*. 20%, p=0.045). At last follow-up, MDI and survival did not differ; mortality was 14.3% in ASyS and 14.9% in OIIM.
Conclusions. The ASyS group showed distinct clinical features compared to OIIM. Mechanic's hand, arthritis, and ILD were more common, while dysphagia was less frequent. Baseline inflammatory markers (CRP, leukocyte, neutrophil) and anti-Ro-52 positivity were higher in ASyS. Early organ damage occurred more often in ASyS due to rapid ILD progression. These findings underscore the unique clinical profile and disease trajectory of ASyS, suggesting differences in management strategies among IIM subtypes.
Key words: antisynthetase syndrome, idiopathic inflammatory myopathies, interstitial lung disease, prognosis, Myositis Damage Index

P-103

IDIOPATHIC INFLAMMATORY MYOPATHIES IN PERU: A SCOPING REVIEW OF PUBLISHED LITERATURE

Yelitza Velarde-Mejia[1]
[1]Essalud, Arequipa, Perú, [2]San Agustin National University, Arequipa, Perú

Background. Idiopathic inflammatory myopathies (IIM) comprise a heterogeneous group of autoimmune diseases characterized by chronic muscle inflammation and variable systemic involvement. While increasing attention has been given globally to IIM through international consortia such as the Myositis Clinical Trial Consortium (MCTC), research output from Latin America – and particularly from Peru – remains limited and fragmented. This scoping review aims to map existing Peruvian evidence on IIM to identify key clinical, epidemiological, and methodological gaps that may guide future collaborative studies.
Methods. We performed a systematic search of PubMed, Scielo, LILACS, Google Scholar, and local Peruvian academic repositories from January 2010 to October 2025. Search terms included "myositis," "polymyositis," "dermatomyositis," "antisynthetase syndrome," and "inflammatory myopathy," combined with "Perú." Studies were included if they involved Peruvian patients or were conducted by Peruvian institutions. Two reviewers independently screened titles, abstracts, and full texts. Data were extracted regarding study design, sample size, IIM subtype, major findings, and research focus.
Results. The search yielded 22 records; 17 met inclusion criteria. Most publications were case reports (82,35%). Dermatomyositis was the most frequently described subtype (70.58%), Two observational, retrospective studies and one observational cross-sectional study based on an international registry were identified. Six studies explored autoantibody profiles, and none addressed standardized disease-activity or remission definitions. Multidisciplinary management approaches were inconsistently reported, and none pediatric or inclusion body myositis cases were documented. Overall, Peruvian research on IIM remains scarce, hospital-based, and largely descriptive, highlighting an urgent need for coordinated multicenter efforts.
Conclusions. Published data on IIM in Peru are limited, reflecting underrecognition of these diseases and restricted access to diagnostic and research resources. Establishing a national or regional registry and integrating Peruvian investigators into international networks such as MCTC could enable standardized data collection, improve patient care, and foster regional representation in global myositis research.
Key words: idiopathic inflammatory myopathies, Perú, scoping review

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DYSPHAGIA HAS A MAJOR IMPACT ON QUALITY OF LIFE IN IDIOPATHIC INFLAMMATORY MYOPATHIES – A PATIENT-REPORTED CROSS-SECTIONAL STUDY

Fulden Sari[1,2], Ingrid Gerhardson[3], Helene Alexanderson[1,4]
[1]Divison of Rheumatology, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden, [2]Department of Physiotherapy and Rehabilitation, Faculty of Physical Therapy and Rehabilitation, Bingol University, Bingol, Turkey, [3]Medical Unit Dermatology, Gastroentology, Rheumatology, Karolinska University Hospital, Stockholm, Sweden, [4]Medical Unit Allied Health Professionals, Karolinska University Hospital, Stockholm, Sweden

Background. Dysphagia is a clinically significant but often underestimated feature of idiopathic inflammatory myopathies (IIM), associated with aspiration risk, malnutrition, reduced quality of life (QoL), and poorer prognosis. Despite its importance, the influence of dysphagia severity on functional and health-related outcomes in IIM remains unclear. This study investigated the impact of dysphagia severity on swallowing-related and general quality of life in patients with IIM.
Methods. This cross-sectional study included 163 IIM patients. Swallowing difficulty, swallowing-related QoL, and general health-related QoL were evaluated using the EAT-10, SWAL-QOL, and RAND-36 scales, respectively. Dysphagia classification was based on the EAT-10, with scores ≥3 indicating clinically significant dysphagia and scores <3 considered normal swallowing function. Group comparisons were performed using non-parametric tests, and the associations between dysphagia severity and QoL measures were analyzed using Spearman correlation and linear regression models ($p<0.05$).
Result: Participants had a mean age of 70.3±12.0 years, 56% were female, and the median disease duration was 4.5 (2–9 years). Dysphagia was present in 27.6%, while 72.4% of patients had normal swallowing function. 24.5% of patients were receiving corticosteroids, 9.8% were on DMARD therapy, and 3% were additionally treated with other immunosuppressive agents. Dermatomyositis (29.4%) and polymyositis (44.8%) were the most prevalent IIM subtypes, followed by inclusion body myositis (6.7%) and antisynthetase syndrome (6.7%). Compared to non-dysphagic individuals, patients with dysphagia showed significantly lower SWAL-QOL and RAND-36 scores (all $p<0.001$), indicating marked impairments in both swallowing-specific and general QoL. EAT-10 demonstrated a strong negative correlation with swallowing-related QoL ($r\approx-0.80$; $p<0.001$) and a moderate negative correlation with general health-related QoL domains ($r\approx-0.60$; $p<0.001$), indicating that increasing dysphagia severity is associated with substantial reductions in functional well-being. Linear regression analyses revealed that dysphagia severity significantly predicted reductions across all SWAL-QOL subscales (all $p<0.001$). The strongest impairments were observed in general burden ($R^2=0.655$; $F=287.99$; $p<0.001$), mental health ($R^2=0.614$; $F=231.91$; $p<0.001$), and fear of eating ($R^2=0.538$; $F=181.95$; $p<0.001$). In terms of overall health outcomes, EAT-10 significantly predicted RAND-36 physical health ($R^2=0.200$, $F=32.69$; $p<0.001$), demonstrating that dysphagia also limits broader physical functioning. Durbin-Watson values (1.592–2.255) confirmed the absence of autocorrelation, supporting model validity.
Conclusions. Dysphagia severity is a key determinant of both swallowing-specific and overall health-related QoL in IIM patients. These findings emphasize the importance of routine screening and early multidisciplinary management of dysphagia to prevent further functional decline and improve patient outcomes
Key words: myositis, dysphagia, quality of life

P-114

GAPS IN TRAINING AND EXPERTISE IN MYOSITIS OUTCOME MEASURES: INSIGHTS FROM THE MCTC INVESTIGATOR SURVEY

Shiri Keret[1], Kaushik Sreerama Reddy[2,3], Iris Yan Ki Tang[4], Akira Yoshida[5], Rachid Smaili[6], Eduardo Dourado[7,8,9], Océane Landon-Cardinal[10], Jennifer Ben Shimol[11], Raisa Lomanto Silva[12], Kendrea L. (Focht) Garand[13], Julián Barahona-Correa[14], Kathryn Cook[15], Kristin Houghton[16], Ana Valle[17], Chester V. Oddis[2], Jiří Vencovský[18], Masataka Kuwana[5], Rohit Aggarwal[2], Prateek C. Gandiga[19]
[1]Bnai Zion Medical Center, Haifa, Israel, [2]Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, USA, [3]Division of Infectious Diseases and International Health, Duke University School of Medicine,

Durham, USA, [4]Division of Rheumatology and Clinical Immunology, Department of Medicine, The University of Hong Kong, Hong Kong, Hong Kong, [5]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [6]Division of Rheumatology, Internal Medicine and Clinical Immunology, Regional University Hospital My Ali Cherif, Errachidia, Morocco, [7]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal., [8]Aveiro Rheumatology Research Centre, Egas Moniz Health Alliance, Aveiro, Portugal, [9]Rheumatology Research Unit, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal, [10]Division of Rheumatology, Centre Hospitalier de l'Université de Montréal, Montréal, Canada, [11]Division of Rheumatology, Barzilai Medical Center, Ashqelon, Israel, [12]Department of Rheumatology, Allergy & Immunology, Massachusetts General Hospital, Boston, USA, [13]Department of Communication Science and Disorders, University of Pittsburgh, Pittsburgh, USA, [14]Department of Immunology and Rheumatology, Stanford University, CA, USA, [15]Division of Pediatric Rheumatology, Akron Children's Hospital, Akron, USA, [16]Department of Pediatrics, Division of Rheumatology, University of British Columbia, Vancouver, Canada, [17]Brigham and Women's Hospital, Harvard Medical School, Boston, USA, [18]Institute of Rheumatology and Department of Rheumatology, 1st Medical Faculty, Charles University, Prague, Czech Republic., [19]Division of Rheumatology, Emory University, Atlanta, USA

Background. The Myositis Clinical Trials Consortium (MCTC) is an international collaboration of clinical investigators, research professionals, patient partners, and industry stakeholders dedicated to advancing clinical trials in idiopathic inflammatory myopathies (IIM). Consistency in performance of standardized outcome measures is essential for reliable assessment in trials, yet the extent of clinical experience and expertise in IIM-specific outcome measures among myositis investigators is not well defined. This study aims to identify gaps in training, certification, and self-reported expertise with myositis outcome measures among IIM investigators.
Methods. The MCTC Investigator Survey was distributed globally to IIM-focused physicians through professional societies, peer networks, and MCTC membership. The survey collected information on professional background, clinical and research experience, and self-reported training or certification in myositis outcome measures. Respondents rated their expertise on a 5-point Likert scale, ranging from "no experience" to "certified", the latter indicating completion of formal training.
Results. A total of 527 investigators responded, representing diverse regions, education, and subspecialties. The majority were affiliated with academic medical centres or hospitals (60.0%). Rheumatology was the most common specialty (74.2%), followed by pulmonology (8.7%), neurology (6.6%), and dermatology (5.5%). Most physicians treated adults (78.6%), while 8.9% were paediatric specialists and 8.9% managed both populations. Investigators reported extensive clinical research experience, with a median (IQR) of 10.0 (5.0-18.0) years in general research and 8.0 (4.0-15.0) years in IIM, with a median of 3.0 (1.0-5.0) myositis research studies and 1.0 (0-2.0) interventional trials in the past five years. Only 22.2% had completed myositis-specific training.
Notable gaps emerged between clinical experience and self-reported expertise in outcome measures. For Manual Muscle Testing (MMT-8 or MMT-9), only 17.9% were certified, while 51.8% reported limited or no experience. For the Total Improvement Score, as defined in the 2016 EULAR/ACR Myositis Response Criteria and used for most myositis clinical trials, 59.6% had limited or no experience, and only 9.6% were certified. For the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI), 60.4% reported limited or no experience. Among physicians managing paediatric patients (n=94), 64.9% and 74.5% reported limited or no experience with Childhood Myositis Assessment Scale (CMAS) and Juvenile Dermatomyositis Activity Index (JDMAI), respectively.
Conclusions. The MCTC Investigator Survey highlights substantial gaps in training and certification related to standardized myositis outcome measures, even among experienced investigators. Strengthening structured training and certification programs will be critical to improve clinical trial readiness, ensure reliable outcome assessment, and advance harmonized research in IIM.
Acknowledgements. Myositis Clinical Trials Consortium (MCTC)
Key words: idiopathic inflammatory myopathies, myositis, outcome measure

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FATIGUE IMPACTS THE QUALITY OF LIFE OF PATIENTS WITH MYOSITIS, REGARDLESS OF AGE, SEX, AND MUSCLE STRENGTH

Maria Diana Pascoal[1,2], Catarina Rebelo Silva[1,2], Graça Costa[1,2], António Fernandes[3], Eduardo Dourado[1,2]
[1]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal, [2]Aveiro Rheumatology Research Centre, Centro Académico Clínico Egas Moniz Health Alliance, Universidade de Aveiro, Aveiro, Portugal, [3]Aveiro Myositis Clinic patient partner, Aveiro, Portugal

Background. Idiopathic inflammatory myopathies (IIM) are rare autoimmune diseases featuring muscle weakness and systemic involvement, reducing quality of life (QoL). Fatigue, a central symptom, is frequently neglected in clinical studies. We aimed to assess the impact of fatigue on the QoL of IIM patients.
Methods. We did a retrospective analysis of prospectively and longitudinally collected data from a single-center specialized IIM clinic. QoL was assessed using the Short Form Health Survey (SF-36) - divided into 8 subdomains compiled in two components - physical (PCS) and mental (MCS). SF-36 variates from 0 to 100, with higher scores indicating better health. Fatigue was assessed using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) questionnaire. Total FACIT-F scores range from 0 to 52, with a higher score indicating less fatigue. Muscle strength was evaluated using Manual Muscle Testing of a Subset of Eight Muscles (MMT8). Spearman's rank-order correlation was used to assess the associations between FACIT-F and other outcome measures. Several linear mixed models were created using the SF-36 subdomains as the dependent (outcome) variables, and the FACIT-F score, MMT8, sex, and age as independent variables.
Results. A total of 28 patients were included, 68% women, median age 62 (IQR 19) years, median 8 (IQR 14) years of disease duration at their first SF-36 assessment. Each patient had a median of 2 (IQR 2) evaluations (total of 61 assessments). The median time between assessments was 6 (IQR 3) months. Most (62%) patients had fatigue that the assisting physician interpreted as a manifestation of their disease. The median SF-36 PCS was 37.8 (IQR 15.2) and MCS 48.4 (IQR 11.6). The median FACIT-F was 33 (IQR 15). Fatigue was inversely correlated with physical ($r=0.766$, $p<0.001$) and mental ($r=0.652$, $p<0.001$) health, as well as with all SF-36 subdomains ($p\leq0.001$ for all subdomains). Moreover, fatigue had a statistically significant influence on both physical ($p<0.001$) and mental ($p<0.001$) health, as well as on all SF-36 domains ($p<0.001$ on all domains), irrespective of age, sex, and muscle strength. For each unit of increase in the FACIT-F score, PCS increased by 0.6 and MCS by 0.5. All sensitivity analyses were consistent with the main results regarding the relationship between fatigue and QoL.
Conclusions. Fatigue significantly impairs physical and mental QoL in IIM patients, regardless of demographic factors or muscle strength. These findings highlight the need to include fatigue as a core outcome in IIM clinical trials, unveiling possible interventions to improve QoL.
Key words: myositis, fatigue, quality of life, patient-reported outcomes

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SYSTEMIC SCLEROSIS-ASSOCIATED FIBROSING MYOPATHY: A DISTINCT ENTITY WITH HIGH MORTALITY

Shane Cameron[2], Payam Mohassel[1], Fred Wigley[1], Ami Shah[1], Laura Hummers[1], Julie Paik[1]
[1]Johns Hopkins University, Baltimore, USA, [2]University of Mannitoba, Canada

Background. Systemic sclerosis (SSc) is a multisystem autoimmune disease in which muscle involvement is common and contributes to morbidity and mortality. Histopathologic subsets of SSc-associated myopathy have been described, including inflammatory, necrotic, fibrotic, and neurogenic forms. Fibrosing myopathy is increasingly recognized as a distinct subset, but long-term outcomes remain poorly defined. We aimed to characterize the clinical features, treatment response, and mortality of patients with SSc-associated fibrosing myopathy.
Methods. Patients enrolled in a large North American Cohort (1990–2023) with muscle biopsy evidence of fibrosing myopathy confirmed by neuromuscular pathology review were included. Demographics, systemic features, muscle involvement, treatments, and outcomes were abstracted. Muscle dis-

ease was assessed by serum creatine kinase (CK) and aldolase, electromyography (EMG), muscle magnetic resonance imaging (MRI), and histopathology. Treatment response was determined by clinician assessment of muscle strength and handheld dynamometry when available, at 6–12 months after therapy initiation.
Results. Sixteen patients were identified. Mean age at SSc diagnosis was 41.2 ± 14.4 years; 62.5% were female and 87.5% had diffuse cutaneous disease. Median CK prior to biopsy was 97 U/L [IQR 46–300]; 44% of patients had persistently normal CK despite weakness. Myopathic features were observed in 93% of EMGs and muscle edema in 92% of MRIs. All biopsies demonstrated hallmark endomysial and perimysial fibrosis. Perifascicular myofiber atrophy localized to fibrotic regions was noted in 56% of patients, a pattern distinct from dermatomyositis. Fourteen patients (88%) received immunosuppressive therapy; mycophenolate (50%), IVIG (56%), and rituximab (25%) were most common. At 6–12 months, 56% of patients had improved strength, 25% showed no improvement, and 19% had inadequate follow-up. After 5.5 ± 4.7 years of follow-up, 50% of patients were deceased, with cardiopulmonary disease the leading cause of death (50% of deaths).
Conclusions. SSc-associated fibrosing myopathy is a distinct clinicopathologic entity with high mortality, frequent cardiopulmonary complications, and characteristic histopathology. Importantly, CK values may be normal despite objective evidence of myopathy, emphasizing the need for multimodal evaluation. While immunosuppressive therapy led to improvement in strength in over half of patients, overall prognosis remained poor. Recognition of perifascicular myofiber atrophy within fibrotic regions may aid diagnosis and further distinguish this subtype from dermatomyositis. Early recognition and aggressive management are critical to improving outcomes.
Key words: overlap syndrome, fibrosing myopathy, systemic sclerosis

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LONG-TERM FOLLOW-UP AND RISK FACTORS FOR RELAPSE IN PATIENTS WITH ANTI-HMGCR NECROTIZING MYOPATHY

Orane Demuynck[1], Romain Batton[2], Noémie Le Gouellec[3], Laure Gallay[4], Alain Meyer[5], Margherita Gianinni[5], Aurore Collet[6], Ygal Benhamou[2], Olivier Boyer[7], Helene Behal[8], Morgane Le Guen[3], Yves Allenbach[11], Jean-Luc Charuel[9], Ludivine Kouton[10], David Launay[1], Olivier Benveniste[11]
[1]Département de Médecine Interne et Immunologie Clinique, Centre Hospitalier Universitaire Lille, Centre de Référence des Maladies Auto-Immunes Systémiques Rares du Nord et Nord-Ouest, Lille, France, [2] CHU de Rouen, Department of Internal Medicine and Clinical Immunology, CHU Rouen, Rouen, France, [3]Department of Nephrology and Internal Medicine, H^opital de Valenciennes, Valenciennes, France, [4]Department of Clinical Immunology, Edouard Herriot Hospital, Hospices Civils de Lyon, Lyon, France, [5]Explorations Fonctionnelles Musculaires, Service de Physiologie, Centre de Référence des Maladies Autoimmunes Rares, Hôpitaux Universitaires de Strasbourg, Strasbourg, France, [6]Institut d'Immunologie, C.H.U de Lille, Lille, France, [7]Laboratoire d'Immunologie et Biothérapies, Centre Hospitalier Universitaire de Rouen, Rouen, France, [8] Biostatistique, CHU de lille, Lille, France, [9]Service d'Immunologie, Département d'Immunochimie, Hôpital La Pitié-Salpêtrière, Paris, France, [10]Service des Maladies Neuromusculaires et de la sla, Hôpital de la Timone, Marseille, France, [11]Médecine Interne, Hôpital Pitié Salpêtrière, Paris, France

Introduction. Among inflammatory myopathies, necrotizing myopathies have the most severe muscle involvement and can sometimes have a slow disease progression, mimicking limb girdle dystrophy. The incidence of necrotizing myopathy associated with anti-HMGCR autoantibodies (anti-HMHCR IMNM) is currently increasing. Little is known about the long-term follow-up and relapses risk factor of anti-HMHCR IMNM.
Methods. Patients were included if they fulfilled the 224th ENMC criteria for anti-HMHCR IMNM. Clinical data were collected retrospectively from seven centres in France. A relapse was defined as a patient presenting, after an initial clinical improvement, a new creatine kinase elevation and/or a worsening of muscle strength that prompted an escalation of immunosuppressive therapy. Patients experiencing two relapses after discontinuing intravenous immunoglobulin (IVIg) treatment were defined as being IVIg dependent.
Results. A total of 165 patients were included in the study, 61% of whom had previously been exposed to statins. The median age was 61 years [IQR 45;69], and 40.6% of patients were male. Among patients followed for over two years, 66% (83/126) experienced at least one relapse. The median time between diagnosis and relapse was 24.5 months [IQR 14.0; 38.0]. Univariate analysis revealed that younger age (hazard ratio (HR) 1.11 for every increase of 10 years; 95% confidence interval (CI): 1.01–1.22), low creatinine rate (HR: 1.26 for every drop of 1 mg/L; 95% CI: 1.09–1.45) and female sex (HR: 1.65; 95% CI: 1.05–2.06) were associated with a higher risk of relapse. However, in the multivariate analysis, only the creatinine level was significantly correlated with relapse (HR: 1.26; 95% CI: 1.04–1.56). Ninety percent of patients received intravenous immunoglobulin (IVIg), and 30.5% were considered IVIg dependent. Following IVIg discontinuation, 57% of patients relapsed within the subsequent year.
Conclusions. The majority of patients with anti-HMGCR IMNM experienced a relapse during the follow-up period in our study. Low creatinine level may indicate relapse risk. IVIg is often used to treat patients, and relapse occurs in half of cases when treatment is stopped. It is important to identify which patients might have a chronic disease course at diagnosis, in order to adapt the treatment strategy.
Acknowledgements. We would like to thank the patients.
Key words: HMGCR, necrotizing myopathy, relapse, intravenous immunoglobulin

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SERTRALINE-INDUCED MADD: TWO CASES OF LIPID STORAGE MYOPATHY AFTER PROLONGED SSRI USE

Swapnasha Panigrahi[1], Ute Pohl[2], Santhosh Nagaraju[2], Hafis Muhammad[3], Thomas Sheeran[3], Latika Gupta[3,4,5]
[1]University of Birmingham, Birmingham, UK, [2]Department of Cellular Pathology, University Hospitals Birmingham, Birmingham, UK, [3]The Royal Wolverhampton NHS Trust, Rheumatology, Wolverhampton, UK, [4]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham, Birmingham, UK, [5]Francis Crick Institute, London, UK

Introduction. Multiple Acyl-CoA Dehydrogenase Deficiency (MADD) is a rare lipid storage myopathy (LSM). Sertraline, one of UK's widely prescribed SSRIs with over 16.7 million prescriptions dispensed in 2019, is rarely associated with drug-induced MADD. Recognition of this potentially reversible adverse effect is crucial. Proposed mechanisms involve mitochondrial fatty acid β-oxidation enzyme inhibition and interference with riboflavin metabolism.
Case presentations. Case 1: A 43-year-old female on sertraline 200mg daily developed progressive proximal myopathy, myalgia, numbness, and fatigue approximately 10 years post-initiation. She presented in 2021 with weakness (MMT8 incapable; hip-flexion 3-4/5, knee-extension 3-4/5). Creatine kinase (CK) ranged from 471 U/L-1362 U/L. Extended myositis panel was negative. Acylcarnitine profile was negligible suggesting impaired fatty acid oxidation.
Muscle biopsy demonstrated LSM featuring fine vacuoles in the sarcoplasm of type 1 fibres with Sudan Black positive lipid droplets and no evidence of mitochondrial abnormality or inflammatory myopathy. Extended genetic testing including Pompe's was unremarkable. EMG demonstrated myopathy with proximal-to-distal denervation. MRI showed bilateral atrophy of glutei and thigh muscles. Ultrasound revealed vastus lateralis/intermedius atrophy, and hyperechoic gastrocnemius changes. Prednisolone during admissions improved symptoms. Sertraline was discontinued after MADD diagnosis (timeline on https://tinyurl.com/3me83pzd).
Case 2: A 46-year-old female on sertraline 150mg daily since 2002 presented with progressive weakness in 2024 – examination revealed a MMT8 score of 80 and bilateral hip-flexion/shoulder-abduction weakness (4+/5). CK was 600 U/L. Extended myositis panel was negative; anti-SRP was positive. Muscle biopsy showed atrophic fibres with small sarcoplasmic vacuoles and mild-to-moderate lipid excess on Sudan Black staining. Mitochondrial enzyme histochemistry demonstrated 10 COX-deficient fibres, suggesting secondary mitochondrial dysfunction. MRI was unremarkable, but ultrasound showed hyperechoic changes in deltoids, forearms, gastrocnemius and tibialis. Prednisolone given 4 months after symptom-onset produced improvement. Sertraline was discontinued after MADD diagnosis.
Discussion. These cases suggest sertraline-induced MADD as a rare but potentially reversible LSM cause. The temporal relationship between prolonged use and symptom development, combined with histopathological findings and negligible acylcarnitine levels without genetic abnormalities, supports a drug-induced mechanism. Symptom onset (10-22 years) and severity varied, despite similar exposure. Anti-SRP positivity in Case 2 is considered false positive given clinical inconsistencies with immune-mediated necrotising myositis. Both patients improved with corticosteroids though unclear how.
Conclusions. Clinicians should monitor for myopathic symptoms in long-term sertraline therapy as discontinuation may reverse symptoms. Secondary mitochondrial dysfunction in Case 2 suggests exposure-dependent injury.

Further research should include systematic acylcarnitine profiling before/after withdrawal, long-term reversibility follow-up, and investigation of riboflavin supplementation.
Key words: sertraline, lipid storage myopathy, drug induced myopathy

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SSRI-ously WEAK: A CASE OF SEVERE MYOPATHY ASSOCIATED WITH SERTRALINE USE

Nikola Wilk[1], Hector Chinoy[2,3], James B. Lilleker[4,5]
[1]Department of Medicine, Division of Rheumatology, The Ottawa Hospital, University of Ottawa, Ottawa, ON, Canada, [2]National Institute for Health Research Manchester Biomedical Research Centre, Manchester University NHS Foundation Trust, The University of Manchester, Manchester, UK, [3]Department of Rheumatology, Salford Royal NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [4]Centre for Musculoskeletal Research, Division of Musculoskeletal and Dermatological Sciences, School of Biological Sciences, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, The University of Manchester, Manchester, UK, [5]Manchester Centre for Clinical Neurosciences, Salford Royal NHS Foundation Trust, Salford, Manchester, UK

Background. In recent years, severe myopathy associated with sertraline has been increasingly recognized. Sertraline has been implicated as a cause of acquired multiple acyl-CoA dehydrogenase deficiency (MADD), presenting with exertional myalgia, proximal limb weakness, sensory disturbances and head drop. We hereby report a severe case illustrating this emerging association.
Case presentation. A 45-year-old woman known for ulcerative colitis, asthma, polycystic ovarian disease and anxiety was admitted to the Salford Royal Hospital in July 2025 with progressive profound symmetrical weakness. Her home medications included Infliximab and sertraline 150mg daily, which had been started 2021 for her anxiety.
She first noticed some intermittent tightness and cramping sensation in her calf muscles in May 2024. This was exacerbated by exertion and relieved with rest. She noted some progressive diffuse myalgias, distal patchy sensory disturbances and weakness in all four extremities over the following months. She requires stick and crutches to ambulate, and by early 2025 she required an electric wheelchair. She also noted head drop, chewing weakness, dysphagia, and lost over 15kg over 4 months.
Physical examination revealed profound muscle wasting, normal cranial nerves and diffuse weakness. Extensive immunology testing for connective tissue disease was unremarkable including ANA, ENA, myositis panel, HMGCR Ab. Her initial CK was initially mildly elevated at 253 (normal 25-200 IU/L) which then normalized. The serum carnitine level was low at 12.5 (normal 20-40 umol/L). Electromyography showed mild myopathic changes in proximal muscles without myotonia, inflammatory features, or abnormal recruitment. FDG-PET-CT demonstrated diffuse muscular uptake without malignancy. MRI thighs revealed subtle myoedema without fatty infiltration, and whole-spine MRI was unremarkable.
Muscle biopsy showed vacuolar myopathy with ragged blue fibers, neutral fat, and pale SDH staining but no inflammation. Given the slow progression, absence of systemic features, low CK, normal immunology, and biopsy findings suggestive of lipid storage disorder, sertraline-induced late-onset MADD was diagnosed. Sertraline was switched to citalopram, and riboflavin 200 mg BID was started, leading to marked strength improvement at two-month follow-up.
Conclusions. Treatment with sertraline, an antidepressant drug, may cause mitochondrial dysfunction by inhibiting oxidative phosphorylation complexes I, II and IV which leads to abnormal lipid storage in muscle fibers, a complication not seen with other SSRIs. Most late-onset MADD patients respond well to high-dose riboflavin and substituting SSRIs. This is an important acquired cause of myopathy which present the rheumatology or neurology clinics with myalgia and exercise intolerance.
Key words: myositis mimics, MADD

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FROM OPERATING ROOM TO OUTPATIENT CLINIC: NEEDLE BIOPSY FOR NEUROMUSCULAR DIAGNOSTICS

Karsten Krause[1,2], Anne-Katrin Güttsches[1,2], Christopher Nelke[1,2], Tobias Ruck[1,2], Felix Kleefeld[1,2,3]
[1]Ruhr University Bochum, BG University Hospital Bergmannsheil, Department of Neurology, Bochum, Germany, [2]BG University Hospital Bergmannsheil, Heimer Institute for Muscle Research, Bochum, Germany, [3]Charité-Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt Universität zu Berlin, and Berlin Institute of Health (BIH), Department of Neurology, Berlin, Germany

Background. Muscle biopsy is a cornerstone in the diagnostic evaluation of neuromuscular disorders. Especially in inflammatory disorders, a muscle biopsy and histopathological work-up is essential to establish the diagnosis. Traditional open biopsies provide sufficient tissue for comprehensive histopathology, but the procedure is invasive and resource-intensive. Percutaneous needle biopsy represents a safe and minimally invasive alternative that can be performed safely in an outpatient setting under local anesthesia (1, 2). Being a minimally-invasive procedure, it improves patient comfort, reduces procedural risks, and facilitates diagnostic workflows in outpatient settings. However, traditional needle biopsy techniques, such as the Bergström method, have been criticized for producing tissue samples of inconsistent and often heterogeneous quality.
We here present our practical experiences with a new, vacuum needle biopsy system, recently established at our institution.
Methods. We conducted percutaneous, sonography-guided muscle biopsies using a vacuum needle biopsy system (10 Gauge, BD EleVation) under sterile conditions and local anesthesia. Biopsies were obtained from the vastus lateralis and gastrocnemius muscles in patients undergoing evaluation for suspected myopathies. Complication rates were recorded. The diagnostic adequacy of each sample was assessed by histology and immunofluorescence microscopy.
Results. A total of 40 biopsies were performed over 12 months. Adequate tissue for full diagnostic work-up was obtained in all cases. Histological and immunofluorescence microscopic analyses showed excellent preservation of muscle fibre morphology and minimal freezing artefacts and allowed for comprehensive histopathological work-up in inflammatory, hereditary, and neurogenic muscle disorders. No complications were observed.
Conclusions. Percutaneous needle biopsy provides diagnostically reliable skeletal muscle samples with minimal patient burden and very low complication rates. This method may replace open biopsies in most clinical diagnostic contexts, offering an efficient, safe, and patient-friendly approach to neuromuscular disease evaluation.
Acknowledgements. We thank the participating patients
Key words: muscle biopsy, needle biopsy, Bergström technique

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SYSTEMIC AND SKELETAL MUSCLE REGULATION OF ANABOLIC PATHWAYS IN IDIOPATHIC INFLAMMATORY MYOPATHIES SHOWS STAGE-DEPENDENT ALTERATIONS

Lucie Lážnovská[1,2], Lucia Vernerová[1], Veronika Balounová[1], Martin Klein[1,3], Heřman Mann[1,3], Sabína Oreská[1,3], Michal Tomčík[1,3], Jozef Ukropec[4,5], Barbara Ukropcová[4,5], Jiří Vencovský[1,3]
[1]Institute of Rheumatology, Prague, Czech Republic, [2]Department of Physiology, Faculty of Science, Charles University, Prague, Czech Republic, [3]Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [4]Institute of Experimental Endocrinology, Biomedical Research Center, Slovak Academy of Sciences, Bratislava, Slovakia, [5]Institute of Pathophysiology, Faculty of Medicine, Comenius University, Bratislava, Slovakia

Background. In idiopathic inflammatory myopathies (IIM), muscle weakness may persist even after inflammation subsides, suggesting that, besides autoimmune destruction, metabolic alterations contribute to residual dysfunction. Previous findings showed differences in circulating myostatin and follistatin and in their gene expression between chronic IIM patients, and healthy controls, indicating the involvement of the myostatin/follistatin axis in the pathogenesis. Suppression of the myostatin pathway activates anabolic signalling cascades. However, anabolic pathways promoting protein synthesis, muscle fibre regeneration, and satellite cell differentiation

– particularly the IGF-1/PI3K/Akt/mTOR and bone morphogenetic protein (BMP) pathways – may be disrupted by chronic exposure to proinflammatory cytokines, thereby impairing muscle regeneration.
Methods. The study cohort included newly diagnosed patients with IIM (IIM-M0), chronic IIM patients (IIM-Ch), and healthy donors (HD). Circulating levels of BMP-2, BMP-4, BMP-7, IGF-1, and hGH were quantified using ELISA assays. In parallel, a preliminary analysis of gene expression of selected components of the BMP and IGF-1/PI3K/AKT1/mTOR signalling pathways was performed on muscle biopsy samples.
Results. Serum levels of anabolic proteins were analysed by ELISA in IIM-M0 (n=21), IIM-Ch (n=19), and HD (n=19) groups. These preliminary data revealed no statistically significant differences in circulating levels of BMP-2, BMP-4, BMP-7, IGF-1, or hGH; moreover, BMP-2 and BMP-7 values were frequently below the detection limit of the assay. Preliminary analysis of BMP pathway gene expression (BMPR1A, BMPR2, SMAD1, SMAD5, SMAD8) in muscle tissue (n=10/10/10 for IIM-M0/IIM-Ch/HD) showed significant differences between groups. Expression of BMPR2 ($p<0.0001$), SMAD1 ($p=0.0003$), SMAD5 ($p<0.0001$), and SMAD8 ($p=0.038$) was markedly decreased in IIM-M0 compared with IIM-Ch, also IIM-M0 is with BMPR2 ($p<0.0001$) and SMAD5 ($p<0.0001$) significantly reduced compared to HD. Within the IGF-1/PI3K/Akt/mTOR signalling pathway, expression of mTOR was significantly altered in IIM-M0 compared with both IIM-Ch ($p<0.0001$) and HD ($p<0.0001$). The number of participants in each subgroup remains limited and will be expanded to increase the statistical power of the study.
Conclusions. Based on the current data, anabolic signalling at the systemic level does not appear to be significantly altered in IIM. Given that the analysed proteins are produced in multiple tissues and exert systemic effects, we hypothesize that compensatory mechanisms primarily operate at the level of local molecular pathways within skeletal muscle tissue – a notion further supported by our gene expression findings.
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Key words: myositis, anabolic pathways, IGF-1, BMP

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ANTI-SYNTHETASE SYNDROME IN ARGENTINA - A REPORT FROM THE ARGENTINE REGISTRY OF INFLAMMATORY MYOPATHIES OF THE ARGENTINE SOCIETY OF RHEUMATOLOGY

Ignacio Lopez[1], Marina Garcia Carrasco[2], Carolina Sánchez Andía[3], Cristian Alejandro Benitez[4], Ana Carolina Costi[5], Graciela Noemi Gomez[6], Micaela Cosatti[7], Mariana Aciar[8], Boris Kisluk[9], Sabrina M. Argüello[10], Melissa Brenda Serna Góngora[11], Anabella Maria Rodriguez[12], Amelia Granel[13], Ramiro Adrian Gómez[14]
[1]Sanatorio Guemes, CABA, Argentina, [2]Hospital de Clinicas Jose de San Martin, CABA, Argentina, [3] Hospital General de Agudos José María Penna, CABA, Argentina, [4]Hospital Nacional Alejandro Posadas, El Palomar, Argentina, [5]H.I.G.A. San Martin La Plata, La Plata, Argentina, [6] Instituto de Investigaciones Médicas Dr Alfredo Lanari, CABA, Argentina, [7]El Centro de Educación Médica e Investigaciones Clínicas "Norberto Quirno" (CEMIC), CABA, Argentina, [8]Hospital Señor del Milagro, Salta, Argentina, [9]Hospital Escuela Eva Perón, Granadero Baigorria, Argentina, [10]Hospital Alta Complejidad en Red El Cruce, Florencio Varela, Argentina, [11]Hospital General de Agudos José María Ramos Mejía, CABA, Argentina, [12]Hospital Britanico, CABA, Argentina, [13]Hospital Britanico, La Plata, Argentina, [14]Hospital Universitario Austral, PIlar, Argentina

Background. The anti-synthetase syndrome (ASyS) in a subtype of Idiopathic Inflammatory Myopathy (IIM), characterized by the presence of anti aminoacil-ARNt-synthetases autoantibodies (ASA) and a variable clinical phenotype including myositis, arthalgia/arthritis, interstitial lung disease (ILD), Raynaud's phenomenon, fever and mechanic hands (1). Data regarding local characteristics of patients with ASyS are scarse, so the aim of this study was to evaluate the clinical, serological and therapeutic characteristics of patients with ASyS included in a multicentric national registry.
Methods. Descriptive, cross-sectional, multicentric study. Patients with a clinical diagnosis of ASyS included in the Registry of Inflammatory Myopathies of the Argentine Society of Rheumatology were included. Data regarding demographics, clinical characteristics, presence of autoantibodies and treatment were collected from the registry. Patients were grouped as Jo-1 (+), Non Jo-1 ASA (+)(PL-7, PL-12, EJ, OJ) and "seronegative". Comparisons between groups were made using Kruskal-Wallis or Chi^2 tests with Bonferroni correction.
Results. A total of 152 patients were included: 74 Jo-1 (49%), 56 Non Jo-1 (37%) and 22 seronegative (14%). Median age at diagnosis was 50 (IQR 39–61) years with a median diagnostic delay of 5 (IQR 1–21) months. Female sex accounted for 70% of patients and 65% were of Mestizo ethnicity. Caucasian ethnicity was more frequent in the Non Jo-1 group ($p<0.05$).
At diagnosis, the most frequent clinical manifestations were myositis (70%), ILD (63%) and arthalgia/arthritis (53%), with the full triad in 23% of patients. Myositis was more frequent in Jo-1 (+) patients compared to the other groups. At the last visit, 22% of patients had developed new clinical manifestations, specially arthritis and myositis, once again more frequently in Jo-1 (+) patients. No difference regarding complementary studies nor treatments were found between groups. Most patients received glucocorticoids and steroid-sparing agents, according to current recommendations
Conclusions. This local cohort of ASyS patients from Argentina shows a clinical and serological profile similar to what has been reported in other international cohorts (2-4). Most patients included here were of Latinamerican Mestizo ethnicity. Myositis was the predominant manifestation in anti Jo-1 (+) patients, both at diagnosis and during follow-up. Treatment strategies were homogeneous in all groups. This study relevant adds relevant local information in a population that is not well characterized in the current ASyS literature.
Key words: anti-synthetase syndrome, intersticial lung disease

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ANTIMITOCHONDRIAL ANTIBODIES IN IMMUNE-MEDIATED INFLAMMATORY MYOPATHIES: A RARE BUT CLINICALLY RELEVANT ANTIBODY

Ignacio Lopez[1,3], Ramiro Adrian Gomez[2], Gonzalo Martin Barros[3], Maria Eleonora Bresan[3], María Julieta Gamba[2], Gustavo Medina[3], Marína García Carrasco[3]
[1]Sanatorio Guemes, CABA, Argentina, [2]Hospital Nacional Alejandro Posadas, El Palomar, Buenos Aires, [3]Hospital de Clinicas Jose de San Martin, CABA, Buenos Aires

Background. Idiopathic Inflammatory Myopathies are a group of heterogeneous diseases characterized by muscular and extramuscular inflammation (1). The presence of certain autoantibodies, whether myositis-specific antibodies (MSA) or myositis-associated antibodies (MAA), confer particular clinical characteristics that delimit specific subgroups. Other groups have described IIM patients with anti M2 mitochondrial autoantibodies (AMA) as characterized by muscle atrophy, axial weakness and cardiac involvement, but no such characterization exists in our region (2-8).
Objective. To study the prevalence of AMA in a cohort of IIM patients and to compare characteristics of patients with and without AMA
Results. A total of 236 patients had AMA determination and 9 were positive (3.8% prevalence in this combined cohort), so 27 matched AMA (-) patients were included for comparison. A final cohort of 36 patients was evaluated; 69% female, mean age 45 ±11.4 years old, median diagnostic delay 6 months (IQR 2-12.3) with a delay in AMA (+) patients ($p=0.02$). The most frequent IIM subtype was Dermatomyositis (DM) (45%). Two of the AMA (+) patients (22%) had concurrent Primary Biliary Cholangitis (PBC). Most patients had muscle weakness and skin involvement, but AMA (+) patients were characterized by muscle atrophy ($p=0.01$) and cardiac involvement ($p<0.001$). Peak CPK was numerically lower in AMA (+) and the coexistence of this autoantibody with other MSA was infrequent.
Regarding treatment, all patients received steroids and AMA (+) patients tended to receive lower doses ($p=0.013$). Most patients received immunosuppressants, without difference among groups.
Conclusions. In this cohort, the presence of AMA associated with muscle atrophy and cardiac involvement, similar to previous reports. Unlike American or Japanese reports, a higher frequency of DM was found, along a lower frequency of axial weakness. This study adds up to the current AMA-IIM literature, including patients from currently underrepresented regions. Determination of AMA-M2 is accessible to most centers in our country and we believe it could offer valuable information to further characterize patients.

Key words: inflammatory myopathy, anti-mitochondrial antibodies, cardiac involvement, auto-antibodies, myositis, chronic clinical course

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THE AUSTRALASIAN MYOSITIS REGISTRY: A NATIONAL PROSPECTIVE DATABASE FOR IDIOPATHIC INFLAMMATORY MYOPATHIES

Merrilee Needham[1,2,3,4], Matthew Parker[5,6,7], Shereen Paramalingam[4,8,13], Jessica Day[9,10], Anna Brusch[11,12,13], Genevieve Fong[5], Kelly Beer[2,3,4], Ian Cooper[2,3,4], Annik Panicker[2,3,4], Althea Doverty[2,3,4], Nataliya Slater[2,3,4]
[1]Department of Neurology, Fiona Stanley Hospital, Murdoch, Perth, Australia, [2]School of Medicine, University of Notre Dame, Fremantle, Perth, Australia, [3]Perron Institute for Neurological and Translational Science, Nedlands, Perth, Australia, [4]Murdoch Univesrity, Murdoch, Perth, Australia, [5]Department of Rheumatology, Royal Prince Alfred Hospital, Sydney, Australia, [6]Faculty of Medicine and Health, The University of Sydney, Darlinghurst,Sydney, Australia, [7]RPA Institute for Academic Medicine, Sydney, Australia, [8]Department of Rheumatology, Fiona Stanley Hospital, Murdoch, Perth, Australia, [9]Department of Rheumatology, Royal Melbourne Hospital, Parkville, Melbourne, Australia, [10]Inflammation Division, Walter and Eliza Hall Institute of Medical Research, Parkville, Melbourne, Australia, [11]Department of Immunology, Sir Charles Gairdener Hospital, Nedlands, Australia, [12]Department of Immunopathology, Pathwest, Perth, Australia, [13]Faculty of Medicine, University of Western Australia, Perth, Australia

Background. Idiopathic inflammatory myopathies (IIMs) are are rare, heterogenous autoimmune diseases often characterised by multisystem involvement, with or without skeletal muscle involvement, and often additional multisystem involvement. Their rarity and clinical diversity can present challenges in advancing understanding and optimising clinical management. While multiple IIM registries exist internationally, until recently there was no coordinated national registry in Australia. The Australian Myositis Registry (AMR) was established to address this gap, providing a unified, longitudinal database to capture clinical, laboratory and patient-reported data across the full spectrum of IIM subtypes and building on the successes and limitations of myositis registries in other regions.
Methods. The AMR is a national, prospective, observational cohort study recruiting adults with a specialist-confirmed diagnosis of IIM. Ethical approval was granted by the Sydney Local Health District Ethics Review Committee (X23-0071). Recruitment began in April 2023 at Murdoch University and Perron Institute (WA) and Royal Prince Alfred Hospital (NSW), with progressive expansion to other states and territories. Data are captured using a REDCap platform, incorporating extensive branching logic for efficiency and data quality. The dataset includes core clinical and laboratory variables, myositis-specific and -associated autoantibodies, IMACS core set measures, and patient-reported outcome measures (PROMs). Consumer involvement is embedded through the Myositis Research Consumer Panel to ensure lived-experience perspectives inform ongoing development.
Results. As of September 2025, the AMR has enrolled 119 patients across three active sites. Another three sites are in set-up, with further expansion planned in 2026. Early enrolment demonstrates feasibility and engagement from both clinicians and consumers. The registry captures a breadth of demographic, diagnostic, and longitudinal clinical data, enabling analyses of disease progression, treatment patterns, and patient experience.
Conclusions. The AMR represents the first nationwide registry for IIM in Australia and one of few globally to integrate both clinician-entered and patient-reported data. Its design supports longitudinal tracking of natural history of disease, facilitates recruitment for interventional and translational studies, and provides infrastructure for registry-based clinical trials. The AMR will be a key platform to improve understanding of myositis epidemiology, outcomes, and lived experience in Australia, and to foster international collaboration in IIM research.
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INCIDENCE OF MYOSITIS IN THE UK, 2010–2024: A RETROSPECTIVE COHORT STUDY USING PRIMARY CARE ELECTRONIC HEALTH RECORDS

Jamie Campbell[1], Kimberly Loh[1,2], Anita McGrogan[1], Juan Jiménez Amaya[1], Sarah Tansley[1,2], Theresa Smith[1]
[1]University of Bath, Bath, UK, [2]Royal United Hospital, Bath, UK

Background. Idiopathic inflammatory myopathies (IIM) are rare autoimmune disorders associated with significant morbidity and mortality. Despite advances in disease classification, population-based incidence estimates in the UK remain limited. Prior studies suggest wide variation in reported incidence rates, ranging from 1.16–19 per million per year (1). Accurate incidence estimates are essential to understand disease burden and plan healthcare resources. The objective of this study was to estimate age- and sex-specific incidence of IIM in the UK from 2010–2024, describe demographics at diagnosis, examine temporal and seasonal trends, and uncover potential associations with influenza and statin exposure.
Methods. A retrospective cohort study was conducted using data from the Clinical Practice Research Datalink (CPRD), a large primary care database comprising over 50 million patients from primary care practices in England. Adults aged ≥16 years with a first-ever IIM diagnosis were identified using two case definitions: 1. Liberal, based on validated code lists as indicating probable, definite or overlap myositis, and 2. Strict, requiring two additional pieces of supporting evidence. Crude and stratified incidence rates per million person-years were calculated, and temporal trends assessed using Poisson generalized additive models.
Results. Among 27 million eligible patients contributing 171.7 million person-years, 6348 incident IIM cases met the liberal definition and 3017 met the strict definition. The corresponding crude incidence rates were 37.0 (95% CI: 36.1–37.9) and 17.6 (16.9–18.2) per million person-years. Incidence was higher in females (19 *vs*. 16.2) and peaked in individuals aged 65–74 years. Rates remained stable over time, with no consistent evidence of seasonal variation or strong correlation with national influenza trends. Evidence of statin prescribing in the three years preceding IIM diagnosis was observed in 36% of the liberal cohort and 38% of the strict cohort. Following diagnosis, recorded anxiety or depression was observed in 39% and 41% of patients respectively, where approximately one-third were first-ever presentations.
Conclusions. This study provides the most comprehensive and up-to-date UK population-based estimates of IIM incidence to date. Strengths include employment of a strict in addition to liberal case definition, enhancing diagnostic capture. Findings confirm the rarity of IIM, a strong female predominance and late-adult onset, with overall rates broadly consistent with prior European studies (2-4). The substantial psychological burden warrants further research and greater mental health emphasis in IIM management. CPRD presents a valuable resource for rare disease epidemiology, although variable diagnostic coding remains a key limitation.

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NUTRITIONAL STATUS AND BODY COMPOSITION IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Stefanie Glaubitz[1,2], Stefanie Meyer[1,2], Leah M Berner[1], Konstantin Schütz[1,3], Rachel Zeng[1,4], Karsten Kummer[5], Lina Hassoun[1], Jan-Gerd Rademacher[6], Jana Zschüntzsch[1,2]
[1]University Medical Center Goettingen, Department of Neurology, Goettingen, Germany, [2]University Medical Center Goettingen, Heart & Brain Center Goettingen, Goettingen, Germany, [3]University Medical Center Goettingen, Department of Geriatrics, Goettingen, Germany, [4]Faculty of Medicine and University Hospital Carl Gustav Carus, Department of Neurology, Dresden, Germany, [5]Immanuel Clinic Ruedersdorf, University Hospital of the Brandenburg Medical School Theodor Fontane, Department of Neurology and Pain Treatment, Ruedersdorf bei Berlin, Germany, [6]University Medical Center Goettingen, Department of Nephrology and Rheumatology, Goettingen, Germany

Background. The positive impact of nutrition on general physical health is well known. In addition to its role in preventing cardiovascular diseases, dietary recommendations are increasingly being developed for rheumatic diseases, suggesting potential benefits of anti-inflammatory diets.
The study aimed to assess the dietary habits and body composition of patients with idiopathic inflammatory myopathies (IIM), and to investigate potential effects of malnutrition in IIM patients
Methods. Patients with all subtypes of IIM were included in the study. Dietary habits were assessed using a study-specific questionnaire and a 7-day food diary was completed by the patients. Daily caloric intake and macronutrient distribution were calculated and compared with the current reference values provided by the German Nutrition Society. Patients underwent a body impedance analysis to assess the body composition. In addition, disease-specific parameters, as well as comprehensive assessments of fatigue, quality of life, and dysphagia were recorded.
Results. A total of 47 patients with IIM (61.7% female, mean age 60.7 ± 14.6 years) participated in the study. The most common subtype was dermatomyositis (n=11), followed by polymyositis and immune-mediated necrotizing myopathy (n=11), followed by polymyositis and immune-mediated necrotizing myopathy (n=9 each).
Based on body mass index (BMI), 31.9% of patients were of normal weight. Overweight was present in 40.4% of patients, while 27.7% were classified as obese.
A total of 89.4% of patients followed a regular mixed diet and one third reported having a prior nutritional counselling. Protein malnutrition was identified in 46.8% of patients, while an increased daily fat intake was observed in 19.1%. No significant differences were found in fatigue or quality of life scores between obese and non-obese patients. However, obese patients showed significantly higher C-reactive protein (CRP) levels (1.94 ± 1.82 mg/L *vs*. 10.27 ± 8.14 mg/L, p=0.003) and significantly higher LDL cholesterol levels.
Conclusions. Due to a combination of glucocorticoid therapy, muscle weakness and pain-related limitations in physical activity, patients with IIM are at increased risk of developing overweight or obesity. Despite a high proportion of patients reporting a regular mixed diet and having received prior nutritional counselling, nearly half exhibited protein malnutrition. Furthermore, the significantly higher CRP levels in obese patients suggest a potential link between excess body weight and systemic inflammation. Although our sample size was limited, these findings support the importance of nutrition and body composition in patients with myositis.
Acknowledgements. The study was supported by the German Society for muscular diseases (DGM).
Key words: myositis, nutrition, body composition

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A PROSPECTIVE DIAGNOSTIC ACCURACY STUDY OF MULTIMODALITY TESTING IN PATIENTS SUSPECTED OF A TREATABLE IDIOPATHIC INFLAMMATORY MYOPATHY (ADAPT-STUDY)

Sanne Evers[1], Pinar Özkaynar[1], Renske Kamperman[1], Hannah Walter[1], Filip Eftimov[1], Johannes Koelman[1], Anne-Fleur van Rootselaar[1], Robert Hemke[2], Frank Smithuis[2], Eleonora Aronica[3], Ester van Leeuwen[4], Paul Baars[4], Nicol Voermans[5], Jessica Hoogendijk[6], Esther Brusse[7], Umesh Badrising[8], Rohit Aggarwal[9], Yves Allenbach[10], Marianne de Visser[1], Ivo van Schaik[1,11], Patrick Bossuyt[12], Camiel Verhamme[1], Joost Raaphorst[1], Anneke van der Kooi[1]
[1]Department of Neurology, Amsterdam University Medical Centre, Amsterdam, The Netherlands, [2]Department of Radiology and Nuclear Medicine, Amsterdam University Medical Centre, Amsterdam, The Netherlands, [3]Department of (Neuro) pathology, Amsterdam University Medical Centre, Amsterdam, The Netherlands, [4]Department of Laboratory Medicine, Laboratory for Specialized Diagnostics and Research, Section Medical Immunology, Amsterdam University Medical Centre, Amsterdam, The Netherlands, [5]Department of Neurology, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Centre, Nijmegen, The Netherlands, [6]Department of Neurology, Utrecht University Medical Centre, Utrecht, The Netherlands, [7]Department of Neurology, Erasmus University Medical Centre, Rotterdam, The Netherlands, [8]Department of Neurology, Leiden University Medical Centre, Leiden, The Netherlands, [9]Division of Rheumatology and Clinical Immunology, University of Pittsburgh University Medical Centre, Pittsburgh, USA, [10]Department of Internal Medicine and Clinical Immunology, Pitié-Salpêtrière University Hospital, Paris, France, [11]Sanquin Blood Supply Foundation, Amsterdam, The Netherlands, [12]Department of Epidemiology & Data Science, Amsterdam University Medical Centre, Amsterdam, The Netherlands

Background. Selecting a diagnostic strategy for Idiopathic Inflammatory Myopathy (IIM) is challenging due to the absence of a gold standard and the uncertainty among physicians regarding the optimal diagnostic approach, mainly due to insufficient evidence. This prospective study evaluated diagnostic strategies for IIM, focusing on high diagnostic accuracy and low patient-reported burden.
Methods. We conducted a prospective diagnostic accuracy study with an over-complete study design. Patients with clinical suspicion of IIM, requiring treatment with high-dosed glucocorticoids, underwent history taking, physical examination and basic laboratory testing, autoantibody testing (Ab), muscle magnetic resonance imaging (MRI), muscle ultrasound (US), electromyography (EMG), and a muscle biopsy. The reference diagnosis (IIM or IIM mimic) was assigned by an expert panel, based on the complete clinical information, including six months of follow-up. Diagnostic strategies, combining these modalities, were evaluated for sensitivity, specificity, positive/negative predictive values, and patient-reported burden.
Results. In total 100 patients (56 females, mean age of 60 years) were included, of whom 67 were classified by the expert panel as IIM and 33 as IIM mimic. Muscle MRI had the highest sensitivity of 96% (CI 89 to 99%) and the lowest specificity of 42% (CI 27 to 59%). Muscle biopsy had the highest specificity of 97% (CI 87 to 100%) and a sensitivity of 81% (CI 70 to 89%), followed by Ab, with a specificity of 94% (CI 82 to 99%) and a sensitivity of 76% (CI 65 to 85%). Patients reported a higher burden from both EMG and muscle biopsy, compared to Ab, MRI, and US. The most optimal diagnostic strategy comprised Ab and MRI in all patients, followed by a biopsy in 34/100 patients. This yielded a sensitivity of 96% (CI 88 to 99%) and a specificity of 94% (CI 82 to 99%) and limited patient-reported burden. Replacing MRI by US or EMG resulted in a similar diagnostic accuracy. Alternative strategies were also assessed.
Conclusions. In patients suspected of treatable IIM, individual diagnostic tests had either limited sensitivity or specificity. Diagnostic strategies including autoantibody testing, combined with either MRI, EMG or US, and a muscle biopsy only in selected cases, were found to yield the optimal combination of highest sensitivity and specificity with a moderate burden reported by patients. Physicians may also select alternative strategies based on availability and expertise.
Acknowledgements. We thank the participants and the referrers.
Key words: diagnostic accuracy, burden, autoantibodies, ultrasound, EMG, MRI, muscle biopsy

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STANDARDIZED INTEROPERABLE DATA COLLECTION FOR MYOSITIS RESEARCH: DEVELOPING COMMON DATA ELEMENTS FOR MYOSITIS OUTCOME MEASURES

Didem Saygin[1], Matthew Diller[2], Varsha Surampudi[3], Mark Bodkin[3], Payam Noroozi Farhadi[4], Adam Schiffenbauer[4], Audrey Kessel[3], Christopher Mecoli[5], Richard H. Scheuermann[2], Lisa Rider[4]
[1]Rush University Medical Center, Chicago, USA, [2]National Library of Medicine, NIH, Bethesda, USA, [3]Social Scientific System Inc, Bethesda, USA, [4]Environmental Autoimmunity Group, Clinical Research Branch, National Institute of Environmental Health Sciences, NIH, Bethesda, USA, [5]Johns Hopkins University School of Medicine, Baltimore, USA

Background. Recent progress has been made in developing validated myositis outcome measures. However, critical deficiencies remain for data standardization across myositis registries. While the National Institute of Health (NIH) Common Data Elements (CDEs) Repository has been developed to facilitate standardized data collection and sharing, few myositis-specific CDEs currently exist. We developed CDEs for myositis outcome measures using novel data science strategies.
Methods. Data dictionaries of myositis registries were examined to understand how outcome measures are currently captured. We used the Linked data Modeling Language (LinkML), an open-source data modeling framework, to develop computable CDEs. After drafting CDEs for myositis core set activity measures (CSMs), an international conference was held with an expert myositis panel to reach consensus on the coding of CDEs, and prioritize additional measures for CDE creation, using Delphi and modified nominal group techniques. This workflow was repeated for the prioritized measures in the second phase of the project.
Results. A standardized workflow was established for CDE creation. CDEs for ten myositis CSMs were drafted. After receiving comments and holding discussions to improve coding of the CSM CDEs, 100% consensus among

participants was reached on the CDEs for the CSMs. The prioritized measures for additional CDE creation included ACR-EULAR myositis response and classification criteria, damage measures (Global damage, Myositis Damage Index), physical function measures (Functional Index-3, Sit-to-Stand, Timed Up-and-Go, two/six-min walk distance), and PROMIS instruments, among others. CDEs for 18 additional measures were discussed at a second consensus conference. Similarly high agreement was achieved (85-100%), resulting in consensus on the CDEs for all forms, except for disease flare criteria (52% agreement). Altogether 852 new CDEs were created for 27 myositis forms and achieved consensus, readying their submission to the NIH CDE Governance Committee and deposit in the NIH CDE Repository. In addition, REDCap data dictionaries and databases for these 27 forms are being created utilizing the consensus CDEs, and will be distributed via the IMACS website for use by the myositis community.

Conclusions. Leveraging multispecialty expertise in myositis and its patient communities and data science expertise of the National Library of Medicine, the first myositis-specific CDEs have been developed to accelerate the ability to conduct interoperable myositis clinical studies and therapeutic trials. The workflow established here should also benefit creation of CDEs and data sharing for other autoimmune and muscle diseases.

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Key words: data sharing, common data elements, core set activity measures

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SURVIVAL AND CAUSES OF DEATH IN IDIOPATHIC INFLAMMATORY MYOPATHIES: FRENCH NATIONAL HEALTH DATA SYSTEM AND NATIONAL DATABASE FOR RARE DISEASES

Dylan Vellas[1,4], Cyril Gitiaux[2], Ludivine Kouton[3], Anne-Sophie Jannot[4], Yves Allenbach[1]

[1]Department of Internal Medicine and Clinical Immunlogy, Sorbonne Université, Pitié-Salpêtrière University Hospital, Paris, France; Sorbonne Université, Institut National de la Santé et de la Recherche Médicale, Association Institut de Myologie, Centre de Recherche en Myologie, UMRS974 Paris, France, Paris, France, [2]Reference Center for Neuromuscular Diseases, Necker-Enfants-Malades University Hospital, APHP, FILNEMUS, Paris, France; Department of Pediatric Neurophysiology, Necker-Enfants malades Hospital, University of Paris, AP-HP, Paris, France, [3]Service de Pathologies Neuromusculaires, Hôpital de la Timone, Assistance Publique des Hôpitaux de Marseille, Marseille, France, [4]French National Rare Disease Registry (BNDMR), AP-HP, Université Paris Cité, Paris, France; HeKA UMR1346, Université Paris Cité, Inserm, Inria, Paris, France

Background. Polymyositis and dermatomyositis (DM) initially composed idiopathic inflammatory myopathies (IIMs). Mortality is increased (main cause of death: cancer). IIMs are now divided into muscle-specific diseases – inclusion body myositis (IBM), immune-mediated necrotizing myopathy (IMNM) – usually not life-threatening, and potentially life-threatening systemic diseases – DM, anti-synthetase syndrome (ASyS).

This study aims to evaluate the survival of IIM subgroups compared to general population and identify their causes of death using nationwide French data combining the National Rare disease registry (BNDMR) recording patients' diagnoses managed by expert centres and the National Health Data system (SNDS) recording healthcare consumptions, dates and causes of death for the whole French population.

Methods. This work, focused on IIMs, is part from the Drómos study that investigates healthcare pathways of French patients affected by rare diseases by combining BNDMR and SNDS data (2010-2022). Dedicated ORPHA codes were used to identy IIM subgroups. Cases were matched to controls on birth year, sex and city of living (1:3 ratio).

Survival was estimated and compared by Kaplan–Meier estimators and a Cox model adjusted for comorbidities. Cause-specific Cumulative Incidence Functions and Fine & Gray model compared causes of death between cases and controls. Causes of death ratios were estimated in IIM subgroups

Results. There were 1,888 IIM cases (DM: n=564; ASyS: n=532; IMNM: n=244; IBM: n=548) and 5,538 controls included. Age at diagnosis was 58.9y [37.35; 80.55] with a female predominance (60%). Survival was 96% one year after diagnosis (95% CI [94.4%; 97.6%]), decreasing to 85.1% five years after (95% CI [82.6%; 87.7%]). IIMs showed a decreased survival compared to controls (HR 3.35 [2.75; 4.08]). DMs displayed the higher hazard ratio (HR 5.15 [3.13; 8.49]) followed by IMNMs (HR 4.27 [2.35; 7.77]), ASyS (HR 3.74 [2.34; 5.96]) and IBMs (HR 2.68 [2.04; 3.52]) without modification after adjustment. Lung involvement presented the highest increase of death risk (sHR 5.36 [2.64; 10.9]) followed by cancer (sHR 3.59 [2.27; 5.7]). The most frequent cause of death in every subgroup was cancer (DM: 50.00% [30.72; 69.28]; IMNM: 27.78% [10.71; 53.59]; IBM: 23.29% [14.52; 34.91]) except for ASyS where it was lung involvement (28.57% [12.19; 52.31]).

Conclusions. An increased mortality for all IIM subgroups is demonstrated in this unprecedented nationwide study. DMs presented the highest mortality (leading cause: cancer). For the first time, an increased mortality in ASyS was identified (leading cause: lung involvement) as well as in IMMNs and IBMs.

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Key words: myositis, mortality, survival

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IMMUNE CHECKPOINT INHIBITOR-INDUCED MYOSITIS: DIAGNOSTIC FEATURES AND FACTORS ASSOCIATED WITH EARLY UNFAVORABLE OUTCOMES

Lucile Duvaltier[1], Molka Tougorti[1], Wafaa Mounfaloti[1], Mathilde Baudet[2], Barouyr Baroudjian[3], Emilien Ezine[3], Celeste Lebbe[3], Baptiste Hervier[1]

[1]Médecine Interne, Hôpital Saint Louis, APHP, Paris, France, [2]Cardiologie, Hôpital Saint Louis, APHP, Paris, France, [3]Deramtologie, Hôpital Saint Louis, APHP, Paris, France

Background. Immune checkpoint inhibitor (ICI)-induced myositis is a rare but potentially severe immune-related adverse event. Diagnosis can be difficult, particularly in atypical or pauci-symptomatic cases, and clinical progression may be unpredictable. This study aimed to identify clinical, biological, and paraclinical features distinguishing confirmed cases from differential diagnoses, and to determine factors associated with early unfavorable outcomes.

Methods. We conducted a single-center retrospective study including 46 patients hospitalized between 2017 and 2024 for suspected ICI-induced myositis. Diagnosis was considered confirmed when classified as "definite" or "probable" according to ACR/EULAR criteria. Patients with confirmed (n=25) and unconfirmed diagnoses (n=21) were compared, as well as those with favorable (n=16) and unfavorable (n=8) evolution among confirmed cases.

Results. Confirmed cases more frequently presented with muscle weakness (56.0% *vs*. 14.3%, p=0.005), axial involvement (24% *vs*. 0%, p=0.025), myocarditis (52% *vs*. 0%, p<0.001), and higher creatine kinase (CK) levels (9.7 n *vs*.2.5 n, p=0.001). The number of ICI cycles before symptom onset was significantly lower in confirmed cases (median 2 *vs*. 4, p<0.001). Sex, age, and ICI type did not differ between groups. Electromyography and muscle MRI were performed with similar frequency. Reintroduction of ICIs was more frequent among unconfirmed cases (65% *vs*.12%, p<0.001).

Among confirmed ICI-induced myositis cases, myocarditis was the only variable significantly associated with an unfavorable early outcome (87.5% *vs*. 37.5%, p=0.033). The initial severity of muscle weakness, the presence of axial involvement, and both baseline and day-3 CK levels did not reliably predict clinical outcome. The delay between CPK elevation and treatment initiation was similar in both favorable and unfavorable groups (5 *vs*. 4 days, p=0.749), as was the proportion of patients treated with corticosteroid pulses at diagnosis (31% *vs*. 37%, p=1.0).

Conclusions. In patients with a non-specific clinical presentation, such as delayed CPK elevation or absence of myocarditis, alternative diagnoses should be actively considered. The presence of myocarditis appears to be the main determinant of early unfavorable evolution, supporting the need for close monitoring and potentially more aggressive initial management. Conversely, severity of the weakness or early CK decrease do not predict favorable outcomes.

Key words: immune checkpoint inhibitors, adverse effects, myositis, chemically induced

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THE INCIDENCE AND MORTALITY OF CONNECTIVE TISSUE DISEASES IN ENGLAND: A POPULATION-LEVEL COHORT STUDY FROM 2012 TO 2023

Samir Patel[1], Mark Russell[1], Katie Bechman[1], Maryam Adas[1], Zijing Yang[1], Edward Alveyn[1], Chris Wincup[1], Alexandru Dregan[1], Kate Bramham[1], Sam Norton[1], James Galloway[1], Patrick Gordon[1]
[1]King's College London, London, UK

Background. The reported incidence and mortality of connective tissue diseases (CTDs) in England has been inconsistent in the literature. Our objective was to describe current trends in the incidence and mortality of systemic lupus erythematous (SLE), Sjögren's syndrome (SjD), systemic sclerosis (SSc), idiopathic inflammatory myopathies (IIM) and mixed connective tissue disease (MCTD).
Methods. We conducted a retrospective population-level study using primary care records in England via the Clinical Practice Research Datalink (CPRD). We included individuals ≥18 years old with new CTD diagnoses between 2012 and 2023. Our outcomes were incidence and all-cause mortality, which included age-standardized mortality rates (ASMRs), standardized mortality ratios and risk of death over time using flexible parametric models.
Results. There was a total of 22,829 incident CTD diagnoses (81.1% female, median age 57). The age and sex-standardised incidence of SLE and SSc fell over the study period 2012 to 2023 (SLE: 4.32 to 3.29 per 100,000 person years (py) and SSc: 2.33 to 1.86 per 100,000 py), whereas SjD and MCTD incidence remained relatively stable. In contrast, IIM diagnoses rose from 3.23 to 4.31 per 100,000 py. ASMRs across the study period were highest for IIM (27.83 per 1,000 py), followed by SSc (24.43), SLE (16.74), MCTD (16.27) and lowest for SjD (9.70). Compared to the general population, mortality was higher in incident SSc, IIM, MCTD and SLE groups (SMRs of 1.74, 1.56, 1.50, and 1.30 respectively). Among all CTDs, the risk of death from time of diagnosis was highest in those diagnosed with IIM or SSc.
Conclusions. Our findings revealed a falling incidence of SLE, a simultaneous rise in IIM incidence and overall high all-cause mortality within IIM and SSc cohorts. Our findings acknowledge the changing landscape of CTDs in England and will aid healthcare resource planning for this vulnerable population.
Key words: idiopathic inflammatory myopathies, incidence, mortality

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A RETROSPECTIVE ANALYSIS OF THE DIAGNOSIS AND TREATMENT OF SARCOID MYOPATHY AT A LARGE ACADEMIC MEDICAL CENTER

Rachel Sauls[1], Anthony Findley[1], Florentina Berianu[1]
[1]Mayo Clinic, Jacksonville, USA

Background. Symptomatic sarcoid myopathy is a rare manifestation of sarcoidosis, estimated to affect fewer than 1% of patients with sarcoidosis. However, it can be associated with significant morbidity. Due to the rarity of this condition, there is currently limited data regarding optimal diagnostic and management strategies. The aim of this study is to describe the clinical manifestations, diagnostic findings, and treatment approaches to managing sarcoid myopathy at a large, tertiary academic center.
Methods. A retrospective cohort was created by identifying all patients diagnosed with sarcoid myopathy who were treated within a large, single institution, multi-center setting between January 2000 and November 2024. Baseline demographic, laboratory, imaging, and clinical variables were gathered from the electronic medical record. Continuous variables were summarized with median and range, and categorical variables were summarized with frequency and percentage (%).
Results. A total of 16 patients were identified who met inclusion criteria. 7 were male, and the median age at sarcoidosis diagnosis was 66. Twelve patients had myopathic symptoms prior to, or at the time of, diagnosis of sarcoidosis. Only 3 patients developed symptomatic sarcoid myopathy more than one year after diagnosis of sarcoidosis. The most common additional sites of sarcoidosis involvement were lymph nodes, lung, eye, and neurosarcoidosis. CK, ESR, and CRP levels were elevated in fewer than 50% at the time of diagnosis of myopathy. Only one patient had positive myositis antibodies. All patients underwent EMGs, with 12 showing a myopathic pattern. 14 patients had a muscle biopsy, of which 12 revealed granulomatous inflammation. Regarding treatment decisions, only one patient received pulse glucocorticoid therapy. 13 patients were started on a glucocorticoid taper, with 8 continuing on glucocorticoid maintenance therapy. The most common second-line agent was methotrexate, followed by infliximab. Half of patients saw improvement in their symptoms or clinical remission, while the other half had stable disease despite immunosuppressive therapy.
Conclusions. Here we describe our institution's experience diagnosing and managing sarcoid myopathy. The majority of patients developed myopathy early in their disease course, and there were no reliable serologic markers for diagnosis. Clinical signs, in addition to EMGs and muscle biopsies, were most important diagnostically. Further efforts are needed to identify optimal treatment approaches.
Key words: sarcoidosis, sarcoid myopathy

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MYOSITIS DISEASE AND TREATMENT LANDSCAPE IN THE UNITED STATES AND GERMANY: RESULTS FROM A QUANTITATIVE PHYSICIAN SURVEY

Leonhard Stross[1*], Shelby C. Wilkinson[1*], Kristin Abramo[2], Tania González Rivera[1], Raj Tummala[1]
[1]Cabaletta Bio Inc., Philadelphia, USA, [2]Lumanity Inc., Boston, USA
[*]Co-first authors

Background. Idiopathic inflammatory myopathies (IIM, or myositis) are characterized by immune-mediated muscle and systemic inflammation, with significant symptom heterogeneity. With increased understanding of myositis pathogenesis, therapeutic development has increased, but the unmet need in myositis remains high, with limited evidence-based treatment guidance. This work aimed to shed light on the real-world myositis disease and treatment landscape in the United States and Germany.
Methods. Following qualitative interviews of 12 U.S. myositis experts, 339 myositis-treating physicians (239 U.S.; 100 German) were recruited between March and May 2025 to complete an online survey exploring treatment approach and refractoriness of their patient population, focused on dermatomyositis (DM), antisynthetase syndrome (ASyS), immune-mediated necrotizing myopathy (IMNM) and juvenile IIM (JIIM).
Results. In the U.S., ~40% of participants were academic tertiary hospital-based and ~60% were community hospital or practice-based. In Germany, ~60% of participants were hospital-based and ~40% were private, office-based. The specialties represented included rheumatologists (adult and pediatric), pulmonologists, and dermatologists. The autoantibody-based classification of myositis into subtypes DM, ASyS, IMNM was adopted by the majority of participants across geographies (~67%), but a significant number (~30%) used dermatomyositis and polymyositis classification only. Antibody testing was routinely performed by ~99% of participants.
Participants estimated mild, moderate, and severe disease in ~30-45%, ~30-40%, and ~25-30% of patients, respectively. U.S. participants reported a higher proportion of moderate-to-severe patients across subtypes. ~20-30% of moderate and ~30-40% of severe myositis patients had reached at least third line, with U.S. participants reporting a more refractory population. ~50% of severe myositis patients were on ≥3 medications versus ~33% of moderate patients.
Intravenous immunoglobulin (IVIg) use was reported in ~25-35% of moderate and ~30-45% of severe myositis cases, with U.S. participants reporting higher rates of use. In the U.S., academic physicians tended to employ IVIg earlier than community-based physicians In Germany, physicians in hospital-based practices used IVIg in later lines compared those in private office-based practices.
Major areas of unmet need identified in this research included increased rates and durability of response, steroid reduction, damage prevention and better treatment options.
Conclusions. Although the myositis landscape was reported as largely similar by U.S. and German physicians, there were differences in the reported population severity and medication use. Participants consistently reported a high unmet need for more effective treatment options with potential for immunomodulator- and steroid-free improvement, such as the opportunity represented by use of CD19-targeting chimeric antigen receptor (CAR) T cells.
Acknowledgements. We thank participating physicians for their contributions
Key words: treatment landscape, unmet need, disease severity

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STEROID INDUCED MYOPATHY AND TOXICITY AMONG DERMATOMYOSITIS PATIENTS USING THE GLUCOCORTICOID TOXICITY INDEX

Ailin He[1], Joshua Prenner[2], Cristina Gerera[3], Lorena Acevado[2,3], John Stone[4], Ruth Ann Vleugels[2], Rochelle Castillo[2,5]
[1]University Of New South Wales, Sydney, Australia, [2]Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, USA, [3]University of Puerto Rico, San Juan, Puerto Rico, [4]Department of Rheumatology, Massachusetts General Hospital, Harvard Medical School, Boston, USA, [5]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Harvard Medical School, Boston, USA

Background. Glucocorticoids remain the cornerstone of treatment for dermatomyositis (DM). However, prolonged courses of glucocorticoids are associated with numerous adverse effects. Steroid-induced myopathy is a well-recognized complication which can clinically mimic DM progression. Distinguishing between these pathologies is critical to reduce treatment-associated morbidity and prevent unnecessary escalation of immunosuppression. Steroid-induced myopathy among DM patients remains underreported in the literature.
Methods. A retrospective cohort study was conducted of DM patients diagnosed with steroid myopathy between 2015 and 2024 at Brigham and Women's Hospital. Patient demographics, clinical and laboratory findings, diagnostic workup and cumulative steroid exposure were analyzed. Total steroid toxicity was quantified using the Glucocorticoid Toxicity Index (GTI), a validated and standardized tool to assess the adverse effects of glucocorticoid therapy.
Results. Thirteen patients were included in the study. The median age was 57 years, and the average BMI was 30.3 kg/m^2. Steroid myopathy was suspected in cases of persistent or refractory muscle weakness with normal or downtrending inflammatory markers and muscle enzymes. Muscle weakness was primarily proximal and symmetric. The mean cumulative prednisone dose at symptom onset was 21,774 mg, with an earlier onset observed among patients who received intravenous pulse steroids. From baseline to the three-month follow-up visit, the majority of patients (69.2%) had a reduction in prednisone dose. Despite dose reduction, four patients continued to experience worsening glucocorticoid toxicity compared to baseline. The overall steroid burden was high, with an average cumulative worsening GTI score of 59.4. This surpassed the minimal clinically important difference score of 10 points. All patients with steroid myopathy experienced at least one additional steroid-related toxicity.
Conclusions. This study highlights the high steroid burden experienced by DM patients, and the importance of accurately diagnosing steroid-induced myopathy in order to minimize treatment morbidity and ensure appropriate management. In our cohort, patients treated with intravenous pulse steroids developed steroid myopathy earlier compared to patients treated with oral steroids alone. Additionally, even following steroid tapering, some patients experienced worsening toxicity, highlighting the importance of early initiation of steroid-sparing therapies in patients with dermatomyositis.
Acknowledgements. Dr Rochelle Castillo and Dr Ruth Ann Vleugels for their guidance and support on the project. Prof. Dedee Murrell for providing the opportunity to A. He to conduct the study at Brigham and Women's Hospital. Dr. Stone who provided an academic use license for the Steritas® Glucocorticoid Toxicity Index 2.0 web application.
Key words: dermatomyositis, steroid toxicity

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COMPARISON OF CLINICAL CHARACTERISTICS BETWEEN ANTI-MDA5 DERMATOMYOSITIS AND ANTI-SYNTHETASE SYNDROME PATIENTS IN A SOUTHEAST ASIAN COHORT

Choon Guan Chua[1], Hwee Pin Phua[1], Wei-Yen Lim[1], Mona Manghani[1]
[1]Tan Tock Seng Hospital, Singapore

Background. Anti-MDA5 Ab dermatomyositis (MDA5-DM) and anti-synthetase syndrome (ASyS) are distinct idiopathic inflammatory myopathies (IIM) subtypes with predilection for lung involvement. MDA5-DM has a strong association with rapidly-progressive interstitial lung disease (RP-ILD) which is highly lethal. We aim to determine the differences between these two IIM-subtypes in this retrospective review.
Methods. Chart review was performed for 119 consecutive IIM patients seen at our hospital between 1 January 2015 and 30 June 2021. Characteristics of IIM-subtypes were compared. All patients fulfilled at least probable disease by Bohan/Peter criteria and were sub-classified into IIM-subtypes based on 2017 ACR/EULAR classification criteria. ASyS fulfilled Connor's/Solomon's classification criteria. RP-ILD was defined as dyspnoea and/or hypoxaemia with worsening radiologic interstitial lung changes within 3 months of respiratory symptoms onset. Myositis autoantibodies were detected using EUROLINE Inflammatory Myopathies 16 Ag (IgG) commercial line immunoblot.
Results. 68/119 (57.1%) had dermatomyositis, 28/119 (23.5%) ASyS, 5/119 (4.2%) immune-mediated necrotising myopathy (IMNM), and 18/119 (15.1%) overlap myositis (OM). Amongst the dermatomyositis, 24/68 (35.3%) was positive for anti-MDA5 Ab. tRNA synthetase-targeted antibodies detected: 14 anti-Jo1, 10 anti-PL7, 4 anti-PL12, 2 anti-EJ (8 had >1 myositis specific autoantibodies). 50/119 (42%) had ILD – 23 ASyS, 18 dermatomyositis, 8 OM and 1 IMNM.
Comparing MDA5-DM and ASyS patients, both groups comprised mainly females (58.3% *vs*. 64.3%), were predominantly Chinese in ethnicity (62.5% *vs*. 82.1%) and with no significant difference in mean age of symptom onset (50.8 *vs*. 55.8; p=0.160). MDA5-DM had predominant cutaneous features compared to ASyS, particularly cutaneous ulcers, palmar papules, and violaceous rash (p<0.001). MDA5-DM also had more Gottron's sign (p=0.003), inverse Gottron's (p=0.003), periungual erythema (p=0.007) and heliotrope rash (p=0.016). No significant difference in predominance of mechanics hands was observed (MDA5-DM 45.8% *vs*. ASyS 35.7%, p=0.458).
ILD was observed in 15/24 (62.5%) MDA5-DM *vs*. 23/28 (82.1%) ASyS group (p=0.111). 8/24 (33.3%) MDA5-DM had RP-ILD *vs*. only 4/28 (14.3%) ASyS (p=0.186). All ASyS RP-ILD received high dose glucocorticoids and cyclophosphamide for induction therapy; 3 achieved disease control and 1 died from disease progression. All MDA5-DM RP-ILD received high dose glucocorticoids with various combinations of immunosuppressants that include cyclophosphamide, calcineurin inhibitors, rituximab, tofacitinib and intravenous immunoglobulin; 1 achieved disease control and the remaining died from disease progression and/or infections.
Conclusions. MDA5-DM and ASyS contribute significantly to our local IIM-ILD cohort. The MDA5-DM patients distinguish themselves from ASyS with distinct cutaneous manifestations. ASyS-RP-ILD was less frequent than MDA5-DM RP-ILD and more responsive to conventional immuno-suppressants.
Key words: anti-synthetase syndrome, dermatomyositis, interstitial lung disease

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SPORADIC LATE-ONSET NEMALINE MYOPATHY (SLONM): DATA FROM A CASE SERIES AND LITERATURE REVIEW OF 144 PATIENTS

Antonio Lauletta[1], Francesca Forcina[1], Gioia Merlonghi[1], Laura Fionda[1], Laura Tufano[1], Luca Leonardi[1], Rocco Costanzo[1], Elena Rossini[1], Demetrio Marando[1], Valentina Vera[1], Giovanni Antonini[1], Stefania Morino[1], Matteo Garibaldi[1]
[1]Neuromuscular and Rare Disease Centre, Department of Neuroscience, Mental Health and Sensory Organs (NESMOS), SAPIENZA University of Rome, Sant'Andrea Hospital, Rome, Italy

Background. Sporadic late-onset nemaline myopathy (SLONM) is an acquired myopathy presenting in adulthood with progressive proximal and axial muscle weakness. A substantial proportion of cases are associated with monoclonal gammopathy of undetermined significance (MGUS), referred to as SLONM-MGUS, suggesting a potential immune-mediated pathogenesis. Although the presence of MGUS has clinical and therapeutic implications, its exact role in disease severity and progression remains unclear. We aimed to characterize clinical, pathological, and prognostic differences between SLONM-MGUS and SLONM without MGUS (SLONM-noMGUS).
Methods. We conducted a systematic review of SLONM case series published over the past 25 years, supplemented by a single-center case series of five additional patients from our institution (Sant'Andrea Hospital, Rome). Eligible subjects included adult patients diagnosed with SLONM based on clinical features and muscle biopsy demonstrating nemaline rods. Data on

demographics, laboratory parameters, histopathological findings, treatments and outcomes were extracted and compared between SLONM-MGUS and SLONM-noMGUS cohorts.
Results. Of the 144 patients analyzed, 47% were classified as SLONM-MGUS. These patients exhibited more severe clinical manifestations, including increased respiratory involvement (p=0.006). Histopathologically, SLONM-MGUS revealed more prominent nemaline rods (p=0.032), often accompanied by cytoplasmic bodies and lobulated fibers, and frequently required repeat muscle biopsies for diagnosis (p=0.0285). Inflammatory infiltrates were less frequent in SLONM-MGUS (p=0.0176). Functional outcomes were significantly worse in this group, with reduced likelihood of full recovery (p=0.013) and higher rates of non-ambulatory status (p=0.01).
Patients receiving dual or more treatment regimens, particularly those including IVIg and/or autologous stem cell transplantation (ASCT), had more favorable outcomes.
Conclusions. These findings indicate that SLONM-MGUS represents a more severe phenotype of SLONM with distinct clinico-pathological features and poorer prognosis. Notably, combined treatment regimens, including IVIg and/or ASCT, were associated with improved outcomes, highlighting the importance of early recognition and aggressive therapeutic strategies in selected patients.
Key words: sporadic late-onset nemaline myopathy (SLONM), nemaline rods, monoclonal gammopathy of undetermined significance (MGUS), immune-mediated myopathy, autologous stem cell transplantation (ASCT), intravenous immunoglobulin (IVIg)

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MIMICKING CONDITIONS OF IDIOPATHIC INFLAMMATORY MYOPATHIES – AN ADAPT SUB-STUDY

Pinar Özkaynar[1], Sanne Evers[1], Saloua Tanan[1], Joost Raaphorst[1], Anneke van der Kooi[1]
[1]*Department of Neurology and Clinical Neurophysiology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands*

Background. Reaching a diagnosis of idiopathic inflammatory myopathy (IIM) can be challenging, due to overlap in clinical presentation with a range of mimicking conditions, so called mimics. This study aimed to provide an overview of IIM-mimics in an overcomplete diagnostic design (the ADAPT study) and identify differentiating clinical and ancillary findings.
Methods. This study is a sub-study of the ADAPT study, in which patients were prospectively included with a clinical suspicion of IIM, defined as subacute (<12 months) proximal muscle weakness leading to functional limitations and justifying immunosuppressive treatment (1). All patients underwent structured clinical and ancillary assessments: history and physical examination, muscle enzymes and line-blot autoantibody testing, muscle imaging, electromyography and muscle biopsy. Mimicking conditions were identified and clinical and ancillary findings were compared between IIM and mimics using descriptive statistics.
Results. 100 patients were included (56% female, mean age 60 years (SD 13.6)), of which 67 had IIM. Mimicking conditions (n=33) included amyloid myopathy (n=3), inclusion body myositis (IBM, n=3), vasculitis (n=3), polymyalgia rheumatica (PMR, n=3), rhabdomyolysis (n=3), axonal polyneuropathy (n=3), chronic inflammatory demyelinating polyneuropathy (n=2), Lambert-Eaton myasthenic syndrome (LEMS, n=2) and other diagnoses (n=11, of which 8 of uncertain etiology). IIM-specific cutaneous lesions (*i.e.* Gottron's papules, heliotrope erythema, periorbital edema, shawl sign or mechanic's hands) were more prevalent in IIM (32% *vs.* 12%, p=0.02). Characteristics of muscle weakness (*i.e.* symmetry, bulbar involvement, progression) did not differ between IIM and mimics. Discriminating ancillary findings between IIM and mimics included serum CK elevation (1.5 times ULN; 82% *vs.* 33%, p<0.001), the presence of myositis specific autoantibodies (MSAs; 66% *vs.* 3%, p<0.001), fascial edema on muscle MRI (37% *vs.* 12%, p=0.01) and MHC class I antigen positivity (76% *vs.* 21%, p<0.001) in muscle biopsies.
Conclusions. This study provides insight in the mimicking conditions of IIM, and explored discriminating clinical and ancillary findings. Early recognition of mimics could aid in the diagnostic trajectory, reduce diagnostic delay and facilitate timely initiation of adequate treatment.
Acknowledgements. We acknowledge the ADAPT study team and participating patients for their contribution to the data this sub-study analyzed.
Key words: IIM, mimicking conditions, diagnosis

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CLINICAL COURSE, THERAPEUTIC MANAGEMENT, AND LIPID-LOWERING THERAPY IN A COHORT OF PATIENTS WITH ANTI-HMGCR IMMUNE-MEDIATED NECROTIZING MYOPATHY (IMNM)

Alberto Paladini[1], Eleonora Antonelli[2], Maria Giovanna Danieli[1], Gianluca Moroncini[1,2]
[1]*Clinica Medica, Department of Clinical and Molecular Sciences, Marche Polytechnic University, Ancona, Italy,* [2]*Internal Medicine Residency Program, Marche Polytechnic University, Ancona, Italy*

Background. Immune-mediated necrotizing myopathy (IMNM) is a rare subtype of idiopathic inflammatory myopathies (IIM) characterized by subacute or rapidly progressive symmetric proximal muscle weakness and markedly elevated serum creatine kinase (CK) levels. Muscle biopsy typically reveals necrosis and regeneration of muscle fibers with inflammatory infiltrates mainly composed of macrophages. The presence of anti-3-hydroxy-3-methylglutaryl-coenzyme-A-reductase (anti-HMGCR) antibodies, frequently associated with prior statin exposure, defines a distinct serological subset.
Methods. We retrospectively analyzed 15 consecutive patients with anti-HMGCR IMNM diagnosed between January 2021 and October 2025 at Clinica Medica, Marche University Hospital (Ancona, Italy). Diagnosis was based on clinical features, serological profile, and muscle enzyme elevation, fulfilling the 2017 ENMC criteria. Demographic, clinical, laboratory, histopathologic and therapeutic data were collected and analyzed.
Results. The cohort included 9 females (60%) with a mean age at diagnosis of 67±9.3 years and a median follow-up of 16.5 months (IQR 8.4–29.4). Six patients (40%) presented with dysphagia, and one with interstitial lung disease. No malignancies were detected at diagnosis or during follow-up. Median CK level at diagnosis was 6468 U/L (IQR 4798–11,145), and median MMT8 score was 135 (IQR 124–138). All patients had prior statin exposure with a median time of exposure of 1.38 years (IQR 1.24–3.08); one patient died three months after the diagnosis due to infectious complications.
Initial treatment was high-dose prednisone (1 mg/kg/day) in all but three patients that also received intravenous methylprednisolone pulses. Methotrexate was the most frequently used first-line steroid-sparing agent (10 patients), followed by mycophenolate mofetil (2) and intravenous immunoglobulins (2). Seven patients required second-line therapy (rituximab, mycophenolate mofetil, or IVIg), and two received third-line treatment with mycophenolate and IVIg.
Lipid-lowering therapy was modified in all patients: six received PCSK9 inhibitors, three inclisiran, and eight bempedoic acid/ezetimibe, with combination regimens in five cases. All treatments were effective and well tolerated, with no adverse events reported. Mean lipid levels at latest follow-up were: total cholesterol 142±23 mg/dL, HDL 60±14 mg/dL, triglycerides 101±43 mg/dL, LDL-C 61±20 mg/dL. All patients, except two with a partial response, achieved complete remission. Median CK level at the follow-up was 99 U/L (IQR 61.5–651.5).
Conclusions. Anti-HMGCR IMNM represents a clinically heterogeneous but potentially severe myopathy. Long-term management requires a multidisciplinary approach considering both immunosuppressant therapy and cardiovascular risk factors. Novel lipid-lowering agents appear to be a safe alternative in these patients.
Acknowledgements. National Recovery and Resilience Plan (NRRP), Project "HEAL ITALIA"
Key words: IMNM, lipid-lowering therapy, necrotizing myositis

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EVALUATION OF GLP-1-RECEPTOR AGONIST USE IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: A RETROSPECTIVE ANALYSIS

Nadean F. Alnajjar[1,2], Joshua C. Prenner[1], Marissa M. Camillucci[1], Ruth Ann Vleugels[1], Rochelle Castillo[1,2]
[1]Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, USA, [2]Division of Rheumatology, Inflammation, and Immunity, Brigham and Women's Hospital, Harvard Medical School, Boston, USA

Background. Glucagon-like peptide-1 receptor agonists (GLP-1-RAs), widely used for diabetes and obesity, may potentially alleviate muscle inflammation (1, 2), but data in idiopathic inflammatory myopathies (IIMs) are limited. This retrospective analysis evaluated their safety by assessing disease activity outcomes in a myositis population.
Methods. Fifty-two patients from a dual-institution database with a confirmed myositis diagnosis who had used a GLP-1-RA were analyzed.
Results. The patient population was predominantly female (75%), with a mean age of 57.7 years at GLP-1-RA initiation. The most common myositis variants were dermatomyositis (48.1%), anti-synthetase syndrome (23.1%), and polymyositis (13.5%). We compared the presence of active skin, muscle, or lung involvement before (average: 2.8 months) and after (average: 25.6 months) GLP-1-RA initiation. The median duration of GLP-1-RA use was 25 months. Before GLP-1-RA initiation, active involvement was present in the skin of 13 patients (25.0%), muscles of 30 (57.7%), and lungs of 14 (26.9%); overall, 41 patients had at least one active domain (78.8%). After initiation, involvement decreased to 9 (17.3%), 23 (44.2%), and 13 (25.0%) patients, respectively, with 33 patients having any active domain (63.5%). There was no statistically significant change for skin (χ^2=0.90, p=0.34), muscle (χ^2=1.56, p=0.21), or lung (χ^2=0.00, p=1.00) between the index pre- and post-GLP-1-RA visits, although the reduction in patients with any active domain approached significance (p=0.07). At the post-GLP-1-RA visit, 82.7% of patients had a stable or tapered immunosuppressive regimen compared with baseline. Creatinine kinase and aldolase levels showed no significant changes between pre- and post-GLP-1-RA visits. Mean BMI decreased by 2.95 kg/m^2 (p<0.001) and HbA1c by 0.79% (p<0.001) with GLP-1-RA use. Thirteen patients (25%) discontinued GLP-1-RAs, primarily due to gastrointestinal side effects or insurance issues. Only one case of increased muscle weakness was attributed to GLP-1-RA use.
Conclusions. Our findings suggest that the addition of GLP-1-RAs to standard treatments was well-tolerated in patients with IIM. Limitations include a small sample size and issues of adherence with GLP-1-RAs. Further multi-institutional, prospective studies are needed to investigate the impact of GLP-1-RAs on disease activity in this population.
Key words: glucagon-like peptide-1 receptor agonist, idiopathic inflammatory myopathy

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PATIENT-BASED MYOSITIS REGISTRY IN GERMANY

Karsten Kummer[1], Martin Hofmann[1], Hans-Werner Rausch[2], Felix Kleefeld[3], Jan-Gerd Rademacher[4], Maggie Walter[5], Jens Schmidt[1]
[1]Medical School Brandenburg, Rüdersdorf, Germany, [2]University Medicine Mannheim, Mannheim, Germany, [3]University Medicine Bochum, Bochum, Germany, [4]University Medicine Göttingen, Göttingen, Germany, [5]Friedrich-Baur-Institute, München, Germany

Background. Myositis disorders include polymyositis (PM), dermatomyositis (DM), anti-synthetase syndrome (ASD), immune-mediated necrotizing myopathy (IMNM) and IBM. All of these diseases are clearly considered rare diseases. The prevalence of IBM in all age groups is thought to be 14.9 per million. The prevalence of polymyositis and dermatomyositis is estimated to be up to 21.5 per 100,000. The inflammatory myopathies are heterogeneous and manifest themselves at any age. They often lead to chronic morbidity and increased mortality. The advances that have been made in recent decades have highlighted the immunological basis of inflammatory myopathies but have not yet led to significant improvements in treatment, particularly in chronic diseases. Natural history data and controlled clinical trials are often lacking.
Small patient populations are the biggest obstacle to progress in the research and treatment of rare diseases.
Methods. A harmonized dataset including clinical data and muscle biopsy reports will be recorded using a dual patient and professional web-based platform, already used and validated in many other rare neuromuscular diseases. The baseline data questionnaire and registry items have been developed in cooperation with the members of MYOSITIS NETZ. To analyse the natural history of inflammatory myopathies follow-up data will be collected. National legislation, data protection laws and ethical recommendations are strictly followed in this process. The registry aims at collecting high-quality, curated and regularly updated longitudinal data of myositis patients.
Results. The patient-based registry will collect data for a better understanding of natural history and to improve standard of care, including epidemiological data, classification of myositis, muscle histopathology, antibody status, organ involvement (*e.g.* interstitial lung disease), present and past medication, comorbidities and PROMs evaluating the Activities of daily live, the Quality of Life, questionnaires for dysphagia and specific PROMs, *e.g.* the IBM functional rating scale (IBM-FRS).
Conclusions. The data derived from the patient-based myositis registry will help to improve diagnostic algorithms and enable successful patient recruitment for treatment studies. In addition, the registry will enable longitudinal studies that provide urgently needed data on the natural course and general care of inflammatory myopathies. In the long term, the proposed registry will help to improve diagnostic and therapeutic efforts in the care of patients with rare inflammatory myopathies.
Acknowledgements. The German patient-based myositis registry was funded by Myositis Netz and Argenx.
Key words: Myositis Registry

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UNMASKING THE COMORBIDITY LANDSCAPE IN IDIOPATHIC INFLAMMATORY MYOPATHIES: A POPULATION-BASED COMPARISON

Miguel Afonso Martins[1,2], Bianca Pulo Correia[1,2], Inês Sopa[1,2], Mariana P. Silva[1,2], Matilde Bandeira[1,2], Ana Rita Henriques[3], Ana Maria Rodrigues[3], João Miguel Pereira[2], Filipa Costa[1,2], Sofia C. Bandeira[1,2], Raquel Campanilho-Marques[1,2]
[1]Unidade Local De Saúde De Santa Maria (ULSSM), Lisbon, Portugal, [2]Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa (CAML), Lisbon, Portugal, [3]Comprehensive Health Research Centre, NOVA Medical School, Universidade NOVA de Lisboa, Lisbon, Portugal

Background. Idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of autoimmune diseases characterized by chronic muscle inflammation and systemic involvement. Beyond organ-specific manifestations, patients with IIM often present multiple comorbidities.
Objectives. To characterize the comorbidity profile of Portuguese patients with IIM and compare it with matched controls without rheumatic disease. Secondary aims included assessing multimorbidity prevalence and associations with clinical subtypes, disease activity, and treatment.
Methods. A cross-sectional, case-control study was conducted using retrospective data from a tertiary Myositis Outpatient Clinic. Controls were selected from the population-based EpiReumaPt study (2011–2013), matched (2:1) by sex, age, and region. Multimorbidity was defined as ≥3 comorbidities from distinct disease categories. Appropriate statistical tests were applied, with Holm–Bonferroni correction for multiple comparisons and binary logistic regression used for multivariable analysis.
Results. We included 133 IIM patients [71.4% female; mean age 56.2±17.4 years; mean disease duration 6.8±5.2 years] and 266 matched controls. Among patients with IIM, the most frequent comorbidities were hypertension (30.1%), dyslipidaemia (21.8%), diabetes (16.5%), gastrointestinal (15.8%), osteoporosis (15.8%), psychiatric (15.8%), and neurological disease (10.5%); 5.3% required hospitalization for severe infection. Skin involvement was associated with lower rates of cardiac disease (p=0.037) and of dyslipidemia (p<0.001), while bDMARD treatment was associated with lower odds of dyslipidemia (OR 0.45, 95% CI 0.22–0.91, p=0.026).

Within IIM patients, lower MMT8 at baseline (p=0.042) and older age (p<0.001) were associated with multimorbidity, but only skin involvement (OR 0.27, 95% CI 0.09–0.81, p=0.020) and age (OR 1.10, 95% CI 1.05–1.14, p<0.001) remained significant in multivariate analysis.
Compared with controls, IIM patients had higher multimorbidity (30.8% *vs*. 13.2%; p≤0.001), and more lung (12.8% *vs*. 4.9%), gastrointestinal (15.8% *vs*. 6.8%), neurological (10.5% *vs*. 1.9%), and osteoporotic disease (15.8% *vs*. 1.5%) (all p<0.045).
In multivariable analysis adjusted for sex and smoking, older age (OR 1.10, 95% CI 1.07–1.13; p<0.001) and IIM diagnosis (OR 4.63, 95% CI 2.32–9.24; p<0.001) were independently associated with multimorbidity.
Conclusions. Comorbidities are frequent in idiopathic inflammatory myopathies, exceeding those in the general population. Older age independently predicted multimorbidity, whereas skin involvement showed a protective association. Biologic therapy was associated with lower dyslipidaemia rates. These findings highlight the need for systematic comorbidity screening and multidisciplinary management in IIM care.
Key words: comorbidities, multimorbidity

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PATIENT PERSPECTIVES ON NUTRITION IN IDIOPATHIC INFLAMMATORY MYOPATHIES: AN ANALYSIS OF ONLINE DISCUSSIONS

Peter Kerkhof[1], Taanya Talreja[2,3], Linda Kobert[4], Latika Gupta[5,6,7]
[1]Dept. Communication Science, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands, [2]Seth GS Medical College, Mumbai, India, [3]KEM Hospital, Mumbai, India, [4]The Myositis Association, USA, [5]School of Infection, Inflammation and Immunology, College of Medicine and Health, University of Birmingham, Birmingham, UK, [6]Royal Wolverhampton NHS Trust, Wolverhampton, UK, [7]Francis Crick Institute, London, UK

Background. Patients with idiopathic inflammatory myopathies (IIMs) increasingly use social media to connect with peers, share experiences, and exchange health information. These platforms allow discussion of topics that receive limited attention in clinical care, such as nutrition and diet. Reddit, a large discussion-based platform organized into topic-specific communities ('subreddits'), offers a valuable setting to observe such patient-driven exchanges. This study analyzed Reddit posts about myositis to examine the frequency, content, and dynamics of diet-related discussions, providing insight into the nutrition-related concerns patients prioritize.
Method: Data were obtained from Reddit data dumps (up to August 2025) hosted on AcademicTorrents.com (>26 billion posts). Posts mentioning IIMs or from IIM-related subreddits were identified (n=43,147). After cleaning, 18,374 posts from 7,033 authors were classified as IIM-related. Posts containing any of 190 nutritional terms were extracted, and a large language model (GPT-4o) identified those written by users with, or suspecting, myositis. Model validation on 200 manually coded posts showed high precision (0.92) and moderate recall (0.75). The resulting 409 posts were analyzed for prevalent nutrition terms and their co-occurrence patterns using semantic network analysis. A parallel dataset on non-inflammatory muscular disease is currently being analyzed to compare the role of nutrition and diet across both disease types.
Results. 'Diet' appeared in 51.1% of the 409 posts. Beyond general words such as eat and food, frequently used terms included protein (11.7%), sugar (9.8%), vitamin (9.5%), gluten (8.1%), and magnesium (5.1%). This reflects a strong focus on diet and micronutrients, indicating patient interest in self-management through nutritional choices.
The semantic network revealed three main clusters. The first cluster concerns supplements and deficiency testing: magnesium, vitamin, iron, and calcium clustered with check, test, and weakness, reflecting discussions of nutrient deficiencies, supplementation, and lab monitoring. The second cluster focuses on macronutrient management: weight, fat, energy, protein, steroid, and meal co-occurred, suggesting attempts to balance diet and manage side effects of corticosteroid therapy. The third cluster highlights specific diets and triggers: gluten, dairy, and inflammation were often mentioned together, indicating experimentation with elimination or 'anti-inflammatory' diets to manage symptoms.
Conclusions. Diet is a central topic in patient discussions about myositis, reflecting active efforts to self-manage the disease through nutrition. Patients focus on correcting deficiencies, managing medication-related effects, and reducing inflammation through dietary adjustments – using nutrition as a tool to influence both symptoms and overall well-being.
Key words: social media, patient self-management, nutrition

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INDUCTION OF EXPERIMENTAL AUTOIMMUNE MYOSITIS BY TIF-1γ MRNA-LNP IMMUNIZATION IN MICE

Xiaoyan Xing[1,2], Liang Zhao[1,2], Yuhui Li[1,2], Jing He[1,2]
[1]Department of Rheumatology and Immunology and Beijing Key Laboratory for Rheumatism and Immune Diagnosis (BZ0135), Peking University People's Hospital, Beijing, China, [2]Center of Clinical Immunology, Peking University, Beijing, China

Background. TIF-1γ (TRIM33)-associated myositis is characterized by TIF-1γ-specific autoimmunity and inflammatory muscle pathology, yet reproducible experimental models remain limited. We evaluated whether lipid nanoparticle-encapsulated TIF-1γ mRNA immunization is sufficient to break skeletal muscle immune tolerance and recapitulate key pathological features of TIF-1γ-associated myositis in mice.
Methods. Female C57BL/6 mice were immunized with LNP-based TIF-1γ mRNA vaccine by intramuscular injection into the hamstring on days 0, 7, 14, and 24 with TIF-1γ mRNA-LNP (10 μg per dose). Serum samples were collected 14 days after the final immunization and anti-TIF-1γ antibody levels were quantified by enzyme-linked immunosorbent assay (ELISA). In parallel, bilateral hamstring and quadriceps muscles were subjected to histopathological evaluation, with muscle pathology scored based on myofiber necrosis and regeneration, lymphocytic infiltration, and interstitial alterations.
Results. Mice immunized with TIF-1γ mRNA-LNP exhibited significantly elevated anti-TIF-1γ antibody levels compared with control mice. Histopathological examination of the hamstring and quadriceps muscles in the TIF-1γ mRNA-LNP group revealed characteristic features of inflammatory myopathy, including endomysial and perimysial lymphocytic infiltration, focal myofiber necrosis, increased numbers of centrally nucleated regenerating fibers, and mild interstitial expansion. Accordingly, pathological scores were significantly higher than those observed in control groups (p<0.05). In a subset of mice, inflammatory infiltrates were also detected in contralateral, non-injected muscles, indicating partial systemic or distal muscle involvement.
Conclusions. Under the dosing and immunization regimen employed, TIF-1γ mRNA-LNP immunization induced robust TIF-1γ-specific antibody responses and inflammatory myositis with characteristic pathological features. These findings support that mRNA-based immunization targeting TIF-1γ is sufficient to overcome local skeletal muscle immune tolerance and establish a reproducible experimental model of TIF-1γ-associated myositis. This model provides a tractable platform for mechanistic investigations and for the preclinical evaluation of targeted immunomodulatory therapies.

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IDENTIFYING IDIOPATHIC INFLAMMATORY MYOPATHIES FROM ELECTRONIC HEALTH RECORD DATA WITH NATURAL LANGUAGE PROCESSING AND MACHINE LEARNING

Valle A.[1], Vo A.[1], Castillo R.[1], Kawano Y.[1], Love Z.[1], Qi Y.[1], Cai T.[2,3], Solomon D.[1], Feldman C.[1*], Liao K.[1,2*]
[1]Division of Rheumatology, Immunology and Inflammation, Brigham and Women's Hospital, [2]Harvard Medical School, [3]Harvard T.H. Chan School of Public Health

Background. Studies of idiopathic inflammatory myopathies (IIMs) using real-world electronic health record (EHR) data have applied published rule-based algorithms with ICD codes to assemble cohorts. In a prior study using EHR data, one rule-based algorithm achieved a positive predictive value (PPV) of 84% at the cost of sensitivity (14%), thus, limiting the size of the study population. We hypothesized that the addition of information from the clinical notes extracted using natural language processing (NLP) for use in a machine learning (ML) algorithm combined with diagnoses codes can increase sensitivity without reducing the PPV.
Methods. We identified subjects with ≥1 ICD 9/10 codes for IIM (359.7*, 710.3, 710.4, G72.4*, M33.*, M36.*) from 1/1/2000 to 9/6/2024 (n=5,684) from a multi-institutional EHR. From this cohort, a random sample of 250 subjects were selected for chart review by two independent reviewers. Charts were classified as definite, possible, probable, or unlikely cases based on the 2017 EULAR/ACR Classification Criteria for IIM. Definite, probable, or possible were considered as cases. ICD 9/10 codes were mapped to parent phenotype codes (phecodes). We applied the knowledge-drive online multi-

modal automated phenotyping system (KOMAP) to develop the algorithm. Briefly, structured, *e.g.* ICD codes, and NLP features related to IIM were extracted for all subjects. An IIM algorithm was developed using unsupervised ML methods. The final algorithm outputs a probability of IIM for each subject. Subjects with a probability of IIM corresponding to a PPV ≥84% (the best PPV from the rule-based approaches) were considered as having IIM. The sensitivity corresponding to the PPV of 84% were calculated to compare KOMAP with the rule-based approach.
Results. Of the 250 subjects, there were 118 IIM cases: 87 definite, 28 probable, 3 possible; the remaining 132 subjects unlikely IIM. At 84% PPV, KOMAP identified subjects with a sensitivity of 46% compared to 14% using the rule-based approach. This difference translated to n=1151 subjects classified as IIM compared to 432 with the rule-based approach. The top 3 features used in KOMAP in order of importance were: mentions of myositis from the notes extracted using NLP, number of encounters with the healthcare system, phecodes corresponding to myositis (359, 709, 770).
Conclusions. An unsupervised ML algorithm incorporating NLP identified 62% more subjects with IIM compared to the rule-based algorithm at the same level of accuracy. This study demonstrated the utility of NLP and ML to advance studies of IIM starting with improving the ability to identify IIM cases for downstream studies.
Key words: myositis, identification, machine learning, natural language processing

Pathogenesis of Inflammatory Myopathy

P-8

PLASMACYTOID DENDRITIC CELLS AND ER STRESS COOPERATE TO DRIVE FIBROBLAST ACTIVATION: IMPLICATIONS FOR MYOSITIS-ASSOCIATED TISSUE FIBROSIS

Mariana D. Machado[1], Beatriz H. Ferreira[1], Carolina Mazeda[2], Catarina R. Silva[2], Eduardo Dourado[2], Camila Castro[1], Fátima Leite-Pinheiro[1], Andreia Mendes[1], Luís Mendes[1], Adrienne W. Paton[3], James C. Paton[3], Philippe Pierre[1,4], Catarina R. Almeida[1]
[1]iBiMED - Institute of Biomedicine; Department of Medical Sciences; University of Aveiro, Aveiro, Portugal, [2]Unidade Local de Saúde da Região de Aveiro, Rheumatology Department, Aveiro, Portugal, [3]Department of Molecular and Biomedical Science, Research Centre for Infectious Diseases, University of Adelaide, Adelaide, Australia, [4]Aix Marseille Univ, CNRS, INSERM, CIML, Centre d'Immunologie de Marseille-Luminy, Marseille, France

Background. Plasmacytoid Dendritic Cells (pDC), major producers of type I interferon (IFN-I), infiltrate inflamed muscle and skin in dermatomyositis and contribute to the strong IFN signature observed in several Idiopathic Inflammatory Myopathies (IIM) subtypes. Because of their high secretory activity, pDC have a prominent endoplasmic reticulum (ER) and basal ER stress, and ER-stress pathways modulate their activation. Here, we are exploring how ER stress in pDC shapes fibroblast activation and may thus contribute to fibrosis development.
Methods. We established an in vitro co-culture system of the human pDC line CAL-1 and human lung fibroblasts (IMR-90). Mono- and co-cultures were exposed to the ER-stress inducers tunicamycin, subtilase cytotoxin (SubAB), and HA-15, with or without the TLR7 agonist CL307. Expression of extracellular matrix (ECM) proteins and activation markers was assessed by immunoblotting and RT-qPCR.
Results. CAL-1 cells established stable physical contacts with IMR-90 fibroblasts in co-culture. Exposure of pDC–fibroblast co-cultures to SubAB or HA-15 increased fibronectin and α-smooth muscle actin (α-SMA) expression compared with untreated co-cultures. This profibrotic effect was lost when PERK (an ER-stress sensor) was absent in CAL-1 cells, whereas STING deficiency did not modify fibroblast responses, demonstrating a PERK-dependent, STING-independent pathway in CAL-1 cells-mediated fibroblast activation. Combining ER-stress induction with TLR7 stimulation synergistically enhanced IFN-I production by CAL-1 cells but did not further increase ECM protein expression in IMR-90 fibroblasts, suggesting that IFN-I is not the main driver of ER-stress-induced fibroblast activation in this setting. Conditioned media from SubAB-treated mono- or co-cultures failed to induce fibronectin or α-SMA up-regulation, indicating that direct cell-to-cell contact between pDC and fibroblasts is required.
Conclusions. Our data show that ER stress in pDC promotes direct, contact-dependent activation of fibroblasts through PERK signalling, independently of STING activation and of increased IFN-I production. Given the major contribution of tissue fibrosis and interstitial lung disease to disability and mortality in IIM, these findings support pDC–ER-stress pathways as potential therapeutic targets to limit progressive fibrotic remodelling in myositis and related connective tissue diseases.
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Key words: pDC, Type I IFN, ER stress

P-36

CD73LOW B CELL PHENOTYPES AND DISTINCT CYTOKINE PROFILES IN PATIENTS WITH ACTIVE ANTI-JO-1 ANTIBODY POSITIVE IDIOPATHIC INFLAMMATORY MYOPATHIES

Nakazawa M.[1], Horuluoglu B.[1], de Vries C.[1], Lodin K.[1,2], Malmström V.[1], Lundberg I.[1,2], Grönwall C.[1]
[1]Division of Rheumatology, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Karolinska University Hospital, Center for Molecular Medicine, [2]Department of Gastro, Dermatology and Rheumatology, Karolinska University Hospital

Background. We performed multi-parameter phenotyping of peripheral B cells in anti-Jo-1 antibody positive idiopathic inflammatory myopathies (IIM) to delineate disease associated immunological profiles and the influence of B cells on disease activity.
Methods. Purified B cells from peripheral blood mononuclear cells from 16 patients with anti-Jo-1 antibody positive IIM (7 with untreated active IIM, 4 with active and treated IIM and 5 with inactive IIM) were analyzed by multi-parameter spectral flowcytometry. Dimensionality reduction and clustering analysis were applied to pre-gated CD19+ B cells. Serum levels of twenty-one cytokines and anti-Jo-1 IgG autoantibodies were determined. All patients with IIM in this study were positive for anti-Jo-1 antibody.
Results. Anti-Jo-1 antibody levels correlated positively to disease activity. Flow cytometry demonstrated B cell dysregulation with a significantly lower CD73 expression on naive, switched memory, and double negative B cells in patients with active IIM. Clustering analysis further revealed expansions of CD73- IgM+ naive B cells and CD73- CD95+ switched memory B cells in active IIM. In unswitched memory B cells, CD73+ CD21+ cells were decreased in active IIM. Patients with active IIM had significantly higher serum levels of BAFF, IP-10, IL-6 and sCD40L which correlated with changes in B cell populations.
Conclusions. Since CD73 has an immunoregulatory function by modulating the ATP/adenosine pathway (1), which is also targeted by methotrexate (2, 3), the low CD73 B cell expression in anti-Jo-1 antibody-positive IIM may lead to B cell hyperactivation. These novel findings further highlight B cells as central in the pathogenesis of IIM and important therapeutic targets.
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Key words: anti-Jo-1 antibody, B cells, CD73

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P-37

INVOLVEMENT OF TYPE I INTERFERON (IFN) RECEPTOR SIGNALING IN SERUM-MEDIATED MUSCLE WEAKNESS IN DERMATOMYOSITIS

Kaewin S.[1], Leijding C.[1], Gastaldello S.[1], Zhong Y.[1,2,3], Andreasson K.[4,5], Horuluoglu B.[2,4], Dastmalchi M.[2,4,6], Lauschke V.[1,2,7,8,9], Alexanderson H.[4,5], Lundberg I.[2,4,6], Andersson D.[1,10]

[1]Department of Physiology and Pharmacology, Karolinska Institutet, [2]Center for Molecular Medicine, Karolinska University Hospital, [3]Pharmaceutical Informatics Institute, College of Pharmaceutical Sciences, Zhejiang University, [4]Department of Medicine, Division of Rheumatology, Karolinska Institutet, [5]Women's Health and Allied Health Professionals Theme, Medical Unit Allied Health Professionals, Karolinska University Hospital, [6]Department of Gastro, Dermatology and Rheumatology, Theme Inflammation and Aging, Karolinska University Hospital, [7]Dr Margarete Fischer-Bosch Institute of Clinical Pharmacology, [8]University of Tübingen, [9]Department of Pharmacy, the Second Xiangya Hospital, Central South University, [10]Heart, Vascular and Neurology Theme, Cardiology Unit, Karolinska University Hospital

Background. Dermatomyositis (DM) is a major subtype of idiopathic inflammatory myopathies (IIMs) and is characterized by muscle weakness, cutaneous lesions and systemic inflammation. Upregulation of type I interferon (IFN)-stimulated genes (ISGs) have been found in muscle, skin and peripheral blood in patients with DM. However, the role of type I IFN and serum-mediated pathology remains unclear for the muscle weakness phenotype in DM. This study aims to study effects of IFN-α/β receptor 1 (IFNAR1) agonists and blockade on muscle force generation to investigate type I IFN signaling in DM serum-induced muscle weakness.

Methods. An experimental platform was used where isolated mouse muscles were exposed to serum from patients with DM or healthy control serum. Flexor digitorum brevis (FDB) muscles were isolated from healthy C57BL/6JRj mice and exposed for 24h to 10% serum from control or serum from patients with DM. To determine whether inhibition of type I IFN protects from DM serum-induced muscle weakness, an IFNAR1 blocking antibody or a JAK/STAT inhibitor (ruxolitinib) was used. Isolated FDB muscles were pre-incubated with IFNAR1 antibody or ruxolitinib for 2h and thereafter incubated in serum. To investigate the effect of IFN-α and/or IFN-β on muscle force generation, muscles were incubated in healthy control serum containing IFN-α and/or IFN-β. Bulk RNA sequencing, followed by bioinformatics analysis, was conducted to identify differentially expressed genes and affected pathways related to blockade of interferon signaling in our DM muscle model.

Results. Serum from patients with DM, but not healthy controls, induced significant muscle weakness in FDB muscle manifested by reductions in muscle force. Inhibition of type I IFN signaling with IFNAR1 antibody or ruxolitinib significantly diminished the detrimental effect of DM serum on muscle force. Exposure to IFN-α or IFN-β for 24h did not induce muscle weakness in FDB muscles. However, concomitant IFN-α and IFN-β exposure induced a decline in muscle force. Bioinformatic analyses revealed down-regulation of IFN1-inducible genes and pathway analysis displayed significant enrichment of numerous IFN-related pathways.

Conclusions. Serum from patients with DM can induce muscle weakness via pathways dependent on type I IFN receptor signaling. Factors in serum from patients with DM activates the type I IFN signaling pathway in mature skeletal muscles, representing mechanisms that ultimately links to muscle weakness in DM. This supports a model where systemic factors contribute to the disease phenotype with muscle dysfunction and highlight therapeutic possibilities of pharmacological interventions that target the IFNAR1 signaling pathway.

Key words: dermatomyositis, muscle weakness, type I IFN, JAK/STAT inhibition, disease model

P-56

THE ROLE OF SIGLEC1 IN THE PATHOGENESIS OF IDIOPATHIC INFLAMMATORY MYOPATHIES

Sylvia Raftopoulou[1], Lefteria Papa[1], Charalampos Skarlis[1], Clio Mavragani[1,2,3]

[1]Department of Physiology, Medical School, National and Kapodistrian University of Athens, Athens, Greece, [2]Department of Pathophysiology, Medical School, National and Kapodistrian University of Athens, Athens, Greece, [3]Department of Pathophysiology, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Background. Idiopathic inflammatory myopathies (IIMs) are rare systemic autoimmune diseases with diverse clinical manifestations. Genomic and proteomic studies have highlighted the importance of type I interferons (IFNs) in IIM pathogenesis, both in muscle tissue and peripheral blood. The sialic acid-binding Ig-like lectin 1 (Siglec1/CD169) has emerged as a candidate biomarker reflecting type I IFN activity. This study evaluated whether Siglec1 expression on monocytes serves as an independent biomarker for type I IFN gene activity in patients presenting with IIM-like symptoms.

Methods. Forty consecutive, untreated patients with suspected IIM, classified according to the 2017 EULAR/ACR criteria, were enrolled. Siglec1 expression on monocyte subsets was measured by flow cytometry using a six-colour panel on a FACSymphony A3 (BD Biosciences). RNA extraction, cDNA synthesis, and qPCR were performed on matched samples to quantify the expression of selected interferon-stimulated genes (ISGs). Myositis-specific and myositis-associated autoantibodies (MSAs/MAAs) were detected using the EUROLINE Autoimmune Inflammatory Myopathies 18 Ag (IgG) line immunoassay. Ten healthy controls (HCs) were included for comparison. All participants provided written informed consent, and data analysis was performed in Python (v3.13).

Results. Siglec1 expression on monocytes was significantly increased in patients versus HCs. Intermediate monocytes showed the highest Siglec1 expression (median 9.5% *vs*.3.8%, p=0.0454), followed by classical monocytes (1.3% *vs*. 0.5%, p=0.0079), while non-classical monocytes showed no difference (0.7% *vs*. 0.9%, p=0.8746). ISGs including MX1 (p=0.0003), ISG15 (p=0.0009), SIGLEC1 (p=0.003), IFI6 (p=0.0004), and GBP1 (p=0.002) were upregulated in patients. Strong correlations were observed between Siglec1 protein expression on classical monocytes and SIGLEC1 (r=0.915), ISG15 (r=0.828), and IFI6 (r=0.740) gene expression. In non-classical monocytes, SIGLEC1 gene expression also correlated with Siglec1 protein levels (r=0.803). TIF-1γ-positive patients exhibited elevated Siglec1 expression across monocyte subsets (classical: p=0.0103; intermediate: p=0.0506; non-classical: p=0.0231).

Conclusions. Siglec1 expression on monocytes closely correlates with type I IFN–induced gene activity in patients with suspected IIM. Elevated Siglec1, particularly on intermediate and classical monocytes, may reflect disease activity or therapeutic response, consistent with the pro-inflammatory roles of these subsets. These findings support Siglec1 as a promising biomarker for type I IFN activity in IIM.

Key words: idiopathic inflammatory myopathies, IFN, SIGLEC1, flow cytometry

P-61

PREVALENCE OF ANTI-NEUTROPHIL EXTRACELLULAR TRAP ANTIBODIES AND THEIR RELATIONSHIP WITH THE CLINICAL CHARACTERISTICS OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Agustin Hernández-López[1], Nancy R. Mejía-Domínguez[1,2], Yatzil Reyna-Juárez[1], Beatriz Alcalá-Carmona[1], Jennifer T. Balderas-Miranda[1,3], Carlos A. Núñez-Álvarez[1], Marta E. Baños-Laredo[1], Álvaro A. Sierra-Salazar[1], Johan Camacho-Pérez[1], Marco A. Martínez-Rivera[3], Diana Gómez-Martín[1], Jiram Torres-Ruiz[1]

[1]Instituto Nacional De Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [2]Red de Apoyo a la Investigación Universidad Nacional Autónoma de México, Mexico City, Mexico, [3]Universidad Nacional Autónoma de México, Mexico City, Mexico

Background. Patients with idiopathic inflammatory myopathies (IIM) have increased production and decreased clearance of neutrophil extracellular traps (NETs), which may promote production of anti-NETs antibodies. The aim of this study was to assess the prevalence of anti-NETs antibodies in IIM and their relationship with clinical features and disease activity.

Methods. We recruited 157 IIM patients according to ACR/EULAR or Connors' criteria. We assessed clinical features, muscle enzymes, disease activity, damage accrual, and myositis antibodies by Lineblot. IgM, IgG anti-NETs antibodies and NETs remnants (neutrophil elastase-DNA complexes) in serum were measured by ELISA. We determined the cut-off point of anti-NETs antibodies assay as 99th percentile of 26 age and sex paired healthy donors (0.183 arbitrary units (AU) for IgG and 0.772 AU for IgM). The positivity for anti-NETs antibodies was corroborated by indirect immunofluorescence (IFI). We assessed associations between anti-NETs antibodies, IIM phenotypes, and clinical features using χ^2, Mann Whitney U, and Spearman rho. In 68 patients with paired serum samples corresponding to active and inactive disease, we compared the amount of anti-NETs antibodies and NETs remnants using Wilcoxon test.

Results. 115 (73.2%) were women with median and interquartile range

(IQR) of age at recruitment of 52 years (40-59). The most frequent diagnosis was dermatomyositis (DM) (n=104, 66.2%), followed by anti-synthetase syndrome (AS) (n=24, 15.2%). 37 patients (23.5%) had positive IgG anti-NETs antibodies, and none were positive for IgM isotype. Figure 1 shows a representative IFI for positive (1A) and negative (1B) anti-NETs antibodies. Positivity for anti-NETs was closely associated to AS (Odds Ratio (OR) 6.1 (95% confidence interval 1.5-27.8), p<0.05), and with positive anti PL12 antibodies (12.1 (95% CI 2.3-91), p<0.05). As shown in Figure 2, IgG anti-NETs antibodies and NETs remnants decreased when disease becomes inactive (0.09 (0.02-0.19) *vs*. 0.008 (0-0.14), p<0.0001) (2A), and (1.19 (1.03-1.52) *vs*. 0.95 (0.86-1), p<0.0001) (2B), respectively.
Among participants with AS, patients with anti-NETs antibodies hp =0.04), erythrocyte sedimentation rate (24 mm/hour (8-36.5 *vs*. 5 (2.2-8), p=0.02), visual analog scale (VAS) of cardiovascular (0 (0-10) *vs*. 0 (0-0), P=0.03) and muscular disease activity (4 (0-7) *vs*. 0 (0-3.5), p=0.04), higher damage extension (0.18 (0.07-1) *vs*. 0.06 (0.06-0.09, p=0.03), and VAS of skeletal damage (0 (0-1) *vs*. 0 (0-0), p=0.05). In Figure 2C, we depict significant correlations between anti-NETs IgG antibodies and clinical features of patients with AS.
Key words: myositis, autoantibodies, neutrophils

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P-74

PHENOTYPE-BASED STRATIFICATION OF IDIOPATHIC INFLAMMATORY MYOPATHIES INTEGRATING PERIPHERAL BLOOD SINGLE-CELL TRANSCRIPTOMES

Shinji Izuka[1], Toshihiko Komai[1], Ikuko Ueda[2], Manabu Fujimoto[2], Hiroyuki Fukui[3], Masaru Takeshita[3], Natsuka Umezawa[4], Shinsuke Yasuda[4], Yuya Kondo[5], Isao Matsumoto[5], Mitsutaka Yasuda[6], Yuichiro Fujieda[6], Tatsuya Atsumi[6], Takeshi Iwasaki[7], Akio Morinobu[7], Toshio Kawamoto[8], Masakazu Matsushita[8], Naoto Tamura[8], Hiroshi Nakajima[9], Ken Yoshida[10], Takeo Isozaki[11], Nobuyuki Yajima[11], Akira Yoshida[12], Takahisa Gono[12], Masataka Kuwana[12], Masanobu Ueno[13], Yoshiya Tanaka[13], Keiichi Sakurai[14], Kimito Kawahata[14], Akari Suzuki[15], Kazuhiko Yamamoto[1,15], Tomohisa Okamura[1,16], Keishi Fujio[1]
[1]Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Japan, [2]Department of Dermatology, Osaka University Graduate School of Medicine, Japan, [3]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Japan, [4]Department of Rheumatology, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, Japan, [5]Department of Rheumatology, Faculty of Medicine, University of Tsukuba, Japan, [6]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Japan, [7]Department of Rheumatology and Clinical Immunology, Graduate School of Medicine, Kyoto University, Japan, [8]Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, Japan, [9]Department of Allergy and Clinical Immunology, Chiba University Hospital, Japan, [10]Division of Rheumatology, Department of Internal Medicine, The Jikei University School of Medicine, Japan, [11]Division of Rheumatology, Department of Medicine, Showa University School of Medicine, Japan, [12]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Japan, [13]The First Department of Internal Medicine, University of Occupational and Environmental Health, Japan, [14]Division of Rheumatology and Allergology, Department of Internal Medicine, St. Marianna University School of Medicine, Japan, [15]Laboratory for Autoimmune Diseases, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan, [16]Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, Japan

Background. Idiopathic inflammatory myopathies (IIM) are heterogeneous and shaped by myositis-specific autoantibodies (MSA) [1]. Within IIM, anti-aminoacyl-tRNA synthetase positivity defines anti-synthetase syndrome (ASyS), while in dermatomyositis, key MSA-based strata include MDA5-positive DM (MDA5), TIF1-γ-positive DM (TIF1-γ), and Mi-2-positive DM (Mi-2). Despite therapeutic advances in other autoimmune diseases, mechanistic stratification in IIM remains incomplete, limiting phenotype-guided treatment optimization.
Methods. In a Japanese multicenter cohort (October 2021–March 2025), we enrolled 94 IIM patients and 22 healthy controls (HC) and performed single-cell RNA sequencing (scRNA-seq) on CD45$^+$ live PBMCs using the 10x Genomics Chromium Single Cell Gene Expression platform. Disease activity was assessed with the International Myositis Assessment and Clinical Studies Group (IMACS) core set. Among untreated, high-activity patients, principal component-based clustering of clinical features identified phenotypically homogeneous groups. Differential expression was performed using MAST with FDR correction. Interferon (IFN) module scores and cell-type composition were compared with HC. Variance partitioning of gene expression was used to infer putative drug-cell type alignments.
Results. We profiled 300,000 cells into 38 populations. Clinical clustering yielded four groups (C1–C4): C1 (ASyS-predominant; mechanic's hands/interstitial lung disease), C2 (TIF1-γ/Mi-2-predominant; rash + myositis), C3 (MDA5-predominant; amyopathic with rash), and C4 (ASyS with rash + myositis). Compared with HC, IL1B$^+$ classical monocytes (cMono) were expanded in C1/C2/C4; S100A$^+$ cMono in C2; plasma cells in C2/C4; and plasmacytoid dendritic cells (pDC) in C3. IFN stimulated gene expression was elevated across multiple lineages, with IFN-α response most enriched in myeloid cells and highest in pDC. The proportion of pDC and the IFN-α response score in cMono were positively correlated, suggesting pDC-derived type I IFN as a driver of monocyte activation. Variance partitioning indicated that IL1B$^+$ monocytes can be targeted with mycophenolate mofetil or calcineurin inhibitors, whereas pDC can be targeted with intravenous immunoglobulin, Janus kinase inhibitors, or intravenous cyclophosphamide.
Conclusions. Integrating clinical phenotypes with PBMC single-cell profiles reveals IIM heterogeneity that transcends MSA classes. Phenotype-led stratification captures differences in cellular composition and interferon signaling, yielding testable therapeutic hypotheses.
Acknowledgements. We thank participating patients and collaborating centers for their contributions.
Key words: anti-synthetase syndrome, dermatomyositis, scRNA-seq

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P-77

NEUTROPHIL EXTRACELLULAR TRAPS PROMOTE INTERFEROGENIC AND PROINFLAMMATORY RESPONSES IN MYELOID AND MUSCLE CELLS: ANALYSIS OF THEIR POTENTIAL ROLE IN THE INDUCTION OF PERIFASCICULAR ATROPHY

Jiram Torres-Ruiz[1], Yatzil Reyna-Juárez[1], Beatriz Alcalá-Carmona[1], Maria, J Ostos-Prado[1], Jennifer, T Balderas-Miranda[1], Miguel Tapia-Rodríguez[2], David, E Meza-Sánchez[3], Carlos Núñez-Álvarez[1], Martha, E Baños-Laredo[1], Diana Gómez-Martín[1]
[1]Department of Immunology and Rheumatology, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [2]Instituto de Investigaciones Biomédicas, Universidad Nacional Autónoma de México, Mexico City, Mexico, [3]Red de apoyo a la Investigación, Cordinación de Investigación Científica, Universidad Nacional Autónoma de México, Mexico City, Mexico, Mexico City, Mexico

Background. Dermatomyositis (DM) and anti-synthetase syndrome (AS) are idiopathic inflammatory myopathies (IIM) with prominent perifascicular pathology. Perifascicular atrophy (PA) is characterized by vasculopathy, inflammatory infiltrate, muscle atrophy, necrosis and regeneration and an intense interferon signature. Neutrophil extracellular traps (NETs) can promote proinflammatory and interferogenic responses in different cell subsets. The aim of this study was to assess the potential role of NETs as inducers of PA.
Methods. We recruited 5 healthy donors (HD), 17 patients with DM and 13 with AS. NETs were detected by confocal microscopy in muscle biopsies. Patient-derived macrophages (PDM) and mDC (PDmDC), healthy donor-derived macrophages (HDM) and mDC (HDmDC) and myotubes differentiated from commercially available human myoblasts were stimulated with spontaneous NETs from patients and HD to assess the differentiation index, area, and interferon production. Interferon signature was assessed by RT-qPCR differential gene expression of ISG15, IFI44, IFI44L, IFIT1, IFI27, CXCL9, CIITA, RSAD2 (ΔΔCt equation) and IFN score was obtained by Z score. Cytokines and chemokines in supernatant of myeloid cells stimulated with NETs were addressed by luminometry.
Results. Twenty-two (73.3%) patients were women. In muscle biopsies, NETs were prominent in the perimysium in close contact with macrophages. In the intravascular compartment, we observed neutrophils undergoing spontaneous NETosis, and NETs were found inside muscle cells. PDM and PDmDCs stimulated with IIM NETs had higher IFN-score, and NETs from DM patients induced a stronger IFN response than those from AS patients in macrophages. NETs from active disease tended to elicit higher IFN-scores.
IL-12p40, IL-15, IFN-γ and MCP-1, IL-RA were markedly increased in NET-stimulated PDM in comparison to HDM. VEGF-A expression was

slightly higher in supernatants from HDM. NET-stimulated PDmDC exhibited marked overexpression of IL-1α, IL-12p40, IL-12p70, IFN-α2, IFN-γ and MIP-1α. IL-10 was more abundant HDmDC, whereas IL-13 predominated in PDmDC. IL-3 and eotaxin were also significantly elevated in PDmDC supernatants. Myotubes internalize NETs, which induces an overexpression of CIITA, CXCL9, IFI44, IFI44L, IFIT1, ISG15 and RSAD2. NET-stimulated myocytes had decreased differentiation index and area.
Conclusions. In muscle biopsies, we detected NETs interacting with key components of the perifascicular pathology. In vitro, NETs promote proinflammatory and interferogenic responses in myeloid cells that may contribute to the pathogenesis of PA. NETs are internalized by myotubes, which induce type I and II IFN signatures and direct muscle damage, hampering the differentiation of myoblasts into myotubes and reducing their size.
Key words: dermatomyositis, anti-synthetase syndrome, NETs, perifascicular atrophy, interferons

P-99

ANTI-MDA5 MONOCLONAL ANTIBODIES FROM PATIENTS WITH DERMATOMYOSITIS – B CELL CHARACTERISTICS AND DIFFERENTIAL TARGETING OF THE HELICASE DOMAINS

Eveline Van Gompel[1,2,3], Marina Galesic[1,2], Nicolas Delaroque[4], Karolin Kern[4], Ragnhild Stålesen[1,2], Antonella Notarnicola[1,5], Deniz Demirdal[1,5], Monika Hansson[1,2], Annika van Vollenhoven[1,2], Edvard Wigren[1,2,6], Susanne Gräslund[1,2,6], Michael Szardenings[4], Vivianne Malmström[1,2], Ingrid E. Lundberg[1,2,5], Begum Horuluoglu[1,2], Caroline Grönwall[1,2], Karine Chemin[1,2], Vijay Joshua[1,2,7]
[1]Division of Rheumatology, Department of Medicine, Solna, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, [2]Center for Molecular Medicine, Stockholm, Sweden, [3]Laboratory of Tissue Homeostasis and Disease, Skeletal Biology and Engineering Research Center, Department of Development and Regeneration, KU Leuven, Leuven, Belgium, [4]Ligand Development Unit, Fraunhofer Institute for Cell Therapy and Immunology (IZI), Leipzig, Germany, [5]Department of Gastroenterology, Dermatology and Rheumatology, Theme Inflammation and Aging, Karolinska University Hospital, Stockholm, Sweden, [6]Structural Genomics Consortium, Division of Rheumatology, Department of Medicine Solna, Karolinska Institutet, Sweden, [7]Division of Immunology and Respiratory Medicine, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden

Background. Autoantibodies targeting melanoma differentiation associated protein 5 (MDA5) are strongly associated with dermatomyositis (DM) and may contribute to its pathogenesis (1). Here we aimed to investigate MDA5+ B cells, their phenotype and generate MDA5 monoclonal antibodies to assess their epitope specificity.
Methods. MDA5-reactive B cells were captured from peripheral blood of patients with anti- MDA5+ DM (n=3) using an MDA5-fluorescent probe. B cell receptor (BCR) sequences were analysed from single-sorted B cells (n=240). Selected clones were re-expressed as IgG1 monoclonal antibodies (mAbs, n=23). Reactivity was assessed using recombinant MDA5 protein constructs, peptide epitope mapping, ELISA, western blot and a commercial line blot assay.
Results. Of 240 anti-MDA5+ sorted B cells, 23 BCRs were re-expressed as mAbs, two of which showed high reactivity and specificity for MDA5. These antibody sequences originated from one CD19+IgD-CD27-CD38+ and one CD19+IgD-CD27+CD38+ IgG+ B cell with low somatic hypermutation (SHM). Both mAbs had nanomolar apparent affinity and bound to sites within the helicase domains of the MDA5 protein but with distinct epitope recognition. Serology screening confirmed targeting of a linear epitope identified in the mAb studies.
Conclusions. Anti-MDA5+ B cells recognize the helicase domains, which are the enzymatically active domains of the protein. These results have implications for understanding the etiopathology of anti-MDA5+ DM and development of new (antigen-specific) therapies. Strong binding despite low SHM level may suggest a low threshold for break of tolerance in predisposed individuals. Patient-derived mAbs will be important tools to further investigate the potential pathogenicity of anti-MDA5 autoantibodies.
Key words: dermatomyositis, MDA5, B cells

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P-104

AUTOREACTIVE T CELLS IDENTIFIED IN PATIENTS WITH ANTI-JO1+ ANTISYNTHETASE SYNDROME RECOGNISE A NEW EPITOPE ON HISTIDYL T-RNA SYNTHETASE

Angeles S. Galindo-Feria[1,2,3], Ravi Kumar Sharma[1,2,4], Anatoly Dubnovitsky[1,2], Christina Gerstner[1,2], Genadiy Kozhukh[1,2], Annika Van Vollenhoven[1,2], Juan Sebastian Diaz Boada[1], Daniel Ramsköld[5], Adnane Achour[6,7], Maryam Dastmalchi[1,2,3], Hugh Reid[8], Tatyana Sandalova[6,7], Jamie Rossjohn[8,9], Karine Chemin[1,2], Vivianne Malmström[1,2], Ingrid E Lundberg[1,2,3], Begum Horuluoglu[1,2]
[1]Division of Rheumatology, Department of Medicine, Karolinska Insitutet, Stockholm, Sweden, [2]Center for Molecular Medicine, Stockholm, Sweden, [3]Department of Gastro, Dermatology and Rheumatology, Karolinska University Hospital, Stockhom, Sweden, [4]Department of Clinical Immunology and Rheumatology, All India Institute of Medical Sciences, India, [5]Department of Cell and Molecular Biology, Karolinska Institutet, Stockholm, Sweden, [6]Division of Infectious Diseases, Karolinska University Hospital, Stockholm, Sweden, [7]Science for Life Laboratory, Department of Medicine, Karolinska Institutet, Stockholm, Sweden, [8]Infection and Immunity Program and Department of Biochemistry and Molecular Biology, Biomedicine Discovery Institute, Monash University, Clayton, Australia, [9]Institute of Infection and Immunity, Cardiff University, School of Medicine, Cardiff, UK

Background. Anti-Jo1+ antisynthetase syndrome (ASyS) is characterised by autoantibodies targeting histidyl t-RNA synthetase (HisRS), association with HLA-DRB1*03:01 and a distinct clinical phenotype including interstitial lung disease, myositis, arthritis, and mechanic's hands. Previous studies of autoreactive HisRS-specific CD4+T cells point to yet undiscovered T cell epitopes. We aimed to identify new epitopes on HisRS to investigate the presence of autoreactive T cells and their corresponding T-cell receptor (TCR) repertoire from patients with ASyS.
Methods. Peptides from HisRS N-terminal region with appropriate major histocompatibility complex (MHC) anchor residues were selected for in vitro binding assays. The peptide (HisRS41-55) with the highest HLA-DRB1*03:01 binding affinity was selected for studies with HLA-class II tetramers. Peripheral blood mononuclear cells (PBMCs) from patients with ASyS with HLA-DRB1*03:01 (n = 12) were stimulated in vitro with peptide and peptide-HLA-DRB1*03:01 tetramers were used to detect HisRS+CD4+T cells. Single TCR sequencing of captured T cells allowed analyses of the underlying TCR repertoire.
Results. We identified a new T cell epitope on HisRS with high affinity for HLA-DRB1*03:01. Autoreactive HisRS+CD4+T cells were detected in PBMCs of patients (n = 6/12). TCR repertoire analysis of HisRS+CD4+T cells revealed shared gene V-alpha and beta usages. Moreover, HisRS+CD4+T cells persisted after treatment in 2 patients (P2 and P4) and 2 identical T cell clones were detected between the initial and follow-up time points in 1 patient (P2).
Conclusions. Autoreactive T-cells targeting a new HisRS epitope were identified indicating T cell reactivity to diverse epitopes of the HisRS protein in patients with anti-Jo1 autoantibodies. Furthermore, we demonstrated the TCR repertoire of autoreactive HisRS+CD4+T cells in patients. Persistence of these T-cells and specific clones may be contributing to disease.
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Key words: anti-Jo1, HisRS, TCR, autoreactive T cells

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STUDY OF PERIPHERAL MICROCIRCULATION WITH LASER DOPPLER FLOWMETRY AND ICE EXPOSURE IN PATIENTS WITH ANTI-SYNTHETASE SYNDROME

Joana Caetano[1,2], Marisa Nicolai[1], Elisabete Silva[1], Clemente Rocha[1], José Delgado Alves[2], Luís Monteiro Rodrigues[1]
[1]Lusófona University, Lisbon, Portugal, [2]Fernando Fonseca Hospital, Amadora, Portugal

Background. Raynaud's phenomenon (RP) is a common manifestation of anti-synthetase syndrome (ASyS) affecting 40–50% of cases, and it can translate a relevant role of microcirculation dysfunction in the physiopathology of ASyS.
Methods. The current study used the controlled exposure to cold (ICE) to

investigate the adaptive impact of fast cooling on the glabrous skin perfusion in patients with ASyS with RP, compared to primary RP (pRP) and healthy controls (HC). Thirty-one female participants, mean age of 55±12 years, were selected (10 ASyS, 11 pRP, and 10 HC). All procedures respected Good Clinical Practice principles. The ICE methodology involved the contact of one randomly chosen hand (ventral side) with a frozen surface for 3 minutes (min). Hemodynamics and local perfusion were measured in both hands by laser doppler flowmetry. Measurements were taken during baseline (10 min phase 1), during ICE (3 min phase 2), and after cooling, during recovery (10 min phase 3), and expressed as blood perfusion units (BPU). Nailfold video-capillaroscopy (NVC) was also performed before ice exposure.

Results. with ICE, statistically significant differences in perfusion were consistently detected between the HC, ASyS, and pRP patients in all experimental phases ($p<0.0001$). In the first minute of recovery, median perfusion significantly increased in HC ($p=0.0003$), while it decreased in pRP (phase 2: 150 BPU *vs*. phase 3: 138 BPU, $p=0.0005$), with no significant response in ASyS (phase 2: 78 BPU *vs*. phase 3: 71 BPU, $p=0.06$). In the late recovery phase, perfusion further increased in HC ($p=0.02$), as well as in ASyS ($p<0.0001$), without reaching baseline values in this latter group, and continued to decrease in pRP ($p<0.0001$). NVC in ASyS patients showed non-specific abnormalities, with reduced capillary density (60%) and dysmorphic capillaries (100%).

Conclusions. These results suggest that ASyS patients react differently to ice exposure compared to pRP and HC. ASyS patients showed a slower perfusion recovery and did not fully recover during the 10-minute evaluation period. These observations suggest that the impairment of vascular adaptation might be a determinant of the RP manifestations, justifying further investigations.

Key words: anti-synthetase syndrome, Raynaud's phenomenon, micro-circulation

P-127

IMPACT OF TREATMENT ON MUSCLE BIOPSIES IN PATIENTS WITH ANTI-HMGCR NECROTIZING MYOPATHY

Orane Demuynck[1,2,3], Yue-Bei Luo[1,2,4], Maryam Dastmalchi[1,5], Inger Nennesmo[6], Andrea Kemp[1,2], Beatriz H. Ferreira[1,2], Ingrid E. Lundberg[1,2,5], Angeles S Galindo-Feria[1,2,5], Begum Horuluoglu[1,2]

[1]Division of Rheumatology, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden, [2]Center for Molecular Medicine, Stockholm, Sweden, [3]Département de Médecine Interne et Immunologie Clinique, Centre Hospitalier Universitaire Lille, Centre de Référence des Maladies Auto-Immunes Systémiques Rares du Nord et Nord-Ouest, Lille, France, [4]Department of Neurology, Xiangya Hospital, Central South University, China, [5]Department of Gastro, Dermatology and Rheumatology, Theme Inflammation and Aging. Karolinska University Hospital, Stockohlm, Sweden, [6]Department of Oncology-Pathology, Karolinska University Hospital, Stockohlm, Sweden

Introduction: Anti-3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) autoantibody necrotizing myopathy is a subtype of idiopathic inflammatory myopathies primarily affecting skeletal muscle. It is often associated with prior statin exposure, which targets the HMGCR enzyme involved in cholesterol synthesis. Characteristic histopathological findings include macrophages infiltrate, necrotic and regenerating fibers, complement deposition along the sarcolemma, sarcoplasmic and sarcolemma accumulation of p62. Despite these well-described features, the relationship between muscle pathology, clinical presentation, and treatment response remains poorly characterized.

Methods. Twenty-one patients diagnosed with anti-HMGCR necrotizing myopathy followed at Karolinska University Hospital between 2018 and 2024 were included. Sections from muscle biopsies taken before and after treatment were stained with anti-human antibodies against CD3, CD68, MHC-I and p62 and analyzed using QuPath and Cellpose software. Clinical parameters including the manual muscle test-8 (MMT8) score, Health Assessment Questionnaire (HAQ), creatine kinase, and anti-HMGCR autoantibody levels were collected at the time of the muscle biopsy. The Spearman´s rank correlation coefficient was used to analyze correlations at diagnosis and after treatment initiation, and the Wilcoxon signed-rank test was used to compare biopsies before and after treatment.

Results. The median age at diagnosis was 67 years [IQR: 62; 71], with 76% (16/21) being male. All patients had been previously exposed to statins. Before immunosuppressive treatment, the number of necrotic fibers and extent of myophagocytosis were inversely correlated with MMT8 ($r= -0.51$, $p=0.02$; $r = -0.591$, $p<0.01$; $r = -0.54$, $p=0.02$, respectively). Every patient received methotrexate, 86% (18/21) received intravenous immunoglobulin (IVIg), and 48% (10/21) received steroids. Median time between the first and second biopsy was 6 months [IQR: 5;11]. At the second timepoint biopsy, 2 of 20 patients were receiving low-dose steroids (5 and 2.5 mg/day), and 19 were on methotrexate. After treatment, necrotic fibers, myophagocytosis, and MHC-I-positive fibers had decreased significantly ($p<0.01$). Necrotic fibers were no longer detected in 14 of 16 patients. However, complement deposition on the sarcolemma persisted in 12 out of 19 post-treatment muscle biopsies. After treatment initiation, $CD3^+$ T cell infiltration remained unchanged and $CD68^+$ macrophage density showed no significant decrease. Myophagocytosis remained negatively correlated with MMT8 ($r = -0.49$, $p=0.03$).

Conclusions. Treatment with IVIg, methotrexate and glucocorticoids descreased muscle necrosis in anti-HMGCR necrotizing myopathy and improved muscle strength. However, persistence of complement deposition on the sarcolemma indicates a persisting subclinical disease activity. Future research should investigate the clinical significance of persistent pathological changes.

Key words: HMGCR, necrotizing myopathy, muscle biospy

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MULTIMODAL SINGLE-CELL PROFILING OF MUSCLE IMMUNE INFILTRATES AND SPATIAL TRANSCRIPTOMICS REVEAL SHARED AND DISEASE-SPECIFIC PROGRAMS IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Tomoya Yoshida[1], Hideyuki Takahashi[1], Takahiro Itamiya[1,2], Takeshi Iwasaki[3], Natsuka Umezawa[4], Hirokazu Sasaki[4], Keita Ninagawa[5], Yuichiro Fujieda[5,8], Yusuke Miyazaki[6], Yasuyuki Kamata[7], Masaru Takeshita[8], Masakazu Matsushita[9], Toshio Kawamoto[9], Meiko Maeda[10], Akatsuki Kubota[10], Tatsushi Toda[10], Naoto Tamura[9], Yuko Kaneko[8], Tsutomu Takeuchi[8,11], Kojiro Sato[7], Shingo Nakayamada[6], Yoshiya Tanaka[12], Ken Yoshida[13], Tatsuya Atsumi[5], Shinsuke Yasuda[4], Koichiro Ohmura[3], Akio Morinobu[3], Kazuhiko Yamamoto[14], Mineto Ota[1], Tomohisa Okamura[1,2], Keishi Fujio[1]

[1]Department of Allergy and Rheumatology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, [2]Department of Functional Genomics and Immunological Diseases, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, [3]Rheumatology and Clinical Immunology, Kyoto University Graduate School of Medicine, Kyoto, Japan, [4]Department of Rheumatology, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, Tokyo, Japan, [5]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan, [6]The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, [7]Division of Rheumatology and Clinical Immunology, Department of Medicine, Jichi Medical University, Tochigi, Japan, [8]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, [9]Department of Internal Medicine and Rheumatology, Juntendo University Faculty of Medicine, Tokyo, Japan, [10]Department of Neurology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan, [11]Saitama Medical University, Saitama, Japan, [12]Department of Molecular Targeted Therapeutics, University of Occupational and Environmental Health, Kitakyushu, Japan, [13]Department of Internal Medicine, Division of Rheumatology, The Jikei University School of Medicine, Tokyo, Japan, [14]Laboratory for Autoimmune Diseases, RIKEN Center for Integrative Medical Sciences, Yokohama, Japan

Background. Idiopathic inflammatory myopathies (IIM) are systemic autoimmune diseases characterized by muscle inflammation, yet the immune processes underlying distinct clinical subtypes remain poorly understood. While histopathology and bulk transcriptomics have identified type I interferon signatures and other disease-associated pathways (1), the cellular-level heterogeneity of immune infiltrates in IIM remain undefined.

Methods. We profiled 43,260 $CD45^+$ immune cells isolated from muscle and blood of 18 patients with IIM, including dermatomyositis (DM) and anti-synthetase syndrome (ASyS), using scRNA-seq, and TCR/BCR repertoire sequencing. Two additional ASyS samples underwent spatial transcriptomics, utilizing Visium platform.

Results. We identified major immune populations, with NK cells enriched in DM muscle and negatively correlated with T cell abundance. Th1 and peripheral helper T (Tph) cells (2) were expanded in muscle compared with circulation, displaying skewed clonal repertoires and differentiation trajectories consistent with the local expansion in muscle. $CD8^+$ GZMKhigh tissue-resident memory T cells (Trm) proliferated locally and acted as IFN-γ producers, distinct from highly cytotoxic CD8+ Temra populations. Disease-specific features included MAIT cell enrichment with type I interferon priming in $Mi2^+$ DM, and clonal expansion of CD8+ HOBIThigh Temra with cytotoxic feature in ASyS. Spatial transcriptomics demonstrated that regions of

T-B cell interaction and type I interferon activation overlapped with muscle damage.

Conclusions. Our multimodal single-cell and spatial transcriptomic analyses define shared and disease-specific immune programs in IIM, linking infiltrating immune populations to tissue damage. These findings refine the immunopathological framework of DM and ASyS and provide a basis for further investigation.

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Key words: single cell transcriptomics, spatial transcriptomics, TCR/BCR repertoire analysis

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ELEVATED CERAMIDASE EXPRESSION LINKS SPHINGOLIPID REMODELING TO MUSCLE INFLAMMATION AND RECOVERY IN A MURINE MODEL OF MYOSITIS

Alfredo Guzman[1], Rita Spathis[1], Elizabeth Bagley[1], Kanneboyina Nagaraju[1], Melissa Morales[1]
[1]*Binghamton University, Johnson City, USA*

Background. Inflammatory myopathies are characterized by immune-mediated muscle damage and activation of both the type I interferon (IFN) and endoplasmic reticulum (ER) stress pathways. Recent studies suggest that dysregulation of sphingolipid metabolism, particularly ceramide accumulation, may contribute to tissue injury and inflammation. Ceramide breakdown by acid (Asah1) and neutral (Asah2) ceramidases generate sphingosine, which can be phosphorylated to sphingosine-1-phosphate (S1P), a lipid mediator with anti-apoptotic, pro-regenerative, and immune-modulatory properties. Because 4-phenylbutyric acid (4PBA) reduces ER stress and inflammatory signaling, we investigated whether ceramidase expression is altered in myositis muscle and how 4PBA treatment modulates this pathway.

Methods. Myositis was induced in 21-day-old female C57BL/6 mice by doxycycline withdrawal. Animals were divided into three groups (n=17/group): untreated myositis (HT), myositis + 150 mg/kg 4PBA (HT-150), and wild-type controls (Bl/6). 4PBA was administered orally once daily for seven weeks. Quadriceps and gastrocnemius muscles were analyzed for mRNA expression of Asah1 and Asah2 by quantitative RT-PCR and for Asah2 protein by western blot using anti-Asah2 (R&D Systems, AF3558). Expression data were compared to ER stress markers (Chop, Grp78, Xbp1s) and IFN-stimulated genes (Ifit1, Irf7, Isg15, Mx1) to assess correlations between ceramidase regulation and stress or inflammatory signaling.

Results. Both Asah1 and Asah2 mRNA levels were significantly elevated in HT muscle compared to Bl/6 controls ($p<0.0001$, $p<0.05$ respectively). Asah2 protein was undetectable or minimally expressed in wild-type muscle but readily detected in myositis muscle, confirming upregulation at the protein level. Treatment with 150 mg/kg 4PBA further increased Asah2 expression over untreated HT mice ($p<0.001$) while weakening correlations with ER stress and IFN-responsive genes. These results suggest that 4PBA amplifies ceramidase expression while uncoupling it from stress-induced inflammation, consistent with a shift toward adaptive lipid remodeling.

Conclusions. Ceramidase upregulation is a prominent feature of myositis muscle and may represent a protective lipid response to inflammation and ER stress. 4PBA treatment enhances Asah2 expression and disrupts its association with stress and IFN signatures, supporting the concept that sphingolipid metabolism contributes to muscle recovery and adaptation. These findings identify Asah1 and Asah2 as potential modulators of myositis pathogenesis and promising markers of therapeutic response.

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Key words: myositis, ceramides, sphingolipid metabolism

P-160

MYOSITIS IN ANTI-U1RNP-POSITIVE PATIENTS: AN IN-DEPTH ANALYSIS

Marie-Therese Holzer[1], Anne Schänzer[2], Sarah Léonard-Louis[3], Olivier Benveniste[4], Yves Allenbach[4], Udo Schneider[5,6], Robert Biesen[6], Ulf Müller-Ladner[7], Dana Lemmer[5], Ina Kötter[1,14], Tobias B. Huber[8,9], Johannes Prudlo[10], Martin Krusche[*1], Corinna Preusse[*11,12,13], Werner Stenzel[*12]
[*]Share last authorship.
[1]*Division of Rheumatology and Systemic Inflammatory Diseases, III. Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany,* [2]*Institute of Neuropathology, Justus-Liebig-University, Gießen, Germany,* [3]*Reference Center of Neuromuscular Pathology Paris-Est, Pitié-Salpêtrière University Hospital, Paris, France,* [4]*Department of Internal Medicine and Clinical Immunology, Pitié-Salpêtrière University Hospital, Paris, France,* [5]*Department of Rheumatology, Clinical Immunology and Osteology, Immanuel Hospital Berlin-Wannsee and Berlin-Buch, Berlin, Germany,* [6]*Department of Rheumatology and Clinical Immunology, Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany,* [7]*Department for Rheumatology, Campus Kerckhoff of Justus-Liebig University Gießen, Bad Nauheim, Germany,* [8]*III. Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany,* [9]*Hamburg Center for Translational Immunology (HCTI), University Medical Center Hamburg-Eppendorf, Hamburg, Germany,* [10]*Department of Neurology, University Rostock, Rostock, Germany,* [11]*Department of Neurology, Charité-Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt Universität zu Berlin, Berlin, Germany,* [12]*Department of Neuropathology, Charité-Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health (BIH), Berlin, Germany,* [13]*Department of Neuropediatrics, Charité-Universitätsmedizin Berlin, Corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health (BIH), Berlin, Germany,* [14]*Department of Rheumatology and Immunology, Klinikum Bad Bramstedt, Bad Bramstedt, Germany*

Background. Mixed connective tissue disease (MCTD) is a very rare autoimmune disease, defined by high titers of U1RNP-antibodies and multiple symptoms of other connective tissue diseases. Patients can exhibit phenotypes of systemic lupus erythematosus, systemic sclerosis and also myositis. Yet, little is known about the morphological aspects of anti-U1RNP-positive myositis. Therefore, the aim of this study is to perform an in-depth histopathological and transcriptional analysis of anti-U1RNP-positive myositis to investigate possible pathomechanisms and/or distinct phenotypes.

Methods. 18 muscle biopsies from anti-U1RNP-positive patients presenting with clinical and morphological features of myositis were analyzed by immunohistochemistry and transcriptomic studies. Clinical data were analyzed retrospectively. Findings were put into the context of biopsies from other myositis entities and non-disease controls.

Results. The mean age of patients was 49 years (range 24–72 years), and 76% were female. 94% of the patients had myalgia and proximal muscle weakness. Arthralgia was reported in 73%, Raynaud's phenomenon in 67%, interstitial lung disease and cardiac involvement in 33%, respectively. Antinuclear antibodies were positive in all patients. Concomitant autoantibodies were present in 94% of the cases (mainly SSA-, CCP-antibodies or rheumatoid factor). Histopathologic analysis indicated three distinct subtypes within the cohort of anti-U1RNP-positive myositis.

33% of the biopsies resembled antisynthetase-syndrome (ASyS) with perifascicular MHC-I and II positivity on myofibers, infiltrates and necrosis, but with additional signs of perivasculitis.

39% of the biopsies resembled immune-mediated necrotizing myopathy (IMNM) with necrosis and myophagocytosis, but without IMNM-like p62 pattern. Additionally, MHC-II positivity was detected in a diffuse, focal enhanced pattern.

Ultimately, 28% of the biopsies had minimal myositis with capillary pathology-like pattern, a common feature of scleromyositis (SM). This entity also exhibited mild necrosis in 100% and a perifascicular pattern in 60% of the cases.

Preliminary transcriptional results using qPCR from all biopsies showed a significantly increased expression of interferon-associated genes (e.g. IFIT1, IFNG, ISG15, MX1), as well as a strongly increased expression of multiple toll-like receptors (e.g. TLR7, TLR8) compared to non-disease controls.

Conclusions. As a result of this detailed analysis, we identified three subtypes of anti-U1RNP-positive myositis, resembling, yet substantially differing from other myositis entities like ASyS, IMNM, SM. These findings raise the question whether anti-U1RNP-positive myositis is one disease entity in the context of MCTD or rather reflects a complex overlap of various pathophysiological mechanisms

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Key words: overlap-myositis, histopathology, transcriptomics

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ENHANCED FIBROGENIC PATHWAYS DEFINE SCLEROMYOSITIS WITHIN THE SPECTRUM OF EULAR/ACR MYOSITIS SUBSETS

Giannini M.[1,2,3], Quiring G.[3], Ellezam B.[4], Troyanov Y.[5], Debrut L.[3], Gilbart V.[6], Geny B.[1,3], Laverny G.[6], Hudson M.[7], Landon-Cardinal O.[8,9], Meyer A.[1,2,3]
[1]Service de Physiologie et Explorations Fonctionnelles, University Hospital of Strasbourg, Strasbourg, France, [2]Centre de Référence des Maladies Autoimmunes Rares, University Hospital of Strasbourg, Strasbourg, France, [3]Unité de Recherche 3072 (UR3072), Centre de Recherche en Biomédecine, University of Strasbourg, Strasbourg, France, [4]Division of Pathology, Centre Hospitalier Universitaire (CHU) Sainte-Justine, Department of Pathology and Cell Biology, Université de Montréal, Montréal, QC, Canada, [5]Division of Rheumatology, Hôpital du Sacré-Coeur, Department of Medicine, Université de Montréal, Montréal, QC, Canada, [6]Université de Strasbourg, CNRS, Inserm, IGBMC UMR 7104-UMR-S 1258, Illkirch, France, [7]Division of Rheumatology, Jewish General Hospital, Department of Medicine, McGill University, Montréal, QC, Canada, [8]Division of Rheumatology, Centre Hospitalier de l'Université de Montréal (CHUM), Autoimmunity Research Laboratory, CHUM Research Center, Montréal, QC, Canada, [9]Department of Medicine, Université de Montréal, Montréal, QC, Canada

Background. The current EULAR/ACR classification criteria recognize four subsets of inflammatory myopathies (IM): dermatomyositis (DM), immune-mediated necrotizing myopathy (IMNM), inclusion body myositis (IBM), and antisynthetase syndrome (ASyS) (1, 2). We and others have identified scleromyositis (SM) as a fifth subset that differs from the above by the presence of scleroderma features (fulfilling or not the 2013 ACR/EULAR criteria for systemic sclerosis (SSc)), SSc-specific or overlap autoantibodies (most frequently anti-PM/Scl, -U1-RNP, and -Ku), and a distinctive muscular capillaropathy (3). These patients are often misclassified as seronegative IMNM or ASyS using current EULAR/ACR IM criteria. We tested the hypothesis that this subset also differs from other IM subsets by a distinct muscle transcriptomic signature.
Methods. In a bicentric cohort (Strasbourg-Montreal), 54 untreated patients with IM at the time of diagnosis were included (SM=23, DM=10, IMNM=8, ASyS=9, IBM=4), along with 7 non-neuromuscular controls. Clinico-seropathological data were collected at diagnosis and at last follow-up. Transcriptomic sequencing was performed using total RNA extracted from diagnostic muscle biopsies, and pathway enrichment analysis was conducted on differentially expressed genes ($|\log FC|>0.5$; adjusted $p<0.05$) using WebGestalt 2024.
Results. Subjects in each subset were comparable regarding age at diagnosis, sex ratio, muscle biopsy site, and sample origin ($p>0.05$). Compared to other IM subsets, SM patients exhibited higher frequencies of sclerodactyly (62%, $p<0.0001$), Raynaud's phenomenon (61%, $p=0.002$), limited cutaneous sclerosis (57%, $p=0.0006$), telangiectasias (52%, $p=0.003$), interstitial lung disease (47.6%, $p=0.03$), puffy fingers (38%, $p=0.02$), and arthritis (38%, $p=0.07$). The SM cohort encompassed a broad serological spectrum of the disease, including 4 anti-PM/Scl+, 5 anti-U1-RNP+, 4 anti-Ku+, 2 anti-RNA Pol III+, 1 anti-NVL+, 1 anti-Scl70+, 1 anti-RuvBL1/2+, and 5 seronegative patients. A total of 239 genes were specifically dysregulated in SM muscle compared with the four other IM subsets and controls (168 upregulated, 71 downregulated). These genes were enriched in pathways related to collagen formation and extracellular matrix remodelling.
Conclusions. Consistent with their distinctive clinical, serological, and histopathological features, SM patients differ from other IM subsets by enhanced activation of fibrogenic molecular pathways in muscle tissue. These findings further support the hypothesis that SM represents a distinct IM subset that should be recognized in future IM classification criteria, and that myositis constitutes a target organ involvement in SSc. Muscle fibrosis activation may represent both a diagnostic biomarker and a potential therapeutic target for SM.

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ANTI-MDA5 DERMATOMYOSITIS IS ASSOCIATED WITH INCREASED RISK OF INFECTIONS: A REVIEW OF THE LITERATURE

Katherine Moore[1,2], Thomas Khoo[1,2,3], Vidya Limaye[1,3], Syed B. Ali[4,5]
[1]Rheumatology Unit, Royal Adelaide Hospital, Adelaide, Australia, [2]Rheumatology Unit, Flinders Medical Centre, Bedford Park, Australia, [3]School of Medicine & Biomedical Sciences, University of Adelaide, Adelaide, Australia, [4]School of Medicine & Public Health, Flinders University, Bedford Park, Australia, [5]Department of Clinical Immunology & Allergy, Flinders Medical Centre, Bedford Park, Australia

Background. Melanoma differentiation-associated gene 5 (MDA5) is an innate pattern recognition receptor that detects cytosolic RNA and induces a type I interferon response essential for antiviral defence.
Dermatomyositis associated with anti-MDA5 antibodies (anti-MDA5 DM) represents a distinct subtype of idiopathic inflammatory myopathy (IIM) characterised by type I interferon-mediated immune activation. It carries high mortality due to rapidly progressive interstitial lung disease (RP-ILD), for which upfront combination immunosuppression is recommended.
Emerging evidence suggests anti-MDA5 DM confers an increased infection risk beyond that attributable to immunosuppressive therapy (1). We evaluated infection risk in anti-MDA5 DM compared with other IIM, focusing on opportunistic infections such as Pneumocystis jirovecii pneumonia (PJP) and cytomegalovirus (CMV).
Methods. A narrative review of the literature was conducted using Embase, Emcare, and MEDLINE for studies (01/25-05/25) reporting infection outcomes in IIM with subgroup data comparing anti-MDA5 DM and other IIM. Clinical outcomes related to infection (infection type, severity, mortality) and immunological features (autoantibody status, lymphocyte or neutrophil counts) were included
Results. Nine studies met the inclusion criteria from East Asia (n=7), Europe (n=1) and North America (n=1). Anti-MDA5 DM was an independent risk factor for serious infection (odds ratio [OR]: 2), particularly pulmonary and cutaneous infections, and PJP infection (OR 6-12). Notably, this increased susceptibility to infection persisted after adjustment for immunosuppressant exposure. CMV occurred more frequently in anti-MDA5 DM than other IIMs (19-63% *vs*. 0-16%).
Conclusions. Anti-MDA5 DM is associated with a higher infection risk than other IIMs. Multifaceted immune dysregulation, including a) impaired host defence intrinsic to the disease, b) persistent interferon signalling and reduced granulocyte release from neutrophils, and c) suppressed T-helper 17 axis, are postulated mechanisms.
Pneumomediastinum (SPM) is a rare but serious complication of anti-MDA5 DM, with CMV and fungal infections identified as independent risk factors (2). SPM may represent an additional downstream consequence of immune dysregulation and infection susceptibility in anti-MDA5 DM.
Routine PJP prophylaxis from the time of diagnosis and continuation beyond high-dose glucocorticoid therapy appears justified in high-risk or RP-ILD phenotypes. Baseline CMV testing and serial surveillance during treatment are also recommended, with emerging evidence for routine prophylaxis.
Key words: infection, prophylaxis, dermatomyositis, interstitial lung disease

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INTERFERON-B TRIGGERS Z-DNA BINDING PROTEIN 1-MEDIATED PANOPTOSIS IN T CELLS OF ANTI-MELANOMA DIFFERENTIATION ASSOCIATED PROTEIN 5 ANTIBODY-POSITIVE DERMATOMYOSITIS

Xinxin Zhang[1,2], Guochun Wang[1,2], Qinglin Peng[1,2]
[1]Peking University China-Japan Friendship School of Clinical Medicine, Beijing, China, [2]Department of Rheumatology, Key Myositis Laboratories, China-Japan Friendship Hospital, Beijing, China

Objective. To investigate the role of PANoptosis activation in anti-melanoma differentiation-associated protein 5 (MDA5) antibody-positive dermatomyositis (anti-MDA5$^+$ DM).
Methods. Transcriptomic profiling of peripheral blood mononuclear cells (PBMCs) from 40 patients with anti-MDA5$^+$ DM and 10 healthy controls (HCs) was performed. The PANoptosis signature score was constructed using single sample gene set enrichment analysis based on the mean enrichment scores of the pyroptosis, apoptosis, and necroptosis gene sets, and the clinical associations of the PANoptosis signature score in patients with anti-MDA5$^+$ DM were evaluated. PANoptosis markers were analyzed via western blotting and the regulatory mechanism of PANoptosis activation was studied in Jurkat cells in vitro.
Results. Transcriptomic profiling demonstrated overactivation of the PANoptosis signaling pathway in patients with anti-MDA5$^+$ DM. The PANoptosis signature score was positively correlated with inflammatory markers, type 1 interferon (IFN) signature score, disease severity, and poor prognosis in patients with anti-MDA5$^+$ DM. Z-DNA binding protein 1 (ZBP1) was identified as a key PANoptosis-related gene in anti-MDA5$^+$ DM. PANoptosis markers, including P-MLKL, GSDMD-N, cleaved caspase-8, cleaved caspase-3, and cleaved caspase-7 were significantly upregulated in T cells from patients with anti-MDA5$^+$ DM. Functional assays demonstrated that IFN-β induced PANoptosis activation in T cells in vitro, which was significantly attenuated following ZBP1 knockdown
Conclusions. PANoptosis overactivation was associated with disease severity and prognosis in anti-MDA5$^+$ DM. Our findings indicated that IFN-β triggered ZBP1-mediated PANoptosis in T cells, highlighting PANoptosis as a novel potential therapeutic target for anti-MDA5$^+$ DM.
Key words: anti-MDA5$^+$ DM, IFN-β, ZBP1, T cell, PANoptosis

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SINGLE-CELL TRANSCRIPTOMIC DIFFERENCES IN ALVEOLAR MACROPHAGES AND NEUTROPHILS IN A MODEL OF MELANOMA-DIFFERENTIATION ASSOCIATED GENE 5-INDUCED INTERSTITIAL LUNG DISEASE

Yuki Ichimura[1,2], Karin Endo[2], Taku Namatame[2], Tadatsune IIda[2], Naoko Okiyama[2]
[1]Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Tokyo, Japan, [2]Department of Dermatology, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, Tokyo, Japan

Background. Anti-melanoma differentiation associated gene 5 (MDA5) antibody-positive dermatomyositis frequently presents rapidly progressive interstitial lung disease (RP-ILD), leading to a high mortality rate during the acute phase. The etiology of the disease was scarcely understood due to the high mortality rate. Recently, we have established new murine model mimicking anti-MDA5 antibody-positive ILD, and the detailed analysis of the model may produce the clue to clarify the mechanism of the disease. Here, we evaluated the cell-specific transcriptome of the model.
Methods. Emulsion containing recombinant murine MDA5 full-length protein and complete Freund's adjuvant (CFA) were injected intradermally to C57BL6/J mice weekly for 4 times. Polyinosinic-polycytidylic acid [poly(I:C)] were administrated intranasally at the time of last immunization. Lung samples were collected 14 days after last immunization, and dissociated them into single cell suspension, following to single cell RNA-sequencing. Control mice were treated with intradermal injections of CFA and transnasal administration of poly (I:C). The data were analyzed with Seurat v5 on R. Gene Set Enrichment Analysis (GSEA) was performed on each annotated cluster using the Gene Ontology database. The differentially expressed genes (DEGs) of each cluster were extracted as well.
Results. Several clusters including the clusters annotated macrophage, T cell, and neutrophil had several DEGs. Neutrophils in the MDA5 group showed high expression of genes related to chemotaxis, such as S100a9 and S100a8, and GSEA showed the enrichment of humoral immune response in neutrophil cluster in the MDA5 group. The alveolar macrophage cluster showed distinct phenotypes in the MDA5 group, including higher expression of cytokines.
Conclusions. MDA5-induced ILD model showed distinct transcriptomic differences in several cell clusters, such as neutrophils and alveolar macrophages. These findings may give a key to understanding the pathogenesis of anti-MDA5 antibody-positive RP-ILD.
Key words: anti MDA5 antibody, interstitial lung disease, murine model

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MUSCLE TRANSCRIPTOMIC PROFILE IN PATIENTS WITH DERMATOMYOSITIS WITHOUT CHARACTERISTIC HISTOPATHOLOGICAL FINDINGS

José Milisenda[1], Enmanuel Leiva-Murillo[1], Ana Matas-García[1], Andrew Mammen[2], Iago Pinal-Fernández[2]
[1]Hospital Clínic de Barcelona, Barcelona, Spain, [2]NIH, Bethesda, USA

Background. Idiopathic inflammatory myopathies (IIM) are a group of autoimmune-based multisystem muscle disorders whose classification relies on clinical features, autoantibody profiles, and muscle biopsy findings. However, the recent characterization of muscle transcriptomic signatures in IIM has enabled highly accurate disease classification. We aim to assess the performance of muscle transcriptomic profiling in a series of patients with suspected dermatomyositis (DM) who lack characteristic histopathological findings.
Methods. Six patients with suspected DM evaluated between 2008 and 2020 at the Muscle Pathology Unit of Hospital Clínic de Barcelona were included. Clinical characteristics and profiles of myositis-specific (MSA) and myositis-associated (MAA) antibodies were collected. Each patient underwent two open muscle biopsies for diagnostic purposes. Histopathological analysis was performed independently by two muscle pathologists. RNA sequencing was conducted on muscle samples from the six patients. Gene expression profiles were compared with transcriptomic data from patients with confirmed DM, other IIMs, and healthy muscle tissue
Results. Six patients (4 women) with a mean age of 53 years at the time of biopsy were included. All presented muscle involvement, five had cutaneous manifestations, and one had dysphagia. The median CK level was 1700 IU/L. Three patients had MSA (2 anti-TIF1 and 1 anti-NXP2), four had MAA, and one was seronegative. None of the initial biopsies showed the characteristic histopathological features of DM. According to the EULAR/ACR criteria, four patients met the criteria for Definite IIM and two for Probable IIM, despite the absence of characteristic biopsy findings. In only one case did a second biopsy change the classification from Probable to Definite IIM.
Transcriptomic analysis of gene expression from the initial muscle biopsies classified all six patients as DM. Moreover, differential expression patterns associated with specific MSA profiles were identified
Conclusions. The current EULAR/ACR criteria for IIM have a sensitivity and specificity of 87% and 82% without muscle biopsy, increasing to 93% and 88% when biopsy is included. Characteristic biopsy features include inflammatory infiltrates (endomysial, perimysial, perivascular), perifascicular atrophy, and rimmed vacuoles, though diagnostic yield varies among IIM subgroups. In clinical practice, muscle biopsy confirms IIM in ~50% of suspected cases. In dermatomyositis, biopsy sensitivity ranges from 35–47% using classical features, but up to 71% with immunohistochemistry. In contrast, transcriptomic profiling classifies IIM phenotypes with >90% sensitivity and specificity and accurately identifies DM even without classic biopsy findings. Muscle transcriptomics therefore provides a distinct molecular signature that may improve future classification criteria and standardize patient selection in clinical trials.
Key words: dermatomyositis, muscle biopsy, transcriptomic profiling

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MUSCLE INFLAMMATION DRIVES MITOCHONDRIAL IMPAIRMENT IN A HUMAN CELL STRESS MODEL OF AUTOIMMUNE MYOSITIS (IIM)

Stefanie Meyer[1,2], Lennart Kazmaier[1,2], Fernanda Ramos-Gomes[3], Daniel Hoffmann[4], Jens Schmidt[1,5,6], Frauke Alves[3,7,8], Jana Zschüntzsch[1,2]
[1]Department of Neurology, University Medical Center Goettingen, Goettingen, Germany, [2]Heart and Brain Center Goettingen, Goettingen, Germany, [3]Max-Planck-Institute for Multidisciplinary Sciences Goettingen, Goettingen, Germany, [4]Department of Trauma Surgery, Orthopedics, and Plastic Surgery, University Medical Center Goettingen, Goettingen, Germany, [5]Department of Neurology and Pain Medicine Immanuel Clinic Ruedersdorf, University Hospital of the Brandenburg Medical School Theodor Fontane, Germany, [6]Faculty of Health Sciences Brandenburg, Brandenburg Medical School Theodor Fontane, Germany, [7]Department of Hematology and Medical Oncology, University Medical Center Goettingen, Germany, [8]Institute for Diagnostic and Interventional Radiology, University Medical Center Goettingen, Goettingen, Germany

Background. Histopathological signs of mitochondrial impairment are a hallmark of inclusion body myositis (IBM), a subtype of autoimmune myositis showing distinct features in muscle pathology, clinical progression and therapy response (1). Despite extensive ongoing research, molecular pathways of IBM pathogenesis, incorporating muscle inflammation, protein accumulation as well as mitochondrial damage remain elusive. Mitochondria are dynamic intracellular networks, constantly engaging in fusion and fission adapting to cellular needs. Previous experiments in our group revealed increased mitochondrial fission in myoinflammation (2), which is further illuminated in this study.
Methods. In a cell culture model for autoimmune myositis, the influence of pro-inflammatory cytokines (IL-1β, IFNγ) on mitochondrial fusion (MFN2, OPA1) and fission (DRP1) was evaluated (qPCR, WB, Imaging). Mitochondrial phenotype and function (Confocal Microscopy, Seahorse XF Analysis) were evaluated in a knock-down of MFN2 and DRP1.
Results. IL-1β and IFNγ exposure resulted in a significant decrease in OPA1 (WB, p=0.016), specifically isoform L-OPA1 (p=0.0497) as well as a significant increase of cells with a fragmented mitochondrial phenotype (p=0.012). Knock-down of DRP1 prevented the fragmentation of the mitochondrial network when exposed to pro-inflammatory cytokines. MFN2-knock-down resulted in a massively fragmented mitochondrial network, with a trend towards COX-IV deficient mitochondria in both-knock-down conditions. In DRP1-knockdown, Seahorse XF Analysis revealed a trend towards increased free respiratory capacity (p=0.12) with significantly reduced coupling efficiency (p=0.005).
Conclusions. Cytokine-dependent myoinflammation disrupts mitochondrial dynamics and function in a cell-culture model for myositis. Increased mitochondrial fission potentially prepares mitophagy, to eliminate damaged mitochondrial mass securing cell survival. Implications of cytokine-mediated cell stress on mitophagy need to be assessed to evaluate downstream mechanisms resulting in failure of internal quality control mechanisms and intramuscular accumulation of damaged mitochondria.
Acknowledgements. S.M. was supported by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) within the Clinician Scientist Program "Cell Dynamics in Disease and Therapy" at the University Medical Center Goettingen (project number 413501650).

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P-280

SPATIAL TRANSCRIPTOMIC ANALYSIS OF TREATMENT-NAIVE INFLAMMATORY MYOPATHY MUSCLE USING XENIUM 5K PRIME PANEL

Jianna He[1,2,3], Lucinda Berglund[2,3], Joanne Reed[1,3]
[1]Westmead Institute for Medical Research, Westmead, Australia, [2]Westmead Hospital, Westmead, Australia, [3]The University of Sydney, Camperdown, Australia

Background. Spatial transcriptomics is a rapidly evolving technology that evaluates gene signature and its locational information within a tissue section at a cellular level. The technology is increasingly applied in autoimmunity research but faces challenges in idiopathic inflammatory myopathy (IIM) due to the highly diverse cell structure and size in skeletal muscle. This is a proof-of-concept study using the Xenium platform to analyse treatment-naive IIM human skeletal muscle section.
Methods. Human vastus lateralis muscle specimen was obtained from a newly diagnosed, treatment-naive TIF1-gamma positive IIM patient with ovarian cancer. The sample was obtained intraoperatively and placed immediately into 10% formalin for formalin-fixed paraffin embedded preparation. Subsequent analysis was performed using the Xenium Prime 5K Gene panel. Cell segmentation of muscle fibres was performed using in-house Xenium large-cell segmentation pipeline, as well as manual segmentation using third party software to optimise cell clustering accuracy and transcript comparison.
Results. The immediate placement of muscle sample in 10% formalin gave a high percentage of high-quality gene transcripts (87.9%). Manual cell segmentation using Cellpose3 out-performed Xenium automated segmentation. A mosaic pattern of type 1 fibres (MYO18B expression) and type 2 fibres (MYH1 and MYH2 expression) was observed. High transcript counts of JAK1, STAT1 and STAT3 was observed along with high transcript count in IL6R and IL6ST but not IL6. While this may reflect the inherent role that JAK/STAT plays in muscle homeostasis, the spatial density of these gene expression correlated to areas of myogenesis and proliferation gene expression (CD34, MEF2A, MYOD1), potentially indicating areas of muscle damage and regeneration. Immune cell markers (BCL6, CD38, FCGR3A, FCGR3B, CD4, CD8A, CD27, CD19, CD79A/B, and MS4A1) were found throughout the sample, with a greater collective density in a perimysial distribution, corresponding to classic histopathology description of IIM. Genes associated with ovarian cancer such as AKT1, ARID1A, CTNNB1, FOLR1, FOLR2, PIK3R1, PP2R1A and PTEN were also expressed, but further analysis is required.
Conclusions. This pilot study demonstrated that Xenium platform and its Prime 5K panel can produce high quality spatial transcriptomic data in human skeletal muscles, but manual cell segmentation is required for optimal accuracy. JAK1/STAT expression is prominent throughout, but its distribution may shed light on IIM muscle damage and regeneration. Cancer-related gene expression in TIF1-gamma IIM was demonstrated, opening new research possibility to investigate the paraneoplastic role of TIF1-1 gamma in IIM and malignancy.
Acknowledgements. Sample preparation and analysis was performed with assistance from Westmead Institute for Medical Research Scientific Platform.
Key words: myositis, spatial transcriptomics

P-301

CHIMERIC NOD SCID MODEL OF MYOSITIS USING PERIPHERAL BLOOD MONONUCLEAR CELLS FROM A PATIENT WITH MDA5+ DERMATOMYOSITIS RECAPITULATES DISEASE FEATURES

Samantha Coss[1], Pamela Gonzalez Manrique[2], Wael Jarjour[2]
[1]Nationwide Children's Hospital, Columbus, USA, [2]The Ohio State University, Columbus, USA

Background. Anti–melanoma differentiation-associated gene 5 (MDA5) dermatomyositis (DM) is a distinct subtype of inflammatory myositis characterized by prominent cutaneous manifestations, minimal myositis, and a high risk of rapidly progressive, potentially fatal interstitial lung disease (ILD)1-2. The pathogenesis of MDA5+ DM remains unclear. Notably, familial cases have not been reported in the literature to date. Here we present the case of a 40-year-old African woman with MDA5+ DM and a family history of anti-MDA5 DM and early ILD in her young son. We also present

the results of murine humanization experiments using immune cells derived from this patient, demonstrating the feasibility and power of this model for studying myositis.
Methods. Peripheral blood mononuclear cells (PBMC) were adoptively transferred into immunodeficient NOD-SCID IL2Rgamma-null mice (NSG) at 10 e6 cells per mouse. Three weeks after injection, tissues were harvested and sent for histological analysis.
Results. A 40-year-old African American woman presented with abrupt polyarticular inflammatory arthritis and a rash consistent with anti-MDA5+ amyopathic DM. She was ultimately hospitalized with non-specific interstitial pneumonia pattern ILD and myocarditis/pericarditis. Her course was complicated at different times by recurrent skin ulceration, macrophage activation syndrome, and several severe infections. Treatments used to achieve remission included high-dose steroids, anakinra, and IVIG. The patient elected to stop treatment, however, and later developed colitis and recurrence of her skin disease, worsening inflammatory arthritis, exertional dyspnea, a reduced cardiac ejection fraction, moderate restrictive pulmonary function tests, though muscle strength was preserved. She was started on upadacitinib and has regained remission.
PBMC isolated from the patient at that time were sufficient to induce organ-specific inflammation, including pulmonary infiltrates, in NSG mice without driving generalized graft versus host disease (GVHD).
Conclusions. This is the first known instance of myositis elicited by adoptive transfer of DM patient-derived cells into NSG mice and represents an important advancement in small animal models of myositis. Additionally, the disease concordance between mother and son suggests a strong genetic/epigenetic component to the disease; further studies are pending and may provide unprecedented insight into the pathogenesis of dermatomyositis.
Acknowledgements. We thank our patients for their generous participation.
Key words: dermatomyositis, MDA5, disease model

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HISTIDYL-TRNA SYNTHETASE-INDUCED MYOSITIS IS MEDIATED BY MEMBRANOPATHY AND AMELIORATED BY REGULATORY T CELLS

Samantha Coss[1], Nicholas Young[2], Shane Bruckner[2], Braden Zeno[2], Gianni Giarrano[2,3], Hannah Bulgart[3], Paula Clemens[4], Jisna Paul[2], Chester Oddis[4], Noah Weisleder[3], Dana Ascherman[4], Wael Jarjour[2]
[1]Nationwide Children's Hospital, Columbus, USA, [2]The Ohio State University, Columbus, USA, [3]University of Kentucky, Lexington, USA, [4]University of Pittsburgh, Pittsburgh, USA

Background/Objective. Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of autoimmune disorders primarily affecting muscle. One common autoantibody associated with IIM is anti-histidyl-tRNA synthetase (HRS; Jo-1). Although the pathogenic mechanisms of IIM are incompletely understood, murine HRS (mHRS) administration in mice has been shown to recapitulate pathology observed in humans with anti-Jo-1 myositis (1). Our group has shown that disruption of muscle membrane repair via genetic knockout (of synaptotagmin VII, Syt VII, a membrane repair protein) or via autoantibody binding (targeting TRIM72) causes a membranopathy that exacerbates inflammatory myositis (2). Human myositis patients commonly harbor anti-TRIM72 antibodies (2), but their pathogenic role is unclear. In this study, we used the mHRS-induced animal model of myositis to evaluate the role of membranopathy in IIM pathogenesis and to investigate the therapeutic potential of regulatory T cells (Tregs).
Methods. Wild-type (WT) C57BL/6 and Syt VII knockout (KO) mice (B6.129S1-Syt7tm1Nan/J) were injected intramuscularly with recombinant mHRS. At experimental endpoints, histopathology of muscle tissue was analyzed and serum was collected. To evaluate suppression of disease pathology, Tregs isolated from WT mice were co-administered with mHRS injections. Sarcolemmal membrane repair capacity in skeletal muscle was also assessed ex vivo by laser injury assays.
Results. HRS-induced myositis leads to the generation of not only anti-HRS but also anti-TRIM72 antibodies. Membrane repair is also delayed or defective in HRS-treated mice as measured by laser injury assay. In mice with mutations in Syt VII, mHRS-induced myositis is exacerbated, including increased levels of autoantibodies compared to WT mice. Regulatory T cells can rescue the inflammatory phenotype in muscle induced by mHRS in Syt VII KO mice.
Conclusions/Discussion. Membranopathy is both a trigger for and a consequence of inflammatory myositis induced by HRS in mice. mHRS administration in WT mice causes myositis associated with delayed membrane repair and increased titers of autoantibodies targeting autoantigens associated with human myositis, including TRIM72. Conversely, in Syt VII KO mice with congenital defects in membrane repair, both histological myositis and autoantibody production are increased. Adoptive transfer of Treg can ameliorate inflammation, highlighting an important role for these cells in protecting against disease.
Key words: membranopathy, Jo-1, Treg

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ASSESSMENT OF INFECTIONS AND ANTIMICROBIALS AS RISK FACTORS FOR IIM

Nhat-han Bui[1], Lisa Rider[2], Kakali Sarkar[2], Ira Targoff[3], Chester Oddis[4], Steven Ytterberg[5], Rohit Aggarwal[4], Lisa Christopher-Stine[6], Ejaz Shamim[7], Paul Dellaripa[8], Sonye Danoff[9], Andrew Mammen[10], Jesse Wilkerson[11], Frederick Miller[2], Adam Schiffenbauer[2]
[1]Haverford College, USA, [2]Environmental Autoimmunity Group, National Institute of Environmental Health Sciences, National Institutes of Health, Bethesda, USA, [3]Veterans Affairs Medical Center, University of Oklahoma Health Sciences Center, Oklahoma Medical Research Foundation, Oklahoma City, USA, [4]Myositis Center, University of Pittsburgh School of Medicine, Pittsburgh, USA, [5]Division of Rheumatology, Mayo Clinic, Rochester, MN., USA, [6]Johns Hopkins Myositis Center, Johns Hopkins University School of Medicine, Baltimore, MD; Departments of Neurology and Medicine, Johns Hopkins University School of Medicine, Baltimore, USA, [7]Department of Neurology, Mid-Atlantic Permanente Research Institute, Kaiser Permanente, Rockville, USA, [8]Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital, Boston, USA, [9]Division of Pulmonary and Critical Care Medicine, Johns Hopkins School of Medicine, Baltimore, USA, [10]Departments of Neurology and Medicine, Johns Hopkins University School of Medicine, Baltimore, MD; National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, USA, [11]Social & Scientific Systems, a DLH Holding Corp. Company, Durham, USA

Background. Idiopathic inflammatory myopathies (IIM) are a group of rare systemic autoimmune rheumatic diseases. IIM is traditionally characterized by inflammation and weakness of the skeletal muscles. The exact pathogenesis of IIM is unknown; however, it is thought that IIM is acquired through a combination of genetic and environmental risk factors. Two environmental influences that have shown an effect on IIM risk are infections and antimicrobial use. As infections and antimicrobial use are heavily correlated, it is difficult to elucidate their individual impact. This study of recent onset IIM patients attempts to understand the individual and combined risk of infections and antimicrobials on the development of IIM.
Methods. This multicenter study enrolled IIM patients meeting possible, probable, or definite Bohan and Peter criteria, to capture patients early in their disease course. Patients had to advance to probable or definite Bohan and Peter criteria at their 4-month follow-up assessment to be included in the analysis. To minimize recall bias, patients were enrolled within two years of their reference date, defined as the date at which the greatest number of Bohan and Peter criteria were reached. Patients were defined as being anti-synthetase syndrome positive (ASyS+) or negative (ASyS-) based on autoantibodies and symptoms. Per the protocol controls were enrolled that had no autoimmune disease and were matched to be within 10 years of age for adults and within 5 years of age for juveniles, as well as by sex, ethnicity, race, and residential geographic location reference date within 150 miles to IIM patients with antisynthetase syndrome.
Results. Infections were positively associated with development of IIM (OR = 4.365, CI [1.955, 9.748], p<0.0001) but were not selective for ASyS- or ASyS+ IIM. Antimicrobials were positively associated with development of IIM (OR = 3.148, CI [1.120, 8.846], p=0.0001). We performed a joint effect

analysis to distinguish the effect of infections and antimicrobials. Risk of IIM was higher in groups that took an antimicrobial and had an infection than the additive frequency of groups that only had infection, and groups that used an antimicrobial only (OR Infections = 3.42, OR Antimicrobials = 4.49, Expected Additive Effect (EAR) = 7.91, Actual Risk = 13.18, Relative Excess Risk of Interaction (RERI) = 5.90).
Conclusions. Our data suggests infections and antimicrobial use and infections are risk factors for IIM with a compounding effect that increases risk.
Key words: environmental risk, infections, antimicrobials

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NOTCH3 SUPPRESSES REGULATORY T CELL CONTROL OF PROINFLAMMATORY MACROPHAGE STATES

Lisa Kimpler[1], Sara Sabbagh[1]
[1]Division of Rheumatology, Department of Pediatrics, Medical College of Wisconsin, Milwaukee, USA

Background. Foxp3+ T-regulatory (Treg) cells are essential regulators of muscle repair. Following injury, Tregs play a key role in the phenotypic switch of macrophages from a proinflammatory (M1) to a regulatory (M2) phenotype via unknown mechanisms. In idiopathic inflammatory myositis, macrophages are skewed to an M1-like state and drive interferon signaling. Here we investigate how loss of the Notch3 receptor on muscle Tregs affects macrophage states following injury
Methods. 10-week-old Foxp3EGFP and Foxp3YFP-Cre mice that express enhanced green or yellow fluorescent protein under control of the Foxp3 promoter (controls, Jax) and Foxp3YFP-CreNotch3Δ/Δ mice, which have a non-functioning Notch3 receptor (gift from Talal Chatila), were injected with 50ul of 10uM cardiotoxin (CTX, Sigma Aldrich) in the tibialis anterior and/or gastrocnemius. Muscle was harvested 1-, 3-, and 7-days post injection and flash frozen in supercooled 2-methylbutane or processed into single cell suspensions (Skeletal Muscle Dissociation Kit, Miltenyi Biotec) and incubated with anti-CD4, -CD8a (ThermoFisher), -F4/80, -CD11b, -Ly6c, -Notch3 (Biolegend), and -JAG1 (Invitrogen). Data were acquired on a Cytek Aurora 5-Laser spectral cytometer utilizing SpectroFlo (Cytek Biosciences) and analyzed using FlowJo (Tree Star). Muscle injury was confirmed via histology. All experiments were performed in triplicate and according to the guidelines of the MCW Institutional Animal Research Committee.
Results. Foxp3EGFP mice express the Notch3 receptor on Tregs, with peak expression one day following CTX injection. On day 7 following CTX injection, Foxp3YFP-CreNotch3Δ/Δ mice have a lower percent of F4/80/CD11b+ macrophages that express the M1 marker, Ly6c, compared to Foxp3YFP-Cre mice (54% *vs*. 71%, p=0.02). Foxp3YFP-CreNotch3Δ/Δ mice also have a lower percent of Ly6c- macrophages with expression of the Notch ligand, Jagged-1 (JAG1), which sustains an M1 phenotype (23% *vs*. 36%%, p=0.04). Lastly, we observed trends of lower expression of JAG1 on F480/CD11b+ (total) macrophages (26% *vs*. 44%, p=0.07) and a lower number of M1s per gram of muscle (1.27E106 *vs*. 1.9E106, p=0.06) in Foxp3YFP-CreNotch3Δ/Δ compared to Foxp3YFP-Cre mice.
Conclusions. Our preliminary data show that lack of Treg-specific Notch3 decreases macrophage M1 polarization. Our data suggest that Notch3 expression on Tregs may suppress a regulatory T cell phenotype and help sustain a proinflammatory environment in early stages of muscle injury. Our data is the first to describe a proinflammatory function of muscle Treg Notch signaling, specifically as a regulator of macrophage polarization. Future work will investigate the role of Treg Notch3 on Treg recruitment and function, muscle regeneration, and microvascular repair.
Key words: T-regs, notch, murine myositis

P-345

SKELETAL MUSCLE EXPRESSION OF IL-17 FAMILY CYTOKINES IN A MOUSE MODEL OF MYOSITIS

Madison King[1], Elizabeth Bagley[1], Alfredo Guzman[1], Rita Spathis[1], Kanneboyina Nagaraju[1], Melissa Morales[1]
[1]Binghamton University, Binghamton, USA

Background. The IL-17 family of cytokines and receptors, most notably IL-17A and IL-17RA, have been shown to be upregulated in patients with inflammatory myopathies, suggesting that it may be a potential novel therapeutic target. IL-17 cytokines contribute to the sustained inflammation present in other auto-inflammatory diseases including psoriatic arthritis, ankylosing spondylitis, and rheumatoid arthritis, and their antagonism has shown positive effects in patients with these conditions. We investigated the expression of IL-17 cytokines in the skeletal muscle of healthy myositis male and female mice.
Methods. The HT myositis mouse model is a conditional model of human myositis that features chronic inflammation and upregulated MHC Class I upon removal of supplemented doxycycline. Mice were removed from doxycycline upon weaning at postnatal day 21. Mice were then observed daily before being euthanized at 50 days old. RNA was extracted from quadriceps muscle of male and female mice using the TRIzol method. The relative expression of IL-17RA, IL-17A, IL-17B, IL-17RC, IL-17C, and IL-17D were evaluated for all groups by rt-qPCR and the 2^-ΔΔCt method.
Results. Expression of IL-17RA were significantly increased compared to wild-type controls in both sexes. In females, HT mice additionally showed increased levels of IL-17B, IL-17C, and IL-17RC. Interestingly, female HT mice showed decreased expression of IL-17D in comparison to wild-type controls.
Conclusions. The HT mouse model of myositis shows elevations in IL-17 gene expression, similar to what is observed in patients with dermatomyositis. We did not observe sex differences between, suggesting this may be a conserved mechanism between sexes that warrants further evaluation. Future studies will explore antagonism of the IL-17 family of cytokines, particularly IL-17RA, as well as the mechanisms of muscle damage.
Acknowledgements. The Myositis Association and Cure JM.
Key words: IL-17, inflammation, models

P-348

THE EFFECTS OF SERUM, CONTAINING MYOSITIS-SPECIFIC AUTOANTIBODIES, ON MUSCLE FIBER CONTRACTILITY IN IMMUNE-MEDIATED NECROTIZING MYOPATHY

Tom Kerkhoff[1,2,3], Sanna Luijcx[1,2], Buram Ardiç[1,2], Patrycja Stachurska[1,2], Anneke van der Kooi[4], Eleonora Aronica[5], Theo Rispens[6,7], Joost Raaphorst[4], Coen Ottenheijm[1,2]
[1]Amsterdam UMC location VUMC, Physiology, Amsterdam, The Netherlands, [2]Amsterdam Cardiovascular Sciences, Pulmonary Hypertension & Thrombosis, Amsterdam, The Netherlands, [3]Amsterdam Movement Sciences, Musculoskeletal Health, Amsterdam, The Netherlands, [4]Amsterdam UMC location AMC, Neurology, Amsterdam, The Netherlands, [5]Amsterdam UMC location AMC, Pathology, Amsterdam, The Netherlands, [6]Research and Lab Services Department, Sanquin Blood Supply, Amsterdam, The Netherlands, [7]Amsterdam UMC location AMC, Immunopathology, Amsterdam, The Netherlands

Background. Immune-mediated necrotizing myopathy (IMNM) is the most severe myositis subtype in terms of muscle weakness. Immunosuppressive therapies are often insufficient and there is a need for better therapies. IMNM is associated with myositis-specific autoantibodies (MSAs) against signal recognition protein-54 (SRP) and 3-hydroxy-3-methylglutaryl CoA reductase (HMGCR), which have been suggested to play a pathogenic role. We have previously shown that the force generating capacity of non-necrotic muscle fibers from untreated IMNM patients is impaired. This may be caused by serological constituents; more specifically IgGs and MSAs, this is however unknown.
Methods. Serum was drawn from treatment naive anti-SRP+, anti-HMGCR+ or seronegative IMNM patients and healthy controls. Subsequently, IgG was isolated from the serum to obtain total IgG and IgG-depleted serum. Healthy intact muscle fibers from the Flexor Digitorum Brevis (FDB) muscle of mice were isolated. After 1 day of culture (to allow the muscle fibers to recover from isolation), fibers were exposed to (IgG-depleted) serum for 2 hours. The muscle fibers were permeabilized and mounted between a force transducer

and length motor; the fibers were then exposed to solutions with incremental Ca2+-concentrations and force was measured.
Results. Our data suggest that muscle contractility is altered after a 2-hour exposure to serum of IMNM patients compared to healthy controls. Maximum normalized force of healthy muscle fibers is lower after exposure to serum from IMNM patients compared to force generated by fibers exposed to serum from healthy controls, whereas Ca2+-sensitivity of force was not altered. Preliminary data from fibers exposed to IgG-depleted patient serum exposure did not replicate the differences as seen after serum exposure, suggesting that IgGs contribute to the force depression.
Conclusions. Serum of IMNM patients has a direct impact on muscle fiber contractility. Since the preliminary data suggest that IgG depleted serum does not affect muscle contractility, it is likely that the IgG of these patients cause the observed effect. To further examine that MSAs play a role in impaired muscle fiber contractility, experiments are ongoing with the IgG and IgG-depleted serum of these patients followed up with purified MSA exposure.
Key words: myofiber contractility, myositis specific autoantibody exposure

P-356

COMBINED RESISTANCE AND ENDURANCE EXERCISE DECREASES DISABILITY AND IMPROVES PHYSICAL CAPACITY IN ESTABLISHED INFLAMMATORY MYOPATHIES: A HOSPITAL- VS COMMUNITY-BASED PROSPECTIVE STUDY

Quentin Toumazeau[1], Léa Debrut[1,2], Pauline Silverstrin[1], Alizée Heit[1], Anne-Laure Charles[1], Bernard Geny[1,3], Margherita Giannini[1,4], Alain Meyer[1,4]
[1]UR3072 Research Centre of Biomedicine Strasbourg, University of Strasbourg, France, Starsbourg, France, [2]Faculty of Sport Sciences, European Centre for Education, Research and Innovation in Exercise Physiology (CEERIPE), University of Strasbourg, Strasbourg, France, Strasbourg, France, [3]Physiology and Function Explorations Department, Strasbourg University Hospitals, France, Strasbourg, France, [4]Physiology and Muscle Function Explorations Department, Referral Centre for Systemic Rare Autoimmune Diseases, Strasbourg University Hospitals, France, Strasbourg, France

Background. Inflammatory myopathies (IM) are autoimmune diseases characterized by chronic skeletal muscle inflammation and weakness. Many patients experience persistent disability despite achieving remission or low disease activity with immunosuppressants. This condition (damage) is frequent, correlates with handicap and mortality. No pharmacological treatment currently targets damage, but combined resistance and endurance exercise (REE) improved exercise capacity (1). However, i) these results have not been replicated, ii) the training program was conducted in a hospital setting limiting access for the patients. This study aimed to validate the efficacy and safety of REE in low disease activity IM patients, compare hospital-based and community-based training and explore the underlying mechanisms.
Methods. Fifty patients with IM (2017 ACR/EULAR criteria) with a disease duration >12 months, CK serum levels <500 IU/L and stable medication for ≥ 6 months were included for a 36-session REE. REE consisted in 30 min of aerobic exercise at 70% of VO_2max followed by 20 min of resistance exercise; 3 sessions per week for 12 weeks (1).
Participants living within 50 km of the university hospital trained under specialist supervision (hospital-based, HB), while others trained with a local physiotherapist (community-based, CB). Adherence to the program, patient-reported outcomes, exercise capacity, muscle strength, body composition, myositis activity, mitochondrial respiration in PBMCs and IMACS damage scores were recorded at baseline and after completion of the 36 sessions.
Results. Twenty-five patients completed the protocol (60% female; 59.7±17 years old; 12.6 ± 5.9 years disease duration; CK=154±182 U/L; VAS physician=2.0±0.8). VO_2max increased to a similar extent after both the HB (Δ=1.68±1.50 mL/min/kg, p=0.0098) and CB (Δ=2.30±2.44 mL/min/kg, p=0.0033) REE.
Power at VO_2max [HB (Δ=17.89±10.55 W, p=0.0009), CB (Δ=14.93±7.38 W, p<0.001)], hand held dynamometer [HB (Δ=14.43±14.48 kg, p=0.008), CB (Δ=9.05±13.32 kg, p=0.019)], 6mWT [HB (Δ=28.64±33.78m, p=0.018), CB (Δ=30.43±54.52m, p=0.057)] similarly improved in both groups.
Perceived fatigue (PROMIS7) decreased in the HB (Δ=–5.82±1.52, p=0.002) as well as in the CB (Δ=–5.75±1.26, p<0.001). Perceived disability (PROMIS20) decreased in the HB (Δ=–5.23±1.6, p=0.006), but not in CB (Δ=–0.38±1.31, p=0.95).
PBMCs mitochondrial respiration improved as shown by complex I leak and complex IV activity (Δ=1.8±3.6 pmol/sec/106cell, p=0.02, Δ=11.05± 23.72 pmol/sec/106cell, p=0.007, respectively).
Conclusions. REE is equally safe and effective for low disease activity IM patients in both hospital-based or community-based settings. Improvement of exercise capacity, muscle strength, perceived disability, and fatigue were associated with an improvement on mitochondrial respiration capacity that may play a role in the efficacy of this non-pharmacological treatment.
Key words: inflammatory myopathies, damage, combined resistance and endurance exercise

P-370

AGGREGATION OF HARS1 AND INTERNALIZED ANTIBODIES IN MUSCLE BIOPSIES OF PATIENTS WITH ANTI-SYNTHETASE SYNDROME AND ANTI-JO1(HARS) AUTOANTIBODIES

Maria Casal-Dominguez[1,2], Iago Pinal-Fernandez[1,2], Katherine Pak[1], Travis Kinder[1], Jon Musai[1], Ana Matas-Garcia[3], Gloria Garrabou[3], Iban Aldecoa[3], Albert Selva-O'Callaghan[4], José Milisenda[3], Andrew L Mammen[1,2]
[1]National Institutes of Health, Bethesda, USA, [2]Johns Hopkins Neurology Department, Baltimore, USA, [3]Clinic Hospital, Barcelona, Spain, [4]Vall d'Hebron Hospital, Barcelona, Spain

Background. Autoimmune inflammatory myopathies (IMs) comprise a diverse group of diseases that primarily affect the muscles and often involve the lungs, skin, and joints. Among them, patients with autoantibodies against aminoacyl-tRNA synthetases develop a distinct clinical entity known as antisynthetase syndrome (ASyS), characterized by inflammatory myopathy, pulmonary fibrosis, arthritis, Raynaud's phenomenon, and mechanic's hands. The most common antisynthetase autoantibody, anti-Jo1, targets histidyl-tRNA synthetase (HARS).
Recent studies have demonstrated that autoantibodies can penetrate muscle fibers and disrupt the function of their target autoantigens. In ASyS patients, this process induces a distinct transcriptomic profile that recapitulates the effects of pharmacologic inhibition of HARS with histidinol.
This study aims to examine the localization of anti-Jo1 antibodies and their cognate antigen, HARS1, in muscle biopsies from anti-Jo1–positive ASyS patients and diseased controls.
Methods. We performed direct immunofluorescence for IgG and HARS1 staining on 10 μm-thick unfixed muscle sections from patients with anti-Jo1 autoantibodies and those with other forms of inflammatory myopathy. Images were acquired using a Leica SP8 high-resolution confocal microscope.
Results. We observed co-aggregation of HARS1 and internalized IgG in muscle biopsies from ASyS patients with anti-Jo1 autoantibodies. This pattern was not detected in samples from patients with other forms of myopathy.
Conclusions. Our data suggest that antibodies from anti-Jo1 patients induce HARS1 aggregation in the cytoplasm of muscle fibers. Notably, similar HARS1 aggregation has been observed in patients with HARS1 mutations and Charcot-Marie-Tooth (CMT) disease. In CMT, this aggregation disrupts HARS1 function, resulting in errors in peptide translation.
Key words: myositis, antisynthetase syndrome, antibodies, HARS1, immunofluorescence

P-380

SPATIAL TRANSCRIPTOMICS DEFINES FOCAL AUTOANTIBODY-DRIVEN MUSCLE INJURY IN ANTI-MI2-POSITIVE DERMATOMYOSITIS

Iago Pinal-Fernandez[1], Katherine Pak[1], Maria Casal-Dominguez[1], Sandra Munoz-Braceras[1], Gustaf Wigerblad[2], Stefania Dell'Orso[2], Faiza Naz[2], Shamima Islam[2], Gustavo Gutierrez-Cruz[2], Travis B Kinder[1], Sandra Amara Ogbonnaya-Whittlesey[1], Andreu Fernandez-Codina[3], Margherita Giannini[4], Benjamin Ellezam[5], Gilles Laverny[6], Valentine Gilbart[6], Oceane Landon-Cardinal[7], Marie Hudson[8], Yves Troyanov[9], Davide Randazzo[10], Aster Kenea[10], Ana Matas-Garcia[11], Gloria Garrabou[11], Iban Aldecoa[12], Albert Gil-Vila[13], Ernesto Trallero[13], Margherita Milone[14], Teerin Liewluck[14], Elie Naddaf[14], Gerard Espinosa[15], Carmen Pilar Simeon-Aznar[13], Alfredo Guillen-Del-Castillo[13], Corinna Preusse[16], Felix Kleefeld[17], Nikolas Bublitz[18], Werner Stenzel[16], Alain Meyer[4], Janet E. Pope[3], Albert Selva-O'Callaghan[13], Jose C. Milisenda[11], Andrew L. Mammen[1]
[1]Muscle Disease Section, National Institute of Arthritis and Musculoskeletal and Skin

Diseases, National Institutes of Health, Bethesda, MD, USA, [2]Genomic Technology Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, USA, [3]Division of Rheumatology, Western University, London, ON, Canada, [4]Explorations Fonctionnelles Musculaires, Centre de Référence Des Maladies Autoimmunes Rares, Centre de Recherche en Biomédecine de Strasbourg, Rhumatologie, Hôpitaux Universitaires de Strasbourg, UR 3072, Université de Strasbourg, Strasbourg, France, [5]Division of Pathology, CHU Sainte-Justine, Department of Pathology and Cell Biology, Universite de Montreal, Montreal, Quebec, Canada, [6]Universite de Strasbourg, CNRS, Inserm, IGBMC UMR 7104- UMR-S 1258, F-67400 Illkirch, France, [7]Division of Rheumatology, Centre hospitalier de l'Université de Montréal (CHUM), Autoimmunity Research Laboratory, CHUM Research Center, Department of Medicine, Université de Montréal, Montréal, Québec, Canada, [8]Division of Rheumatology, Department of Medicine, Jewish General Hospital, Lady Davis Institute and McGill University, Montreal, QC, Canada, [9]Division of Rheumatology, Hôpital du Sacré-Cœur de Montréal; Department of Medicine, Université de Montréal, Montréal, Québec, Canada, [10]Light Imaging Section, Office of Science and Technology, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, USA, [11]Muscle Research Unit, Internal Medicine Service, Hospital Clinic, IDIBAPS, CIBER, UB, Barcelona, Spain, [12]Pathology, Neurological Tissue Bank. Hospital Clinic of Barcelona-CDB-IDIBAPS/FCRB-University of Barcelona, Barcelona, Spain, [13]Systemic Autoimmune Disease Section, Vall d'Hebron Institute of Research, Barcelona, Spain, [14]Division of Neuromuscular Medicine, Department of Neurology, Mayo Clinic, Rochester, MN, USA, [15]Department of Autoimmune Diseases, Reference Centre for Systemic Autoimmune Diseases (UEC/CSUR) of the Catalan and Spanish Health Systems, Member of ERN-ReCONNET, Hospital Clinic, Barcelona, Spain, [16]Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universitit Berlin, Humboldt-Universitit zu Berlin, and Berlin Institute of Health (BIH), Department of Neuropathology, Berlin, Germany, [17]Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt- Universitit zu Berlin, and Berlin Institute of Health (BIH), Department of Neurology, Berlin, Germany, [18]Division of Rheumatology and Systemic Inflammatory Diseases, III. Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Background. Anti-Mi2-positive dermatomyositis is characterized by autoantibodies directed against Mi2, a core component of the nucleosome remodeling and deacetylase (NuRD) complex, a transcriptional repressor. Prior studies demonstrated that anti-Mi2 muscle biopsies exhibit a highly specific transcriptional program marked by ectopic expression of genes normally repressed by Mi2/NuRD. Purified anti-Mi2 immunoglobulin G (IgG) is sufficient to induce this transcriptional program in vitro, and immunofluorescence demonstrates nuclear accumulation of IgG in muscle cells, consistent with the nuclear localization of Mi2. However, the spatial organization of these events within tissue and their relationship to muscle fiber injury in vivo have remained unclear.
Methods. We performed spatial transcriptomic profiling of diagnostic muscle biopsies from patients with anti-Mi2-positive dermatomyositis using a targeted in situ gene expression panel. Analyses focused on the Mi2-specific gene set identified by bulk RNA sequencing, markers of mature and regenerating muscle fibers, immunoglobulin genes, interferon-responsive pathways, and interferon receptor expression.
Results. Spatial transcriptomics revealed that anti-Mi2-associated transcriptional derepression is highly focal, affecting discrete subsets of myofibers in a perifascicular distribution rather than muscle uniformly. Fibers expressing high levels of Mi2-specific transcripts showed coordinated loss of canonical adult muscle genes, including TTN and myosin heavy-chain isoforms, indicating intrinsic muscle fiber injury. These fibers selectively overexpressed TGFB1 and IL11, linking autoantibody-associated transcriptional reprogramming to profibrotic and atrophic signaling pathways. Notably, fibers expressing the Mi2-specific gene set exhibited reduced expression of type I interferon–inducible genes and the type I interferon receptor subunit IFNAR1. In contrast, adjacent muscle cells demonstrated robust induction of interferon-stimulated genes such as ISG15 and MX1. This spatial dissociation indicates relative interferon unresponsiveness within affected fibers and suggests a paracrine type I interferon response in the surrounding microenvironment. Plasma cells were frequently located adjacent to fibers expressing the Mi2-specific gene set, and immunoglobulin transcripts extended beyond plasma cell boundaries into neighboring muscle cells, consistent with intercellular transfer of antibody-encoding material.
Conclusions. Spatial transcriptomics demonstrates that in anti-Mi2-positive dermatomyositis, autoantibody-associated transcriptional derepression is spatially restricted to perifascicular muscle fibers, directly linked to muscle fiber injury and induction of profibrotic signaling. This process is accompanied by suppression of type I interferon signaling within affected fibers alongside a probable paracrine interferon response in surrounding cells. The close spatial relationship between plasma cells and affected fibers supports a localized mechanism by which plasma cells may directly deliver antibody-encoding material or autoantibodies to muscle.
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Key words: anti-Mi2, spatial transcriptomics, dermatomyositis

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PREDICTORS OF MORTALITY IN IDIOPATHIC INFLAMMATORY MYOPATHY: A NATIONWIDE MULTICENTER COHORT STUDY

Inês Sopa[1,2,*], Mariana Pereira Silva[11,2,*], Filipa Costa[1,2], Bianca Paulo Correia[1,2], João Miguel Pereira[2], Miguel Martins[1,2], Sofia Barreira[1,2], Ana Teresa Melo[1,3], Matilde Bandeira[1,4], Tânia Santiago[5,6], João Oliveira[5,6], Eduardo Dourado[7,8], Cláudia Oliveira[7,8], Sofia Azevedo[7,8], Vanessa Fraga[9], Susana Matias[9], Bárbara Esteves[10], Margarida Rocha[11], Anita Cunha[12], Hugo Gonçalves[13], Rita Cunha[14], Susana Fernandes[15], Ana Leão[15], Catarina Rua[16], Raquel Marques[1,2]
[*]Contributed equally as first authors
[1]Rheumatology Department, Unidade Local de Saúde de Santa Maria, Centro Académico de Medicina de Lisboa (Lisboa, Portugal), [2]Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa (Lisboa, Portugal), [3]Rheumatology Department, Unidade Local de Saúde de São José (Lisboa, Portugal), [4]Rheumatology Department, Unidade Local de Saúde de Viseu (Viseu, Portugal), [5]Rheumatology Department, Unidade Local de Saúde de Coimbra (Coimbra, Portugal), [6]Faculdade de Medicina, Universidade de Coimbra (Coimbra, Portugal), [7]Rheumatology department, Unidade Local de Saúde da Região de Aveiro (Aveiro, Portugal), [8]Centro de Investigação em Reumatologia de Aveiro, Centro Clínico Académico Egas Moniz Health Alliance (Aveiro, Portugal), [9]Rheumatology Department, Unidade Local de Saúde de Almada-Seixal (Almada, Portugal), [10]Rheumatology Department, Unidade Local de Saúde de São João (Porto, Portugal), [11]Reumatology Department, Unidade Local de Saúde do Algarve (Algarve, Portugal), [12]Rheumatology Department, Unidade Local de Saúde do Alto Minho (Ponte de Lima, Portugal), [13]Rheumatology Department, Unidade Local de Saúde de Braga (Braga, Portugal), [14]Rheumatology Department, Unidade Local de Saúde Tâmega e Sousa (Penafiel, Portugal), [15]Rheumatology Department, Instituto Português de Reumatologia (Lisboa, Portugal), [16]Rheumatology Department, Unidade Local de Saúde de Vila Nova de Gaia (Vila Nova de Gaia, Portugal)

Background. Idiopathic inflammatory myopathies (IMM) are associated with considerable morbidity and increased mortality. Evidence on long-term outcomes and mortality risk factors is limited.
Methods. Nationwide cohort study using the Portuguese Rheumatic Diseases Registry (Reuma.pt). Adult IIM patients registered between January 2015 and January 2025 were included and classified using established criteria for polymyositis/dermatomyositis, immune-mediated necrotising myopathy, antisynthetase syndrome and overlap myositis. Cancer-associated myositis (CAM) was defined as malignancy diagnosed within 3 years of myopathy onset. Sociodemographic, clinical, immunological and treatment data were extracted; causes of death were recorded. Survival was analysed using Kaplan-Meier methods and predictors of mortality using Cox proportional hazards regression.
Results. A total of 294 patients were included; most were female (65.6%) and Caucasian (88.6%). The most frequent diagnoses were dermatomyositis (30.2%), anti-synthetase syndrome (15.6%) and overlap syndromes (11.2%). During the 10-year period, 38 deaths were recorded (13%). Patients were followed for 27.5 ± 29.0 months, and time from diagnosis to death was 1.9 ± 3.0 years. Deceased patients were older at disease onset (66.0 *vs*. 50.5, p<0.001) and diagnosis (67.1 *vs*. 52.0, p<0.001). CAM was more frequent among deceased patients (27.0% *vs*. 6.4%, p<0.001), and anti-TIF1-γ positivity was higher (21.2% *vs*. 8.4%, p=0.032). Kaplan-Meier survival was 93.4% at 1 year, 87.7% at 3 years, 85.9% at 5 years and 70.6% at 9 years. Cancer was the leading cause of death (n=10), followed by infection (predominantly pneumonia; n=7) and cardiovascular causes (n=4). Survival differed significantly across IIM subtypes (p<0.001) and between CAM and non-CAM patients (p<0.001), mean survival time was 4.727 years in CAM versus 8.786 years in non-CAM. Among deceased CAM patients, three deaths were directly attributable to malignancy (breast, lung and neuroendocrine cancers). In multivariable Cox regression, older age at diagnosis remained independently associated with mortality, and CAM conferred an approximately five-fold higher hazard of death.
Conclustion. Mortality was highest shortly after diagnosis, with older age at diagnosis and CAM emerging as the principal independent predictors of death. Malignancy was the leading cause of mortality, followed by infection. These findings support early risk stratification, systematic malignancy screening and longitudinal surveillance, particularly in high-risk phenotypes such as CAM and anti–TIF1-γ-positive patients.
Key words: mortality, prognostic predictors, cancer associated myositis, cohort study

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SPATIAL CHARACTERIZATION OF THE PERIPHERAL IMMUNE LANDSCAPE IN MYOSITIS

Barath Ramanathan[1,2], Hao Cheng Shen[3,4,6], Marie Hudson[3,5,6], Yves Troyanov[4,7], Océane Landon-Cardinal[7,8], Geneviève Gyger[3,6], Erin O'Ferrall[6,9], Benjamin Ellezam[7,10], Jason Karamchandani[6,11], Celia del Carmen Crespo Oliva[2], Dominique Jean[2], Zoé Gerber[2], Marilyne Labrie[2], Valérie Leclair[3,5,6], Hugues Allard-Chamard H.[1,12]
[1]Department of Medicine, Université de Sherbrooke, Sherbrooke, Quebec, Canada, [2]Department of Immunology and Cell Biology, Faculty of Medicine and Health Sciences, Cancer Research Institute of the Université de Sherbrooke (IRCUS), Université de Sherbrooke, [3]Division of Rheumatology, Jewish General Hospital, Montreal, Quebec, Canada, [4]Division of Rheumatology, Hôpital du Sacré-Coeur de Montréal, Montreal, Quebec, Canada, [5]Lady Davis Institute, Montreal, Quebec, Canad, [6]Department of Medicine, McGill University, Montreal, Quebec, Canada, [7]Department of Medicine, Université de Montréal, Montreal, Quebec, Canada, [8]Division of Rheumatology, Centre hospitalier de l'Université de Montréal, Montreal, Quebec, Canada, [9]Division of Neurology, Montreal Neurological Institute, Quebec, Canada, [10]Division of Neuropathology, Ste-Justine Hospital, Montreal, Quebec, Canada, [11]Division of Neuropathology, Montreal Neurological Institute, Montreal, Quebec, Canada, [12]Division of Rheumatology, Centre Hospitalier de l'Université de Sherbrooke (CHUS), Sherbrooke, Quebec, Canada.

Background. Idiopathic inflammatory myopathies (IIMs) are systemic autoimmune disorders marked by chronic skeletal muscle inflammation, progressive muscle weakness, and immune-mediated tissue destruction. Although skeletal muscle is not a conventional immune or tolerogenic organ, it is persistently exposed to self and stress-induced antigens as a result of repeated microinjury associated with normal muscle use. In steady-state conditions, myofibers exhibit low antigen-presenting capacity and minimal costimulatory signaling, promoting peripheral tolerance. In IIMs, this balance is disrupted, leading to immune infiltration with distinct spatial organization, including features such as perimysial inflammatory infiltration and muscle fiber atrophy in some IIM such as dermatomyositis.
To elucidate the spatial dynamics of immune cell infiltration in myositis, we applied Cyclic Immunofluorescence (CycIF), a highly multiplexed, spatially resolved imaging platform that enables detailed single-cell phenotyping in situ. We aimed to map immune cell populations, their localization and costimulatory molecule, and interactions within inflamed muscle tissue to better understand mechanisms of tolerance breakdown and autoimmune propagation
Methods. We developed and optimized a multiplex CycIF assay capable of profiling over 60 immune and structural markers on a single tissue section. This approach enabled high-resolution spatial analysis of key immune subsets, including T peripheral helper (Tph) cells, $CD4^+$ and $CD8^+$ T cells, B cells, macrophages, and dendritic cells, within muscle tissue. A custom computational pipeline was implemented for single-cell segmentation, phenotypic classification, spatial mapping, and analysis of cell–cell interactions, including proximity-based signaling potential and immune-myofiber crosstalk.
Results. We have successfully identified several immune cell types, including B and T cells, macrophages, dendritic cells, and stromal populations such as vascular endothelial cells and myocytes.Our ongoing analysis is advancing along two main research directions. First, we are investigating autoimmune organisation within muscle tissue by uncovering spatial relationships and functional interactions between T peripheral helper (Tph) cells, B cells, and other immune subsets within ectopic lymphoid-like structures present in IIM muscle. These analyses will reveal key insights into the local breakdown of immune tolerance and mechanisms driving autoantibody production. Second, we are characterizing the architecture and immune composition of tertiary lymphoid structure and immune aggregates, with a particular focus on the co-localization of antigen-presenting cells and lymphocytes and their correlation with clinical markers of disease activity.
Conclusions. Together, these findings will provide a spatially resolved framework for understanding the immunopathology of myositis, how immune tolerance is broken down and may inform the development of targeted immunotherapies aimed at disrupting pathogenic immune niches within affected muscle tissue.
Acknowledgement: Myositis Canada
Key words: B cells, T peripheral helper (Tph) cells, cyclic Immunofluorescence (CycIF), idiopathic inflammatory myopathies (IIMs)

Patient Perspectives

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'YOUR BODY IS DOING SOMETHING YOU DON'T WANT IT TO': UNDERSTANDING THE HEALTH JOURNEYS OF ABORIGINAL PEOPLE WITH MUSCLE DISEASES

Thomas Khoo[1,2,3], Janet Kelly[1], Jackie Lamshed[4], Kim Morey[1,5], Odette Pearson[1,5], Vidya Limaye[1,2]
[1]Faculty of Health and Medical Sciences, University of Adelaide, Adelaide, Australia, [2]Rheumatology Unit, Royal Adelaide Hospital, Adelaide, Australia, [3]Rheumatology Unit, Southern Adelaide Local Health Network, Adelaide, Australia, [4]Patient Research Partner, Adelaide, Australia, [5]Aboriginal Health Equity Research and Strategy, South Australia Health and Medical Research Institute, Adelaide, Australia

Background. Aboriginal and Torres Strait Islander peoples in Australia experience significant health service inequities, contributing to detrimental outcomes. Current models of healthcare, through diagnosis, treatment and follow-up, do not adequately integrate the perspective and priorities of Aboriginal patients. We aimed to understand the experiences of Aboriginal peoples with muscle diseases through focusing on the patient journey.
Methods. Individual interviews were undertaken with six Aboriginal participants diagnosed with muscle diseases. Health journey mapping approaches were utilised to enable detailed discussion cross-sectionally (encompassing physical, emotional, cultural/spiritual and social/community dimensions) and longitudinally (considering disease progress and geographical journey). Reflexive thematic analysis was paired with journey mapping to identify both meaning and context.
Results. Three main themes and one central theme were identified. In 'the importance of connection', participants described hospitals as isolating and identified the importance of family connections and understanding. Conversely, interpersonal conflict was felt to trigger illness in some instances. In 'the high burden of symptoms', the impact of muscle weakness on basic tasks, and the severity and unpredictability of symptoms were discussed. 'The difficulty of understanding and coping with a rare condition' focused on trying to understand muscle disease by comparing to more familiar conditions such as cancer or infection, and recognition of the shared challenges that rare conditions pose to both doctors and patients. Central to these experiences was 'striving to maintain the self', a determination to meet one's physical and family-role expectations despite the limitations of muscle diseases.
Journey mapping illustrated what participants described as the 'rollercoaster' of muscle diseases. Improvements often parallelled geographical progression: intensive care unit (ICU) to ward, city to local country hospital, and hospital to home. Deteriorations were highlighted when complications, new symptoms or medication side effects occurred. Although events such as going to ICU were recognised as important, these were not necessarily perceived as being as significant as some symptoms which had a greater impact on quality of life.
Conclusions. These data uniquely capture the experiences of Aboriginal peoples with muscle diseases. The impact of muscle dysfunction extended beyond weakness, additionally disconnecting the sense of self from physical and family-role expectations. Strength was predominantly derived from connection with family, and through partnering with doctors in meeting the challenge of rare diseases. Asking participants to map their journeys through verbal discussion and visual illustration highlighted that patient perspectives were often goal-oriented; returning home and controlling symptoms were high priorities, often more important than seeking a diagnosis.
Key words: qualitative research, patient perspective, Aboriginal health research

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CONTEXTUALIZING SEXUAL WELL-BEING IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Hannah Maher[1], Lekshmi, Minikumari Rahulan[2], Jasmine Parihar[3], Laura Andreoli[4,5,6], Luis, Fernando Perez-Garcia[7], Vidya, Sadanand Limaye[8,9], Allison Foss[10], Stephen Reddel[11,12], Tsvetelina Velikova[13], Uzma Rasheed[14], Chongbo Zhao[15], Xicheng Li[15], Masataka Kuwana[16], Vahed Maroufy[17], Vikas Agarwal[2], Mazen M. Dimachkie[18], Latika Gupta[19,20], on behalf of the COVAD Study Group

[1]University Of Minnesota Medical School, Minneapolis, USA, [2]Department of Clinical Immunology and Rheumatology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India, [3]Department of Neurology, All India Institute of Medical Sciences, New Delhi, India, [4]Rheumatology and Clinical Immunology Unit, ERN ReCONNET, ASST Spedali Civili and University of Brescia, Brescia, Italy, [5]Danish Centre for Expertise in Rheumatology (CeViG), Danish Hospital for Rheumatic Diseases, Sønderborg, Denmark, [6]Department of Regional Health Research, University of Southern Denmark, Odense, Denmark, [7]Department of Rheumatology, Erasmus University Medical Center, Rotterdam, Netherlands, [8]Rheumatology Department, Royal Adelaide Hospital, Adelaide, Australia, [9]Discipline of Medicine, University of Adelaide, Adelaide, Australia, [10]Myasthenia Gravis Association, Kansas City, USA, [11]Faculty of Medicine and Health, University of Sydney, Sydney, Australia, [12]Neurology Department, Concord Repatriation General Hospital, Sydney, Australia, [13]Medical Faculty, St. Kliment Ohridski University, Sofia, Bulgaria, [14]Department of Rheumatology, Pakistan Institute of Medical Sciences Islamabad, Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad, Pakistan, [15]Department of Neurology, National Center for Neurological Disorders (NCND), Huashan Hospital, Fudan University, Shanghai, China, [16]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [17]Department of Biostatistics and Data Science, School of Public Health, University of Texas Health, Austin, USA, [18]Neurology Department, Neuromuscular Division, The University of Kansas Medical Center, Kansas City, USA, [19]Department of Rheumatology, Royal Wolverhampton Hospitals NHS Trust, Wolverhampton, UK, [20]Division of Musculoskeletal and Dermatological Sciences, Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, The University of Manchester, Manchester, UK

Background. Sexual well-being is an often-overlooked component of health, particularly for people living with idiopathic inflammatory myopathies (IIM), a condition in which disease-related factors impact sexual functioning.
Methods. This cross-sectional study compares the sexual well-being of patients with IIM and patients with other rheumatic musculoskeletal diseases (oRMD) with healthy controls (HC). An additional neuromuscular comparator group of patients with myasthenia gravis (MG) was used. Predictors of sexual well-being in IIM were identified. The validated Short Sexual Well-being Scale (SSWBS) was integrated into the Collating the Voice of People with Autoimmune Diseases-3 (CoVAD-3) e-survey. Comparisons of SSWBS between groups were conducted using Kruskal-Wallis and Mann-Whitney U-tests. Results are expressed as standardized β-coefficients (95% CI).
Results. Of 2339 respondents, 308 had IIM, 74 had MG, 1591 had oRMD, and 236 were HC. The majority identified as heterosexual (≥85%) and were married or living with their partner (≥93%). Median SSWBS was 22 (IQR 17–28) in IIM, 23 (15.3–28) in MG, 23 (18–29) in oRMD, and 26 (20–30) in HC. SSWBS was significantly lower in IIM than oRMD (p=0.002) and HC (p<0.0001) but comparable to MG (p=0.688). There was no significant difference in SSWBS between IIM subtypes (1).
Hierarchical linear regression models identified demographic, disease-related, psychosocial, and socioeconomic predictors of sexual well-being among patients living with IIM. Among demographic factors, older age (β=0.089, p=0.006) and female gender (β=3.76, p<0.001) were positively associated with SSWBS. Among disease-related factors, fatigue was negatively associated with SSWBS (β= -0.69, p=0.006; 95% CI -0.36 to -0.06). Among psychosocial factors, loneliness was negatively associated with SSWBS (β= -0.69, p=0.004). Among socioeconomic factors, higher family functioning was positively associated with SSWBS (β=0.70, p<0.001). The final multivariate model (n=295; R^2 =0.244, adjusted R^2 =0.200; AIC=1946) affirmed that loneliness predicted lower SSWBS (β= -0.839, p<0.001) (1).
Conclusions. Patients living with IIM reported lower sexual well-being when compared with patients with oRMD and HC; no differences were seen when compared with MG. Loneliness was identified as an independent predictor of poor sexual well-being, highlighting the psychosocial burden on patients living with IIM. Fatigue emerged as a disease-related negative predictor. Targeted interventions such as patient support groups addressing loneliness and fatigue may be beneficial to sexual well-being in this patient population.
Acknowledgements. Thank you to the COVAD study group.
Key words: sexual well-being, idiopathic inflammatory myopathies, myasthenia gravis

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MYOSITIS PATIENT JOURNEY QUALITATIVE RESEARCH AND CO-CREATION

Edward Banfe[1], Paula Eichenbrenner[2], Susan Helm[2], Sandy McInnis[3], Steven Tucker[1], Hailey Miser[4], Monica Grant[5], Tyler Thompson[5]

[1]Keenova Therapeutics, Bridgewater, USA, [2]The Myositis Association, Columbia, USA, [3]SM Consulting, Marietta, USA, [4]Florida State University, Tallahassee, USA, [5]Ideas To Go, Minneapolis, USA

Background. The journey of a person with chronic disease can be mapped in many ways: documenting symptoms, tracking lab results, or listing treatment history. However, these ignore the human element to living with disease. Keenova Therapeutics (KT) and The Myositis Association (TMA) partnered to better understand emotional journeys and develop resources for people with myositis (PwM).
Methods. Ideas To Go (ITG) recruited and trained 8 creative patients, diagnosed with dermatomyositis (DM) or polymyositis (PM), from TMA's database. Patients completed a homework assignment designed to bring to life their individual journeys with myositis. Participants from ITG, KT, and TMA, plus the patients then worked in a virtual co-creation session to generate patient resource possibilities, followed by a session to prioritize and categorize the ideas.
Results. Myositis comes with significant emotional strain, from grief over lost ability to anticipatory fear of disease progression and treatment failure. The sudden shift from a healthy self-image to living with myositis is jarring, and patients struggle to reconcile "the old me" with now limited physical ability. Because the disease may be invisible, patients feel the impact of the disease on their lives is underestimated by others. Patients believe that myositis is misunderstood, not only by the public but also among their families and even their healthcare providers (HCPs). Several patients indicated they believed themselves to be the only PwM treated by their rheumatologist. Patients cycle through powerful medications that weigh heavily on everyday life, and fear that HCP inexperience with myositis limits treatment options offered to them. At the same time, they do not want to leave their current HCP, having been through so much together. Many patients noted the importance of online and in-person community groups, such as TMA support forums or Facebook groups, as places to learn, share stories, compare experiences, and feel less alone. All expressed a desire to improve their ability to advocate for themselves throughout their journey.
Conclusions. People with myositis want more education on myositis, for themselves and for their healthcare providers and families. They want education to include mental health as a component of treatment, to broaden the pharmacological treatment options offered by HCPs, and to improve their ability to communicate their concerns so that the HCP will act on the information. PwM also want more opportunities to connect with each other with the goal of improving their quality of life by learning from others with their disease.
Key words: dermatomyositis DM, polymyositis PM, patient journey

P-342

MENTAL HEALTH BURDEN IN IDIOPATHIC INFLAMMATORY MYOPATHIES: A COMPARATIVE POPULATION-BASED STUDY

Bianca Paulo Correia[1,2], Ana Rita Henriques[3], João Miguel Pereira[2], Sofia C. Barreira[1,2], Inês Sopa[1,2], João Aguiar[1,2], Filipa Costa[1,2], Miguel Afonso Martins[1,2], Gonçalo Boleto[1,2], Ana Maria Rodrigues[3], Raquel Campanilho-Marques[1,2]

[1]Rheumatology Department, Unidade Local De Saúde De Santa Maria (ULSSM), Lisbon, Portugal, [2]Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa (CAML), Lisbon, Portugal, [3]Comprehensive Health Research Centre, NOVA Medical School, Universidade NOVA de Lisboa, Lisbon, Portugal

Background. Idiopathic inflammatory myopathies (IIMs) are chronic systemic diseases that impair quality of life. While muscular and extramuscular involvement are well characterized, the psychological burden – particularly anxiety and depression – remains underexplored.
Objectives. To assess the prevalence and severity of anxiety and depression symptoms in adults with IIM compared to a matched control group without rheumatic disease, and to explore clinical and treatment-related predictors of psychological distress.
Methods. We conducted a cross-sectional, case-control study with pros-

pective data collection from adults with IIM followed at a tertiary Myositis Clinic between March–September 2025, using the Hospital Anxiety and Depression Scale (HADS). Controls (3:1) were selected from the population-based EpiReumaPt study (2011–2013), matched by sex, age, and region of residence. HADS-A and HADS-D scores ≥8 and ≥11 defined possible and probable cases. Holm-Bonferroni correction was applied for multiple comparisons. Multivariable logistic regression identified factors associated with anxiety and depression.

Results. We included 100 IIM patients [75% female; mean age 52.8±15.6 years; median disease duration 7.0 (IQR 12.0) years] and 300 matched controls. No significant differences were found in body mass index (BMI) (p=0.561) or employment status (p=0.712).

Compared with controls, IIM patients more often had gastrointestinal (29% *vs*. 7.4%), pulmonary (13% *vs*. 4.3%), thyroid (16% *vs*. 5.4%), and neoplastic diseases (20% *vs*. 3.4%), as well as osteoarthritis (21% *vs*. 2.7%) and osteoporosis (25% *vs*. 1.4%) (all p≤0.004).

IIM patients had higher HADS-A and HADS-D scores, with 42% *vs*. 16% scoring ≥8 and 17% *vs*. 4.3% ≥11 for anxiety, and 27% *vs*. 7.3% scoring ≥8 and 9% *vs*. 2.7% ≥11 for depression (all p≤0.001).

In multivariable analysis adjusted for sex, age, smoking, thyroid disease, and employment, IIM diagnosis (OR 4.62, 95%CI 2.61–8.19, p<0.001) and higher BMI (OR 1.07, 95%CI 1.01–1.13, p=0.032) were associated with anxiety. Both IIM (OR 7.87, 95%CI 3.88–15.94, p<0.001) and BMI (OR 1.09, 95%CI 1.02–1.17, p=0.010) were associated with depression.

Among IIM patients, lower MMT8 was associated with depressive symptoms (p=0.043), but only corticosteroid use (OR 5.12, 95%CI 1.50–17.45, p=0.009) and retirement (OR 10.3, 95%CI 1.85–57.33, p=0.008) remained significant in multivariable analysis.

Conclusions. IIM patients have a higher psychological burden than the general population, with anxiety and depression affecting nearly half and one-third of patients, respectively. IIM diagnosis and higher BMI were associated with anxiety and depressive symptoms, while corticosteroid use and retirement were associated with depression within IIM. These findings underscore the importance of systematic mental health assessment in IIM care.

Key words: idiopathic inflammatory myopathies, mental health, anxiety and depression

P-347

ESTABLISHMENT OF A GLOBAL PATIENT-CENTERED REGISTRY FOR IDIOPATHIC INFLAMMATORY MYOPATHIES – THE MY PACER STUDY

Kaushik Sreerama Reddy[1], Akira Yoshida[2], Raisa Silva[3], Eduardo Dourado[3,4,5], Edoardo Conticini[7], Saadia Sasha Ali[8], Siamak Moghadam-Kia[1], Thomas Moulinet[9], Alexandre Santos[10], Anushka Aggarwal[11], Cristiana Sieiro Santos[12], Iris Tang[13], Nantakarn Pongtarakulpanit[14,15], Maha Almackenzie[16], Rohit Aggarwal[1]

[1]Division of Rheumatology and Clinical Immunology, University of Pittsburgh School of Medicine, Pittsburgh, USA, [2]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [3]Department of Rheumatology, Allergy & Immunology, Massachusetts General Hospital, Boston, Japan, [4]Rheumatology Department, Unidade Local de Saúde da Região de Aveiro, Aveiro, Portugal, [5]Aveiro Rheumatology Research Centre, Egas Moniz Health Alliance, Aveiro, Portugal, [6]Rheumatology Research Unit, Instituto de Medicina Molecular, Faculdade de Medicina Universidade de Lisboa, Lisboa, Portugal, [7]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University of Siena, Siena, Italy, [8]Epsom and St Helier Uinversity Hospital, department of Rheumatology, London, UK, [9]Department of Internal Medicine and Clinical Immunology, Regional Competence Center for Rare and Systemic Auto-Immunes Diseases and Auto-Immune cytopenias, Nancy University Hospital, Lorraine University, Vandoeuvre-lès-Nancy, France; UMR 7365, IMoPA, Lorraine University, CNRS, Nancy, France, [10]Departments of Pharmacology, Institute of Biological Science, Federal University of Minas Gerais, Belo Horizonte, Brazil, [11]Department of Rheumatology, Indraprastha Apollo Hospital, New Delhi, India, [12]Rheumatology Department, Complejo Asistencial Universitario de León, León, León, Spain, [13]Division of Rheumatology & Clinical Immunology, Department of Medicine, The University of Hong Kong, Hong Kong, China, [14]DLH, LLC, Bethesda, USA, [15]Division of Allergy, Immunology and Rheumatology, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand, [16]Division of Rheumatology, Medical Cities of the Ministry of the Interior, Riyadh, Saudi Arabia

Background. Idiopathic inflammatory myopathies (IIM) are rare, heterogeneous systemic autoimmune diseases, making patient recruitment for clinical studies challenging. Advancing equitable therapeutic development requires efficient, standardized global patient data platforms that overcome geographic barriers. The NIH-funded Myositis Patient-centered Tele-Research (My Pacer) Study demonstrated the feasibility of remote enrollment and direct-to-patient data collection, establishing a successful model for global IIM research.

Methods. The My Pacer Registry is a first-of-its-kind, global, direct-to-patient, longitudinal observational registry. The primary objective is to establish the registry by incorporating remote patient enrollment through our website www.mypacerstudy.org and data collection through a mobile application (MyCap app) developed by Research Electronic Data Capture (REDCap). Adult IIM participants will be enrolled globally, with an initial target of 1,000 patients per year. Enrollment will be facilitated by patient support organizations, physician partners, professional myositis groups like MIHRA, MCTC, IMACS, and social media. After electronic consent and pre-screening, baseline and semiannual follow-up assessments where participants will provide patient-reported outcomes (PROs) in several domains and perform one physical test (Sit- To- Stand) at home. A beta survey assessed app usability and patient understanding pre-launch.

Results. A group of 17 myositis investigators from 13 countries (and 4 continents), and two patient-partners, have joined the My Pacer registry. To date, the team has: (1) deployed the study website and participant portal; (2) built and iteratively refined REDCap instruments and MyCap workflows; (3) completed internal pilot runs and patient/clinician beta testing to assess usability and feasibility; (4) established data governance, security, and standard operating procedures (SOPs) for remote enrolment; and (5) instituted standing monthly investigator patient partner meetings to review milestones, recruitment operations, and language/localization plans (expansion to 10 languages). Preliminary feedback from patient beta testers indicated that the MyCap app was easy to use, intuitive, and clear in its instructions. Active enrollment is underway, and ongoing data collection will provide cross-sectional and longitudinal summary statistics on disease characteristics and patient outcomes across various myositis subtypes and geographical regions.

Conclusions. The My Pacer Registry gathers data on disease progression, epidemiology, and outcomes in IIM using PROs via remote assessments. Currently active in 13 countries with plans for further expansion, the initiative emphasizes international collaboration, with future growth focused on engaging patient partners and broadly sharing findings to maximize its scientific impact.

Key words: patient-reported outcomes, direct to patient, registry

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COMPARISON BETWEEN IDIOPATHIC INFLAMMATORY MYOPATHIES AND RHEUMATOID ARTHRITIS: FROM A SHARED PHYSICAL IMPAIRMENT TO DIFFERENT QUALITY OF LIFE OUTCOMES

Linda Carli[1,2], Elenia Laurino[1], Federico Fattorini[1], Michele Diomedi[1], Chiara Cardelli[1,2], Simone Barsotti[3], Marta Mosca[1,2]

[1]Rheumatology Unit, University of Pisa, AOUP, Pisa, Italy, [2]European Reference Network RECONNET, EU, [3]Rheumatology Unit, Versilia Hospital, Viareggio, Italy

Background. Idiopathic inflammatory myopathies (IIM) and rheumatoid arthritis (RA), despite their improved prognosis, still correlate with a significant impairment in patients' quality of life (QoL). Since they are the systemic autoimmune diseases with the greatest impact on patients' physical functioning, we compared QoL outcomes of patients with IIM and RA to clarify which clinical and epidemiological parameters were most implicated in its impairment.

Methods. We conducted a retrospective analysis of monocentric cohorts of patients diagnosed with MII according to the EULAR/ACR 2017 classification criteria and with RA according to the EULAR/ACR 2010 classification criteria, followed at our specialist clinics.

In IIM disease activity was assessed with Manual Muscle Testing 8 (MMT8) and Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI); in RA, Clinical Disease Activity Index, Simple Disease Activity and Disease Activity Score; Patient Global Assessment, Physician Global Assessment and Visual Analogue Scale for pain were collected. QoL and disability were assessed with the following patient-reported outcomes (PROs): Short-form 36 (SF36), Functional Assessment of Chronic Disease Therapy-Fatigue Scale and Health Assessment Questionnaire (HAQ).

Results. Two hundred patients were enrolled, 100 with RA and 100 with IIM [mean age 63.4 years, female 136/200 (68%)].

The two groups were comparable in terms of mean age and gender. Patients with IIM were older at diagnosis and had a shorter disease duration (p<0.001).

Patients with IIM consumed a higher mean daily GC dose (p<0.001), with no difference in cumulative dose between the two conditions. Patients with RA showed worse HAQ scores and impairment in social activities (SF domain of the SF36) compared to IIM (p<0.02). In the RA group, the main factors impacting QoL were age, disease duration, cumulative and mean daily GC dose, depression, osteoporosis (OP), fibromyalgia (FM) and disease activity (p<0.04). In patients with IIM, the parameters with the greatest impact on QoL were GC therapy, depression and chronic kidney disease (CKD) (p<0.05). MMT8 and CDASI damage values correlated inversely and directly, respectively, with HAQ scores (p=0.006).
Conclusions. QoL of patients with IIM and RA is largely comparable, although RA patients appear to experience greater physical and social impairment. GC therapy has a negative impact on both patient groups, as do disease activity and the presence of depression. Furthermore, opportunities emerge to optimize the management of FM and OP in RA patients and CKD in those with IIM, thus suggesting more targeted interventions to improve patients' outcomes.
Key words: idiopathic inflammatory myopathies, quality of life, glucocorticoids, comorbidities, quality of care

P-360

MENTAL HEALTH COPING STRATEGIES PRACTICED BY PEOPLE LIVING WITH MYOSITIS: RESULTS OF A QUALITATIVE SURVEY

Paula Eichenbrenner[1], Laurie Boyer[1], Holly Jones[1], Terry Richardson[2]
[1]The Myositis Association, Columbia, US, [2]Impact Education, LLC, Blue Bell, USA

Background. Living with a chronic, rare disease places a heavy burden on an individual's mental health. The prevalence of depression (39% of patients with rare diseases) and anxiety (44% of patients with rare diseases) is substantially higher in patients with rare diseases than in the general population (depression 11-21%; anxiety disorders 17%) (Uhlenbusch *et al*.). A myositis diagnosis, coupled with continued disease progression and the possibility of overlapping diseases, profoundly affects the emotional well-being of patients, care partners, families, and the communities that support them.
Methods. During Myositis Awareness Month (May 1-31, 2025), The Myositis Association (TMA) conducted a ten-question qualitative survey to capture patient perspectives. The online survey was disseminated via email and social media channels. A total of 24 TMA members participated, representing individuals with lived experience across myositis subtypes, including antisynthetase syndrome, dermatomyositis (including MDA5 DM), inclusion body myositis, immune-mediated necrotizing myopathy, overlap myositis, polymyositis, and myositis-associated interstitial lung disease. Open-ended responses were analyzed using thematic analysis to identify key patterns and insights.
Results. The most common tools used by myositis patients to address their mental health were sleep management (n=9 or 38%); pharmaceutical treatment and/or therapy with mental health providers (n=7 or 30%); mindfulness practices like meditation (n=7 or 30%); exercise and/or physical therapy (n=6 or 24%); and social support networks (n=5 or 21%). Additional coping strategies included nutrition, self-compassion, maintaining a positive outlook, emotional processing, boundary setting, and creative outlets. People living with myositis also noted the importance of care partner resources and self-care for their loved ones.
Conclusions. People living with myositis face mental health challenges, like many patients navigating rare conditions. These include the misunderstood nature of their disease, limited disease knowledge among health care professionals, challenges in treatment, and difficulty coping with stigma and uncertainty (Richardson et al). Individuals affected by myositis employ a myriad of practices to overcome isolation, connect with others, seek support, and manage stress. Families benefit from the resources and peer-to-peer connections made possible through patient foundations like TMA.
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Key words: mental health, anxiety, depression, emotional well-being, coping, peer support, quality of life

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Therapeutic Advances

P-18

RESPIRATORY MUSCLE STRENGTH TRAINING IN THE MYOSITIS POPULATION

Meaghan Arnold[1,2], MacKenzie Bradley[1], Kelly Salmon[3]
[1]Speech Swallowing and Neurological Rehabilitation PLLC, Tyler, USA, [2]Myositis Support and Understanding, Lincoln, USA, [3]Drexel University, Philadelphia, USA

Background. Idiopathic inflammatory myopathies (IIM), including inclusion body myositis (IBM), dermatomyositis (DM), and polymyositis (PM), are rare autoimmune disorders often associated with dysphagia and respiratory dysfunction. Respiratory muscle strength training (RMST) has demonstrated benefits in other neuromuscular conditions, but evidence in myositis is limited. The primary aim of this study was to examine the effects of expiratory muscle strength training (EMST) using the EMST150® device on expiratory function and self-reported swallowing in individuals with myositis.
Methods. Nineteen participants (7 males, 12 females; mean age 62.7 years) completed 25 RMST repetitions per day, 5 days per week, for 5 weeks at 70% of maximum expiratory pressure (MEP). Outcome measures included the Eating Assessment Tool (EAT-10), peak expiratory flow (PEF), and MEP. Pre- and post-intervention changes were analyzed using paired-sample t-tests.
Results. Statistically significant improvements were observed for all outcomes. EAT-10 scores decreased from 17.95 (SD = 10.51) to 11.63 (SD = 9.03), p < .001. PEF increased from 297.63 L/min (SD = 83.39) to 338.16 L/min (SD = 107.56), p < .001. MEP increased from 81.26 cm H_2O (SD = 20.86) to 87.95 cm H_2O (SD = 18.46), p=0.004. Exploratory correlations revealed a moderate, non-significant association between improvements in MEP and reductions in EAT- 10 scores (r = -0.37). Changes in PEF demonstrated a moderate-to-strong, statistically significant association with EAT-10 improvement (r = 0.53, p=0.02), suggesting that enhanced expiratory airflow may relate to reduced dysphagia symptom burden.
Conclusions. This pilot study provides preliminary evidence that expiratory muscle strength training may improve expiratory pressure generation, expiratory airflow, and self-reported swallowing symptoms in individuals with myositis. The significant relationship between PEF gains and reductions in EAT-10 scores suggests a potential functional link between expiratory airflow and perceived swallowing improvement. Although the MEP–EAT-10 association did not reach significance and the study was not powered for correlational inference, the observed patterns support further investigation of the respiratory-swallowing relationship in myositis. Larger, controlled studies incorporating instrumental swallowing measures are needed to confirm these findings and clarify underlying mechanisms.
Key words: idiopathic inflammatory myopathies, inclusion body myositis, dysphagia, expiratory muscle strength training, respiratory muscle strength training

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P-39

LOW-DOSE IL-2 ADD-ON THERAPY REDUCES INFECTION INCIDENCE IN IDIOPATHIC INFLAMMATORY MYOPATHY: A PROSPECTIVE COHORT STUDY

Liang Zhao[1], Ke Ma[2], Xiaoyan Xing[1], Jingxuan Liu[2], Wanxing Mo[1], Yirui Lian[1], Tian Liu[1,3], Yuhui Li[1,2]
[1]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China, [2]Department of Rheumatology and Immunology, Qingdao Women and Children's Hospital, Qingdao, China, [3]Department of Rheumatology and Immunology, Shijiazhuang People's Hospital, Shijiazhuang, China

Background. Infections contribute to disease exacerbation in patients with idiopathic inflammatory myopathy (IIM) and represent a leading cause of mortality. Although glucocorticoids and immunosuppressants remain cornerstone therapies, their use increases infection risk, which can further exacerbate disease outcomes. Low-dose IL-2 (Ld-IL-2), known for its immunomodulatory properties in autoimmune diseases, may mitigate these risks.
Objectives. To evaluate the frequency of infections in patients with IIM receiving Ld-IL-2 add-on therapy compared to standard of care (SOC) over a 12-month period.
Methods. In this prospective cohort, multicenter study, patients were divided into subcutaneous Ld-IL-2 (1×10^6 IU every other day for 12 weeks) with SOC group or SOC group. The occurrence of infectious complications was identified over a 12-month follow-up period, based on supportive clinical features, positive microbial cultures, and/or responses to antibiotic therapy. Baseline demographics, clinical characteristics, and treatment details were systematically recorded. Infection rates between the Ld-IL-2 and SOC groups were compared using chi-square tests.
Results. Overall, 914 patients with IIM were included in the study. Among the 813 patients who completed follow-up period, 132 received Ld-IL-2 add-on therapy, and 681 received standard therapy. A total of 225 (27.7%) cases experienced infectious episodes. The infection rate in the Ld-IL-2 group (14.4%, 19/132) was significantly lower than that in the SOC group (30.2%, 206/681) ($p<0.001$). Pulmonary infections were the most common among all identified infection sites (65.8%, 148/225). The most common pathogen was bacteria (40%, 90/225), followed by viruses (35.1%, 79/225), mixed infections (12.9%, 29/225) and fungi (12%, 27/225). Compared to the SOC group, patients treated with Ld-IL-2 exhibited a significantly lower incidence of bacterial infections (5.3%, 7/132 *vs*. 12.2%, 83/681; p=0.021) and a marked reduction in viral infections (4.5%, 6/132 *vs*. 10.7%, 73/681; p=0.028). Fungal infections were rare and showed no significant difference between the groups.
Conclusions. This study underlines the high frequency of infections in patient with IIM. Ld-IL-2 add-on therapy significantly reduces the risk of infection, suggesting a promising adjunctive therapeutic strategy for IIM.
Key words: idiopathic inflammatory myopathies, infection, risk factor, low-dose IL-2

P-60

TREATMENT PATTERNS AND DRUG USE IN IDIOPATHIC INFLAMMATORY MYOPATHIES. DESCRIPTION OF THE FIRST YEAR AFTER DIAGNOSIS IN A SWEDISH MYOSITIS COHORT

Irene Peralta Garcia[1,2], Naz Haque[1], Dag Leonard[3], Anna Glasin[4], Silva Puksic[5], Balsam Hanna[6], Theodoros Lappas[5], My Axelhed[7], Fabricio Espinosa Ortega[1,2], Karin Lodin[1,2], Nils Eckerdal[1], Helene Alexandersson[2,8], Elisabeth Hsia[9], Ingrid E. Lundberg[2,8], Marie Holmqvist[1,2]
[1]Karolinska Institutet, Clinical Epidemiology Division, Department of Medicine Solna, Stockholm, Sweden, [2]Karolinska University Hospital, Medical Unit of Gastroenterology, Dermatology, Rheumatology. Theme Inflammation and Ageing, Stockholm, Sweden, [3]Rheumatology, Department of Medical Sciences. Uppsala University, Uppsala, Sweden, [4]Rheumatology Department, Linköping Hospital., Linköping, Sweden, [5]Rheumatology Department, Örebro University Hospital, Örebro, Sweden, [6]Rheumatology Department, Sahlgrenska University Hospital, Gothemburg, Sweden, [7]Rheumatology Department, Västmanlands Hospital, Västerås, Sweden, [8]Karolinska Institutet, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden, [9]Johnson & Johnson, Spring House, USA

Background. Most of current treatment practice in idiopathic inflammatory myopathies (IIM) is based on case reports or is adapted from other diseases. We investigated the occurrence of IIM subgroups over time and described immunosuppressive treatment during the first year after diagnosis in different calendar periods and IIM-subtypes.
Methods. SweMyoNet is a nationwide study following IIM patients longitudinally. Information is prospectively collected by healthcare providers. For this study, we included IIM patients diagnosed from 31/12/2007 to 15/03/2025, with at least two registered visits, the first within six months of diagnosis. IIM subtypes were: polymyositis (PM), dermatomyositis (DM), anti-synthetase syndrome (ASyS), immune-mediated necrotizing myopathy (IMNM) and inclusion body myositis (IBM). Patients were divided into three calendar periods according to year of diagnosis: 2008-2013, 2014-2019 and 2020-2025. Continuous variables are described as mean±SD/median and IQR; categorical as frequencies and percentages.
Results. We identified 544 patients, 316 women (58%), mean age 60 years at diagnosis. The most frequent IIM subtype was DM (n=159.29%) followed by ASyS(n=130.24%), PM(n=113.21%), IMNM(n=76,14%) and IBM(n=65.12%). The subtype distribution has changed over time with a rise of ASyS and IMNM (20% and 2% in 2008-2013 to 24% and 27% in 2020-2025, respectively) and a drop in PM (35% in 2008-2013 to 12% in 2020-2025).
During the first 12 months after diagnosis, glucocorticoids (GC) were the most used (n=367.74%). Methotrexate (MTX) was the most prescribed immunosuppressant (68% of all patients, 93% of all IMNM) followed by rituximab (RTX) (23%). Forty-nine patients received no drug therapy the first year after diagnosis, 34% were IBM patients. 86% of all DM, 79% of PM and ASyS, 65% of IBM and 46% of IMNM patients were treated with GC. Forty-seven % of ASyS patients received cyclophosphamide and 44% RTX. Intravenous immunoglobulins (IVIG) were used in all subtypes except IBM, but predominantly in IMNM (n=58.78% of IMNM).
Over time, GC use decreased: 82% patients during 2008-2013 received GC in comparison to 67% during 2020-2025. In contrast, IVIG increased from 2% of patients during 2008-2013 to almost 40% during 2020-2025. RTX was not widely used in 2008-2013 (3%) but increased from 2014 onwards (35% and 24%, respectively in 2014-2019 and 2020-2025).
Conclusions. ASyS and IMNM occurrence increased and PM decreased from 2008 and onwards. Over time, drug use has changed with decrease of GC and increase of IVIG. Prescription patterns differed between IIM subtypes but MTX was the most used immunosuppressor in all subtypes.
Key words: register, epidemiology, treatment, treatment patterns

P-67

SUSTAINED DISEASE CONTROL WITH RITUXIMAB MAINTENANCE IN ANTI-SYNTHETASE SYNDROME: INSIGHTS FROM A REAL-LIFE COHORT

Silvia Grazzini[1], Paolo Cameli[2], Luca Cantarini[1], Bruno Frediani[1], Edoardo Conticini[1]
[1]Rheumatology Unit, University of Siena, Siena, Italy, [2]Pneumology Unit, University of Siena, Siena, Italy

Background. Myositis, arthritis and interstitial lung disease are the pivotal manifestations of anti-synthetase sydrome (ASyS): due to its rarity, no clear guidelines exist about therapy and a combination of immunosuppressive drugs (IS) is often necessary to control all disease domains. Rituximab (RTX) seems to be an overall effective treatment, but literature evidence is limited to cases with predominant lung involvement and optimal treatment duration is unknown. The aim of our study was to assess the long-term efficacy and safety of RTX as maintenance therapy in patients affected by ASyS.
Methods. We retrospectively included adult patients from Siena Myositis Clinic affected by ASyS and treated with RTX for at least 12 months. Demographic and clinical data were collected at baseline, at 1st RTX administration and at last follow-up: disease activity was scored on a 4-point Likert scale (0 remission, 1 low, 2 moderate, 3 severe disease activity).
Results. We included 15 patients (2 males) with a mean age of 53.2 ± 14.2 years. The most frequent specific antibody was anti-Jo1 (11), while anti-SSA/Ro52 was found in 12 subjects. At the time of RTX administration (1 g ev twice, 2 weeks apart), after a median of 12 (range 1–240) months from diagnosis and 2 previous IS, patients had a median of 2 (range 1–5) affected organs – lungs being the most common (12), followed by skin (10), joints (7) and muscle (4) – and a median disease activity of 2. RTX was prescribed as monotherapy in 11 subjects, together with a mean daily dose of 25 mg prednisone (PDN). At last follow-up, after a mean of 4 ± 3 (range 2–12) administrations, 8 (60%) patients were on monotherapy while the others were taking also MTX (3), BARI (2) or MMF (1): RTX dosage was tapered to 1 g and 500 mg

every 6 months in 4 and 1 patient, respectively. Mean daily dosage of PDN was 1.5 mg (p=0.001), whereas median disease activity and involved organs were both 0 (p<0.001). We reported mild infectious episodes in 4 patients (≃ 27%, recurrent urinary infections in 2 subjects, sinusitis and Herpes Zoster in other 2, respectively) and only one pneumonia requiring hospitalisation.
Conclusions. Our results demonstrate an overall good efficacy and safety of RTX, which also guaranteed a steroid-sparing effect, providing useful insights into its role as long-term maintenance therapy in patients affected by ASyS.
Key words: anti-synthetase syndrome, rituximab, long-term treatment

P-83

EFFICACY OF RITUXIMAB IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES REFRACTORY TO CSDMARDS – PRELIMINARY RESULTS OF A PROSPECTIVE OBSERVATIONAL MONOCENTRIC STUDY OVER 24 MONTHS

Daniel Zavada[1], Sabina Oreska[1,2], Anna Bobrova[1], Katerina Bobrova[1], Eliska Sudkova[1], Emma Polouckova[1], Martin Klein[1,2], Herman Mann[1,2], Karel Pavelka[1,2], Ladislav Senolt[1,2], Jiri Vencovsky[1,2], Michal Tomcik[1,2]
[1]Institute of Rheumatology, Prague, Czechia, [2]Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czechia

Background. The evidence of efficacy of bDMARDs in patients with idiopathic inflammatory myopathies (IIM) with active, progressive disease non-responsive to glucocorticoids and csDMARDs is limited. The aim of this study was to assess the efficacy of rituximab in bDMARDs-naive IIM patients.
Methods. 24 patients, who fulfilled the 2017 ACR/EULAR classification criteria (7 males / 17 females; 10 antisynthetase syndrome (ASyS) / 6 immune-mediated necrotizing myopathy / 4 dermatomyositis (DM) / 2 DM + ASyS / 1 cancer-associated DM, 1 polymyositis; mean±SD age 56.8±14.6 years, disease duration 6.7±5.2 years) were treated with 1 (month (M)6, n=24), 2 (M12, n=17) or 4 (M24, n=10) cycles of rituximab (1g i.v. at day 0 and 14, every 6 months). Before each cycle, patients were assessed using the Myositis Disease Activity Assessment Visual Analogue Scale (MYOACT), Myositis Intention to Treat Index (MITAX) and Manual Muscle Testings (MMT-8) and filled out questionnaires assessing disability (Health Assessment Questionnaire, HAQ), quality of life (Medical outcomes study Short Form 36, SF-36), fatigue (Fatigue Impact Scale, FIS), depression (Beck's Depression Inventory-II, BDI-II), physical activity (Human Activity Profile, HAP) and pulmonary symptoms (St. George´s Respiratory Questionnaire, SGRQ). Peripheral blood was analyzed for routine laboratory parameters (CRP, ESR). At each visit, patients performed lung function testing (FVC, FEV1, DLCO).
Results. Results are presented in brackets as mean±SEM in the order visits at M0–M6–M12–M24, with asterisks indicating statistical significance from baseline (p<0.05*, p<0.01**, p<0.001***). Over 24 months of follow-up, we observed significant improvement in disease activity assessed by MYOACT (0.10±0.01; 0.06±0.01**; 0.05±0.02**; 0.05±0.02**), specifically in pulmonary domain, and MITAX (0.20±0.02; 0.11±0.02***; 0.11±0.03**; 0.11±0.03*), muscle strength (MMT-8: 68.83±1.60; 71.74±1.65*; 71.69±1.83; 72.48±2.01) and serum markers of muscle injury myoglobin, lactate dehydrogenase). Prednisone equivalent dose significantly decreased (9.12±0.77; 7.03±0.80*; 5.61±0.93***; 3.15±1.08*** mg/day). Lung function improved, specifically: FVC (79.5±3.8; 83.9±3.8; 88.7±4.2*; 88.2±4.4 %), FEV1 (78.4±3.8; 83.2±3.8; 86.4±4.0*; 86.5±4.3 %), DLCO (60.8±3.8; 66.8±3.8; 65.9±4.0; 70.58±4.34* %), and SGRQ Activity domain at M12. We observed significant improvement in mental health (SF-36 Mental Component Score) at M6 and M24. Only numerical non-significant improvements were observed in creatine kinase, CRP, ESR, disability (HAQ), fatigue (FIS), and depression (BDI-II).
Conclusions. These findings suggest that long-term use of rituximab provides clinical benefit in patients with IIM refractory to csDMARDs, particularly in improving global disease activity, muscle strength, serum markers of muscle damage, lung function, and mental health, while allowing for a reduction in glucocorticoid dose.
Acknowledgements. Supported by MHCR023728.
Key words: rituximab, idiopathic inflammatory myopathies

P-101

TECLISTAMAB-INDUCED RAPID REMISSION IN REFRACTORY ANTI-JO-1 ANTISYNTHETASE SYNDROME

Elpida Phithak[1], Fredrik Albach[1], Ioanna Minopoulou[1], Robert Biesen[1], Arnd Kleyer[1,2], Edgar Wiebe[1], Elise Siegert[1], Veronika Scholz[1], Marie Rehm[1], Qingyu Cheng[2], Arne Sattler[1,2], Stefano Bianco[1], Anja Fleischmann[1], Kay-Geert Hermann[3], Thula Walter-Rittel[3], Moritz Wagner[3], Jan Zernicke[1], Vincent Casteleyn[1], Martin Nielsen[4], Thomas Rose[1], Antonia Busse[5,6,7], Marie Luise Hütter-Krönke[5], Ulrich Keller[5,6,7], Udo Schneider[1,4], Leona Kawelke[8], Nikolas Ruffer[9], Werner Stenzel[8], Gerhard Krönke[1,2,10], Tobias Alexander[1,2], David Simon[1,2,10]
[1]Department of Rheumatology and Clinical Immunology, Charité Universitätsmedizin Berlin, [2]German Rheumatism Research Centre (DRFZ), [3]Department of Radiology, Charité Universitätsmedizin Berlin, [4]Immanuel Hospital, Berlin, Germany, [5]Department of Hematology,Charité Universitätsmedizin Berlin, [6]Max Delbrück Center of Molecular Medicine in the Helmholtz Association, [7]German Cancer Consortium (DKTK), [8]Department of Neuropathology, Charité Universitätsmedizin Berlin, [9]Division of Rheumatology and Systemic Inflammatory Diseases, III. Department of Medicine, University Medical Center Hamburg-Eppendorf, Hamburg, Germany, [10]Fraunhofer Institute for Translational Medicine and Pharmacology, Allergology and Immunology, Berlin, Germany

Background. B-cell dysregulation and abnormal autoantibody production against aminoacyl-transfer RNA synthetases play a central role in the pathogenesis of antisynthetase syndrome (ASyS). Emerging bispecific T-cell engagers targeting BCMA may enable immune reset and drug-free remission in ASyS (1, 2).
Methods. We report the case of a 57-year-old patient with rapidly progressive, Jo-1- and Ro-52-positive ASyS (disease duration: 6 months) presenting with interstitial lung disease, inflammatory myopathy, and perimyocarditis. Despite previous treatment with glucocorticoids, cyclophosphamide, intravenous immunoglobulins (IVIG), rituximab, and tofacitinib, the disease rapidly progressed.
At baseline, creatine kinase (CK) was 14,695 IU/L, manual muscle testing (MMT-8) was 115/150, and forced vital capacity (FVC) was 62% of predicted. Chest CT showed nodular and ground glass opacities. Baseline skeletal muscle biopsy revealed perifascicular myofiber atrophy with necrotic muscle fibers. Teclistamab, a CD3×BCMA bispecific T-cell engager, was initiated with a step-up regimen (d1: 0.06; d3: 0.3; d5,14,21,28: 1.5 mg/kg), while all previous therapies except 25 mg prednisolone were discontinued.
Results. Teclistamab was well tolerated, with no cytokine release syndrome or neurotoxicity observed. Severe hypogammaglobulinemia (3.77g/l) at week 10 necessitated IVIG substitution. Treatment resulted in rapid and significant clinical improvement, allowing discontinuation of prednisolone by week 12.
At 6 months, a major TIS response of 72.5% was achieved, with normalized MMT-8 and significant pulmonary improvement (FVC: +26%; DLCO: +9%; KCO: +14%). Correspondingly, chest CT imaging revealed near-complete resolution of interstitial changes by week 12, and cardiac MRI at week 20 showed improvement of perimyocarditis. CK, myoglobin, CK-MB, and troponin T levels normalized by week 18.
Rapid and sustained seroconversion of anti-Jo-1/Ro-52 and antinuclear antibody levels was observed. Flow cytometry revealed complete depletion of $CD38^{+}CD138^{+}$ plasma cells in bone marrow and peripheral blood by week 8. A follow-up muscle biopsy demonstrated striking histopathological improvement, with reduced atrophy, necrosis, complement deposition, and B/plasma-cell infiltration.
Conclusions. Teclistamab induced rapid and complete drug-free clinical and serologic remission in refractory, rapidly progressive Jo-1-positive ASyS, with a favorable safety profile. BCMA-targeted therapy may represent a novel disease-modifying strategy in idiopathic inflammatory myopathies.
Acknowledgements. We thank the patient for their participation and consent, as well as the clinical care team and funders for their contributions.
Key words: antisynthetase syndrome, BCMA, teclistamab, plasma cell depletion, inflammatory myopathy, seroconversion, remission

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P-129

CASE SERIES: SUCCESSFUL RESCUE TREATMENT OF 3 CASES OF REFRACTORY ANTI-MDA5 AUTOANTIBODY POSITIVE DERMATOMYOSITIS WITH RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE USING DARATUMUMAB

Choon Guan Chua[1], Rachel Wei Shan Lim[1], Ruth Xian Lynn Yap[1], Tsui Yee Lian[1], Gin Tsen Chai[2], Xin Rong Lim[1], Mona Manghani[1], Bernard Pui Lam Leung[3], Li Wearn Koh[1]
[1]Department of Rheumatology, Allergy and Immunology, Tan Tock Seng Hospital, Singapore, [2]Department of Respiratory and Critical Care Medicine, Tan Tock Seng Hospital, Singapore, [3]Health and Social Sciences, Singapore Institute of Technology, Singapore

Background. Anti-melanoma differentiation-associated 5 gene autoantibody (anti-MDA5 Ab) positive dermatomyositis (DM) with rapidly progressive interstitial lung disease (RP-ILD) (anti-MDA5 disease) has high mortality despite aggressive immunosuppressive treatment. We report three patients with refractory anti-MDA5 disease that did not respond to Methylprednisolone-Rituximab-Tofacitinib (MEP-RTX-TOF) combination therapy but eventually achieved disease remission with daratumumab at our centre.
Methods. Clinical records were extracted from recruitment/hospital admission to 31 Oct 2025. All patients fulfilled Bohan/Peter criteria and the 2017 ACR/EULAR classification for idiopathic inflammatory myopathy. RP-ILD was defined as dyspnoea and/or hypoxaemia with worsening radiologic interstitial lung changes within 3 months of respiratory symptoms onset. EUROLINE Inflammatory Myopathies 16 Ag (IgG) commercial line immunoblot was used for detection of myositis specific/associated antibodies at diagnosis.
Results. Three patients with refractory anti-MDA5 disease received daratumumab to date: Case 1 30-year-old male, Case 2 65-year-old female and Case 3 66-year-old male (all were Chinese). Diagnoses were made 3-to-5 weeks from symptoms onset. All had fever, exertional dyspnoea, DM rashes (Gottron's papules, Gottron's sign, inverse Gottron's, skin ulcers, mechanics hands, periungual erythema). Case 1 was hypomyopathic [no weakness, peak creatine kinase 488U/L (50-350)]; Cases 2 and 3 had proximal weakness but normal serum creatine kinase. All were anti-MDA5 Ab strongly positive on line immunoblot; Cases 2 and 3 were also anti-Ro52 strongly positive. Ground-glass opacities/consolidation were detected in all 6 lung fields in all patients' HRCT. All had poor prognostic markers at diagnosis (high serum ferritin, lactate dehydrogenase and neutrophil:lymphocyte ratio).
MEP-RTX-TOF was given to all patients upon diagnosis. Plasmapheresis was also prescribed for Cases 1 and 2. Intravenous daratumumab (16mg/kg weekly x 4) was given at month 6 (M6) after diagnosis for Case 1, M1 for Case 2 and M2 for Case 3. All patients exhibited symptoms and signs of worsening lung disease despite moderate-to-high dose glucocorticoids and TOF at time of daratumumab therapy decision. Clinical remission (prednisolone tapered to 5mg/day, Myositis Disease Assessment Tool score 0) were achieved at 7, 10 and 4 months after daratumumab treatment for Case 1, 2 and 3 respectively. All achieved sustained anti-MDA5 Ab serological remission, normalisation of ferritin and improvements in serum KL-6 levels, spirometry readings and radiological scans (Table 1).
Conclusions. Daratumumab can be considered in refractory anti-MDA5 disease by depleting CD38-positive long-lived autoantibody-secreting plasma cells that drive chronic inflammation in autoimmune diseases.
Acknowledgements. We express gratitude to Veredus Laboratories Pte Ltd and Sekisui for sponsoring the Nanopia KL-6 test kits.
Key words: dermatomyositis, MDA5, daratumumab

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USE OF ANIFROLUMAB IN A PATIENT WITH REFRACTORY DERMATOMYOSITIS: A CASE REPORT

Alsayed Osman[1], Tanya Chandra, Rohit Aggarwal
[1]University Of Pittsburgh Medical Center, Pittsburgh, USA

Background. Dermatomyositis (DM) is an idiopathic inflammatory myopathy marked by characteristic cutaneous manifestations such as Gottron's papules and heliotrope rash. A subset of patients with amyopathic or hypomyopathic forms have limited muscle involvement yet experience chronic, treatment-refractory skin disease. Conventional therapies including corticosteroids, immunosuppressants, and intravenous immunoglobulin (IVIG) often fail to induce sustained remission. Type I interferon (IFN-I) pathway activation is increasingly recognized as a key pathogenic driver in DM. We describe a case of anti-TIF1-γ- positive hypomyopathic DM refractory to multiple agents who achieved complete remission with anifrolumab, an inhibitor of type I interferon receptor subunit-1 approved for treatment of Systemic lupus erythematosus (SLE).
Methods. A 44-year-old female diagnosed in 2015 with anti-TIF1-γ- positive hypomyopathic DM presented with severe cutaneous disease and minimal muscle involvement. Treatment history included systemic corticosteroids, hydroxychloroquine, methotrexate, mycophenolate mofetil (MMF), and IVIG with incomplete or transient responses. Given persistent disease activity and intolerance to maximal MMF dosing, anifrolumab 300 mg intravenously every four weeks was initiated in February 2024 and was later continued as monotherapy.
Results. Within eight weeks of therapy, the patient demonstarted marked improvement in cutaneous erythema and pruritis. By month four, complete clearance of lesions was achieved without recurrence of weakness or elevation of muscle enzymes. No corticosteroids or additional immunuosuppressive therapy were required. The patient maintained remission through August 2025 with no infectious or systemic adverse events. The observed remission aligns with emerging retrospective data demonstarting rapid and durable improvements in Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) scores with anifrolumab in refractory adult and juvenile dermatomyositis.
Conclusions. Anifrolumab resulted in steroid-free remission in this case of anti-TIF1-γ-positive hypomyopathic dermatomyositis refractory to multiple standard therapies. The favorable safety profile and rapid clinical response align with emerging real-world data supporting IFN-I pathway inhibition as a rational therapeutic strategy in cutaneous-predominant DM. Larger controlled trials are warranted to define efficacy, optimal duration, and long-term safety.
Key words: dermatomyositis, anifrolumab, type I interferon (IFN-I)

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P-185

RECONSTITUTION OF THE B-CELL COMPARTMENT FOLLOWING ANTI-CD19 CAR T-CELL THERAPY IN REFRACTORY PATIENTS WITH JUVENILE DERMATOMYOSITIS (JDM)

Rebecca Nicolai[1], Andrea Ariolli[1], Marco Becilli[2], Claudia Bracaglia[1], Pietro Merli[2], Maria Isabella Petrone[1], Francesca Del Bufalo[2], Mattia Algeri[2], Maria Giuseppina Cefalo[2], Franco Locatelli[2,3], Fabrizio De Benedetti[1], Emiliano Marasco[1]
[1]Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, [2]Department of Hematology/Oncology, Cell and Gene Therapy, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, [3]Catholic University of the Sacred Heart, Rome, Italy

Background. CAR T-cell therapy is an innovative strategy to induce profound B-cell depletion in patients with refractory juvenile dermatomyositis (JDM). Our aim was to characterize the reconstitution profile of B-cell subsets and investigate changes in molecular signatures in peripheral blood in three patients with JDM treated with anti-CD19 CAR T-cell therapy.
Methods. Three patients with refractory JDM received a single infusion of fresh autologous, second-generation anti-CD19 CAR T cells (lentiviral vector), following lymphodepletion with cyclophosphamide and fludarabine. After treatment, all three patients achieved an ACR-EULAR major clinical response using the Total Improvement Score. B-cell immunophenotyping was performed according to standard operating procedures (SOPs) before and after CAR T-cell infusion. RNA-seq was performed on RNA samples obtained from peripheral blood. A group of 10 JDM patients treated with rituximab (RTX) was included as controls.
Results. B-cell reconstitution occurred at a median of 8 weeks (IQR: 8.0-12.0) post-CAR T therapy, with an immature transitional B-cell phenotype, followed by naive B-cells and memory B-cells starting from month 3. B-cell phenotyping in bone marrow showed a complete depletion of CD19+ B-cells at month 1, with the presence of CD19- pro-B-cells. At 6 months the

frequency of peripheral blood CD19+ B-cells was higher in patients treated with CAR T cells than patients treated with RTX (respectively, 11.9% [IQR: 11.4-13.2] *vs*. 0.9% [IQR: 0.02-1.75], p=0.014). At 6 months peripheral B-cells of patients treated with CAR T cells were transitional and naive B-cells, and only <5% of memory B-cells, whereas patients treated with RTX showed a more heterogeneous pattern of B-cell subsets, with an expansion of switched memory B-cells and double negative B-cells. RNA seq analysis of peripheral blood sampled obtained 6 months after CAR T cell treatment compared to baseline showed a modulation of 201 differentially expressed genes (DEGs): 117 genes were downregulated and 84 genes were upregulated. Overrepresentation analysis of DEGs showed an enrichment for the interferon pathways among the down-regulated genes, and of cellular growth among the up-regulated genes.
Conclusions. CAR T cell treatment induces a deep B-cell depletion, followed by a reconstitution of B-cells starting from immature progenitors. RTX is associated with a long-lasting peripheral B-cell depletion and a heterogeneous B-cell reconstitution with persistence of memory B-cells. CAR T cell treatment induces a downregulation of genes in peripheral blood associated with interferon pathway and immune activation and an upregulation of genes associated with cellular growth.
Key words: CAR-T cell therapy, juvenile dermatomyositis

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PROGNOSTIC FACTORS AND TREATMENTS FOR IMMUNE MEDIATED NECROTIZING MYOSITIS

Charlotte Sierra[1], Lucas Pacoureau[2], Antoine Briantais[3], Baptiste Hervier[1], Sharam Attarian[4], Nicolas Schleinitz[5]
[1]Internal Medicine, [2]Internal Medicine, [3]Internal Medicine, [4]Neurology, [5]Internal Medicine

Background. immune mediated necrotizing myositis (IMNM) is characterized by severe muscle damage, with acute to sub-acute motor deficits that can lead to functional disability and even loss of walking ability. The prognostic factors described in the literature are based on a few retrospective cohorts, and the treatment of this condition is based on recommendations from expert centers.
We set out to describe the prognostic factors associated with this condition, and to compare the efficacy of immunosuppressive agents that may be prescribed during the course of the disease.
Methods. A retrospective, multicenter study was carried out, including patients followed up for IMNM between January 2013 and September 2022, via the BaMaRa database. We defined two groups depending on the status at the end of follow-up: mild and severe. The severe group was defined as patients having a modified Rankin score between 4 and 6 (loss of walking or death). Survival analyses with time to treatment discontinuation were used to assess the efficacy of treatments (Rituximab, Azathioprine, Methotrexate and MMF).
Results. We identified 43 patients with IMNM, with 53%, 37% and 9% anti-HMGCR, SRP and seronegative IMNM respectively. At the end of follow-up, 14 patients (33%) had lost the ability to walk or had died (n=4), and 29 patients (67%) were walking without assistance. The presence of axial muscle damage was statistically significantly associated with loss of walking in univariate and multivariate analysis (OR 6.97 (IC95% (1.72–36.44)) and 8.08 (IC95% (1.86–46.61)) respectively.
In case of anti-SRP and HMGCR IMNM, treatment with Azathioprine or Methotrexate had a significantly higher risk of treatment discontinuation (HR at 1.95 (IC95% (1.32–2.92)) and 1.45 (IC95% (1.01–2.08))
Conclusions. Axial muscle involvement appears to be associated with a poor prognosis in IMNM. Treatment with Rituximab appears to be more effective and better tolerated in seropositive IMNM.
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Key words: necrotizing, immune mediated myositis, rituximab prognosis

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DRUG-INDUCED MYOSITIS IN ONCOLOGY: IMMUNE CHECKPOINT INHIBITORS MYOTOXITIES AND BEYOND

Yacine Khitri[1], Paul Gougis[2], Kevin Bihan[3], Bénédicte Lebrun-Vignes[3], Julian Sanchez-Dal Cin[1], Yves Allenbach[1]
[1]Sorbonne Université, Assistance Publique Hôpitaux de Paris, National Reference Center for Inflammatory Myopathies, Pitié-Salpêtrière Hospital, Paris, France, [2]Department of Medical Oncology, Pitié-Salpêtrière, Assistance Publique - Hôpitaux de Paris (AP-HP), Paris, France, [3]Département de Pharmacologie, AP-HP, GHU Sorbonne Université, Centre Régional de Pharmacovigilance Pitié-Saint-Antoine, Paris, France

Background. Myositis may arise from cancer itself or from anticancer therapies. Beyond statins, immune checkpoint inhibitors (ICIs) have emerged as a major cause of fulminant and life-threatening myositis in oncology. Drug-induced myotoxicity ranges from mild creatine kinase (CK) elevation to rhabdomyolysis, yet large-scale data describing incidence, drug-class profiles, severity, and predictors of fatal outcome remain limited. We aimed to characterize anticancer and immunomodulator-induced myotoxicity using global pharmacovigilance data and to validate mechanistic signals through in silico skeletal muscle transcriptomic analysis.
Methods. Pharmacovigilance analysis: A retrospective observational study was conducted using VigiBase, the WHO global pharmacovigilance database (>130 countries; 40 593 689 deduplicated individual case safety reports (ICSRs) at extraction, 17 March 2025). All ICSRs reporting suspected myotoxicity related to anticancer or immunomodulators were included. Disproportionality analyses (Information Component, IC) detected CK-related myotoxicity signals; severity was classified; predictors of death were assessed by multivariate logistic regression.
In silico validation: Public single-nucleus and single-cell atlases of healthy human skeletal muscle were interrogated using Drug-to-Target predictions to identify targeted muscle-tissue cell types and pathways for drugs highlighted in the pharmacovigilance step.
Results. Signal detection: Among 4 475 drugs (87 331 ICSRs), 366 (≈8%) were associated with myotoxicity, including 39 anticancer/immunomodulators (≈10%). The strongest signals involved lipid-lowering drugs (cerivastatin IC 7.4), anti-infectives (daptomycin IC 6.1) and neuroleptics (loxapine IC 4.4). Among anticancer drugs, MEK (selumetinib IC 5.3), ALK (brigatinib IC 4.8) and BRAF inhibitors (dabrafenib IC 3.3) showed the strongest associations; ICIs, RET inhibitors and conventional chemotherapies were also implicated. Immunomodulators with significant signals included colchicine, calcineurin, JAK and mTOR inhibitors.
Most events occurred within one month; 60% were serious. Independent predictors of death were anti-PD1 exposure (aOR 2.18), severe clinical complications (aOR 3.62) and metabolic abnormalities (aOR 2.72). Targeted therapies (MEK, ALK, BRAF inhibitors) were mainly associated with mild to moderate toxicity.
In silico validation: All 39 anticancer/immunomodulating drugs were predicted to target pathways within skeletal muscle tissue. Targeted cells included muscle fibers, fibroblasts, endothelial cells, adipocytes and immune cells. As expected, drugs within the same class displayed similar pathway signatures. MEK, ALK, BRAF inhibitors showed widespread pathway activation across muscle-tissue cell types, whereas ICIs selectively targeted immune subsets (T/B/NK lymphocytes) within muscle tissue.
Conclusions. Combining large-scale pharmacovigilance data with skeletal muscle transcriptomic atlases, this study shows anticancer myotoxicity is frequent and heterogeneous: ICIs drive severe immune-mediated forms, while targeted therapies largely induce milder toxicity patterns. These data are clinically useful for guiding myotoxicity management and open perspectives on muscle homeostasis.
Key words: anticancer agents, immunomodulating agents, myotoxicity

P-385

CORTICOSTEROID DEPENDENCY AMONG ADULT PATIENTS WITH DERMATOMYOSITIS IN THE UNITED STATES

Rohit Aggarwal[1], Iazsmin Bauer Ventura[2], Joel Arackal[3], Raquel Campanilho-Marques[4], Hector Chinoy[5], Zoltan Griger[6], Antonia Valenzuela[7], Maria Francisca Bozan[7], Margitta Worm[8], Athiveeraramapandian Prabu[9], Prateek C. Gandiga[10]

[1]Division of Rheumatology and Clinical Immunology, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA, [2]Division of Rheumatology, Department of Medicine, University of Chicago, Chicago, IL, USA, [3]Roivant Sciences, New York, NY, USA, [4]Department of Rheumatology, Unidade Local de Saúde Santa Maria, Centro Académico de Medicina de Lisboa, Lisbon, Portugal, [5]Department of Rheumatology, Salford Royal Hospital, Northern Care Alliance NHS Foundation Trust, Manchester Academic Health Science Centre, Salford, UK, [6]Division of Clinical Immunology, Department of Internal Medicine, University of Debrecen, Debrecen, Hungary, [7]Section of Rheumatology, Department of Medicine, Hospital Clínico Universidad de Chile, Santiago, Chile, [8]Division of Allergy and Immunology, Department of Dermatology and Allergy, Charité - Universitätsmedizin Berlin, Berlin, Germany, [9]Department of Rheumatology, University of Birmingham, Birmingham, UK, [10]Division of Rheumatology, Department of Medicine, Emory University, Atlanta, GA, USA

Background. Toxicities associated with systemic corticosteroid (SCS) use in dermatomyositis (DM) are well documented (1, 2). Although conventional immunosuppressants (ISTs) and intravenous immunoglobulin (IVIg) have historically been relied upon to facilitate steroid tapering, the extent to which these approaches achieve meaningful steroid-sparing outcomes in real-world clinical practice remains unclear. To address this gap, we evaluated treatment patterns for adults with DM in the United States utilizing historic claims data.
Methods. This retrospective analysis characterized DM immunomodulatory (IM) treatment patterns utilizing closed claims data from Inovalon. Adults with ≥2 claims for DM (ICD-10 codes M33.1x or M33.9x) separated by ≥30 days, with an index diagnosis on or before December 31, 2023, were included. Continuous enrollment from January 1, 2019 through December 31, 2024 was required. Population-level weighting was applied using U.S. Census Bureau-derived multipliers for age, sex, and insurance status. Treatment utilization of DM-related medications was assessed during the 2024 calendar year. SCS exposure was standardized to prednisone-equivalent dosing. Polypharmacy burden was quantified as the number of distinct generic medications utilized in 2024, with the entire SCS class counted as one, regardless of formulation or route of administration.
Results. DM patients were frequently treated with multiple concurrent IM therapies: 65% of treated patients received ≥2 therapies and 35% received ≥3 therapies, including conventional ISTs, IVIg, and off-label systemic IM agents. Despite this high degree of polypharmacy, corticosteroid dependence remained substantial across treatment approaches. Among patients receiving regimens containing ISTs, 69% received concomitant SCS for an average of139 days during the year, of which 63% received prednisone-equivalent doses ≥10 mg/day for an average of 73 days. Among patients receiving IVIg, 77% received concomitant SCS for an average of 150 days, of which 65% received prednisone-equivalent doses ≥10 mg/day for an average of 90 days. Among patients receiving off-label therapies, 91% received concomitant SCS for an average of 146 days, of which 59% received prednisone-equivalent doses ≥10 mg/day for an average of 86 days.
Conclusions. In contemporary U.S. clinical practice, DM patients continue to experience substantial systemic corticosteroid dependency despite concurrent use of ISTs, IVIG, and off-label therapies, underscoring the challenge of achieving adequate disease control with existing treatments. Taken together, these findings highlight an urgent need for more effective, targeted therapies in DM capable of achieving rapid, durable clinical improvement while reducing reliance on corticosteroids.
Key words: corticosteroids, unmet need, dermatomyositis

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Biomarkers & Imaging

OP-11

TELL ME YOUR ANTIBODY AND I WILL TELL YOU YOUR CAPILLAROSCOPY PATTERN

Sara Alves Costa[*1], João Oliveira[1*], Fabiana Gouveia[1], Maria João Cadório[1], Mariana Luís[1,2], Tânia Santiago[1,2]

[1]Rheumatology Department, Local Unit Health of Coimbra, Coimbra, Portugal, [2]Faculty of Medicine of the University of Coimbra, Coimbra, Portugal
[*]Contributed equally

Background. Nailfold videocapillaroscopy (NVC) abnormalities are promising clinically useful markers in idiopathic inflammatory myopathies (IIM) but data remain limited. This study aims to characterise microvascular abnormalities assessed by NVC in IIM and explore their associations with clinical and laboratory parameters.
Methods. A cross-sectional single-tertiary center study was conducted including consecutive patients with IIM, enrolled between January and October 2025. Demographic, clinical and laboratory data were collected within +/- 3 months of the NVC. The NVC were performed by a certificated trained rheumatologist using a 200x probe (VideoCap 3.0; DS Medica, Italy). Quantitative parameters were analysed using the Capillary.io software.1 Between-group comparisons were performed using the Mann-Whitney U or independent-samples t-test for continuous data, Fisher's exact test for categorical data, and the Kruskal-Wallis test for comparisons involving more than two groups. Statistical significance was set at $p<0.05$.
Results. 36 patients with IIM were included (72.2% female). The mean age was 57.9 ± 12.2 years, with a disease duration at NVC of 7.9 ± 2.3 years and a median MMT-8 score of 150 [140–150]. The most frequent diagnoses were antisynthetase syndrome (33.3%), dermatomyositis (25.0%), and overlap myositis (25.0%).
VC abnormalities were found in half the IIM patients. In subsets of patients classified by autoantibody specificities, the prevalence of NVC abnormalities was significantly higher in patients with myositis-specific autoantibodies.
Patients with Raynaud's phenomenon exhibited more abnormal- shaped capillaries (p=0.002). No other clinical or laboratory characteristic showed to influence the NVC pattern. The presence of myositis-specific autoantibodies was associated with the presence of giant capillaries (p=0.002) and haemorragies (p=0.006) compared with patients with myositis-associated autoantibodies. Anti-PL12 positivity was linked to a lower number of giants (p=0.045) and hemorrhages (p=0.025), whereas anti-Mi-2β positivity showed the opposite trend, being associated with an increased number of hemorrhages (p=0.045). Anti-SSA52 positivity was associated with a higher capillary density (p=0.021) and with fewer giants (p=0.018) and hemorrhages (p=0.025). A single positivity autoantibody was significantly associated with a higher number of giant capillaries (p=0.001) and hemorrhages (p=0.029).
Conclusions. These findings underscore the close link between specific autoantibodies profiles and microvascular abnormalities in IIMs, highlighting NVC as a tool for microvascular assessment and potential phenotypic stratification of these patients.
Key words: myositis, capillaroscopy, autoantibodies

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OP-158

PSOAS MUSCLE ATROPHY CAN DIFFERENTIATE SPINAL BULBAR MUSCULAR ATROPHY FROM AMYOTROPHIC LATERAL SCLEROSIS: A RETROSPECTIVE STUDY

Jin-Sung Park[1], Hyunjin Kim[2], Hee-Jae Jung[2]
[1]Department of Neurology, School of Medicine, Kyungpook National University, Kyungpook National University Chilgok Hospital, Daegu, South Korea, [2]Department of Neurology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

Background. Spinal bulbar muscular atrophy (SBMA) and amyotrophic lateral sclerosis (ALS) are adult-onset motor neuron disease (MND), that share similar clinical manifestations including progressive muscular atrophy dysarthria, dysphagia. The aim of this study was to differentiate the two diseases by measuring the skeletal muscle from abdominal computed tomogram (CT) which is less time consuming and cost effective, compared to muscle magnetic resonance imaging.
Methods. All ALS and SBMA patients were recruited from Kyungpook National University Chilgok Hospital MND registry. CT images were retrospectively reviewed and we utilized the Skeletal muscle index (SMI, cm^2/m^2) at L3 level of the abdomen CT, which included abdominal, psoas, paraspinalis and quadratus lumborum muscles, and total gluteal muscle at the level of anterior superior iliac spine. Clinical and laboratory data of both groups were also retrieved for the analysis
Results. 25 SBMA patients and 41 male ALS patient`s abdomen CT were analyzed. The mean age (58.12 *vs*. 59.80, p=0.541), revised amyotrophic lateral sclerosis functional rating scale (ALSFRS-R, 38.92 *vs*. 38.27, p=0.714), and body mass index (22.99 *vs*. 21.98, p=0.244) were statistically insignificant in both groups. Creatine kinase was higher (707.48 *vs*. 291.39, p<0.001) and serum creatine level was lower (0.47 *vs*. 0.69, p<0.001) in the SBMA group. L3 level skeletal muscle index (cross sectional area/height2, cm2/m2) of SBMA and ALS was 37.29 and 45.69 (p=0.001). The total psoas muscle at L3 level was 3.86 with SBMA 5.83 in ALS which was statistically lower in the SBMA (p<0.001), Moreover, the total gluteus muscle SMI was also lower in SBMA group with statistical significance (p=0.001). In intragroup correlation analysis, the ALSFRS-R score and their subscore were correlated to L3 SMI, gluteus muscle index
Conclusions. The muscular atrophy of axial muscles in L3 level, especially psoas muscles in SBMA was an independent factor that differentiated from ALS while BMI, functional status, and age showed no statistical significance. In conclusion, the under-recognized axial muscular mass measurement via CT may be a good diagnostic marker that can differentiate SBMA from ALS.
Key words: motor neuron disease, differential diagnosis, computed tomography, psoas muscle

Cancer Myositis

OP-122

CANCER INCIDENCE AND PROGNOSTIC IMPACT OF MALIGNANCY TIMING IN DERMATOMYOSITIS: DATA FROM THE INMYRE REGISTRY

Marco Fornaro[1], Angela Carenza[1], Laura Coladonato[1], Sergio Del Vescovo, Gianmarco Roselli, Florenzo Iannone[1]
[1]Rheumatology Unit, Department of Precision and Regenerative Medicine and Ionian Area (DiMePReJ), University of Bari Aldo Moro, Bari, Italy

Background. To evaluate the incidence of new cancer cases (excluding non-melanoma skin cancers) in patients with dermatomyositis (DM) compared with other forms of idiopathic inflammatory myopathy (IIM), and to assess the impact of cancer diagnosis timing (before or after DM diagnosis) on survival.
Materials and Methods. Data from the local INMYRE registry of patients with IIM were analyzed. For the incidence analysis, patients with at least one follow-up visit and no baseline neoplasia were included. The cancer incidence rate per 100 patient-years (p/y) was calculated for the DM and other IIM (oIIM) groups. Survival analyses were performed using Kaplan-Meier curves and Cox regression models adjusted for age, sex, and lung involvement.
Results. The cohort included 145 patients with IIM: 81 with DM and 64 with oIIM (23 antisynthetase syndrome, 30 polymyositis, 7 immune-mediated necrotizing myopathy, and 4 inclusion body myositis). Sixteen cancer cases were identified in DM (6 breast, 3 intestinal, 2 melanoma, 2 hematologic, 1 lung, 1 ovarian, 1 neuroendocrine): 6 diagnosed before DM (median [IQR] 2 [1–2] years) and 10 after DM diagnosis (median [IQR] 2 [0.5–5] years). In the oIIM cohort, 3 cancers were identified, all after diagnosis. Among patients without baseline neoplasia, 10 and 3 new cancers occurred during follow-up in the DM and oIIM groups, respectively, corresponding to incidences of 2.2 and 0.71 per 100 p/y. In the DM cohort, patients with cancer had worse survival than those without cancer (log-rank 5.5; p=0.019), with a hazard ratio (HR) for death of 3.55 (95% CI 1.01–12.52). Patients with cancer diagnosed before DM had poorer survival compared with those diagnosed after DM (log-rank 4.6; p=0.032), although no difference was observed when survival was calculated from cancer diagnosis (log-rank 1.7; p=0.186).
Conclusions. Patients with DM have more than twice the cancer incidence of those with other IIMs. The timing of cancer onset relative to DM significantly influences prognosis: cancers diagnosed after DM appear to be associated with better survival, whereas preexisting malignancies confer worse outcomes. These findings underscore the importance of vigilant cancer screening at DM onset and throughout follow-up.
Key words: myositis, cancer, survival

OP-137

CLINICAL PROFILE AND OUTCOMES OF PATIENTS WITH IMMUNE-RELATED ADVERSE EVENTS TO IMMUNE CHECKPOINT INHIBITORS

Annie Rose Ammar, Rica Keiza King, Leandro Jose Dado, Geraldine Zamora, Aileen Agbanlog Dimatulac, Brigitte Yu Lao
St. Lukes Medical Center, Philippines

Background. Immunotherapy is a new trend in the treatment of cancer and had improved outcomes of patients. Among the available cancer immunotherapy, immune checkpoint inhibitors (ICI) have been the most widely used. ICI blocks intrinsic down regulators of the immune system, thus increasing antitumor activities. These results in increase T cells response in recognizing and attacking cancer cells. But despite the benefits of ICI, it can also lead to serious immune and inflammatory adverse events called immune-related adverse events (irAEs). 1 2 They have been already described in case series and retrospective observational studies but still with limited data.3 As of this writing, there is one published study on irAEs in the Philippines. This paper aims to determine the profile and outcome of irAEs evaluated and managed by the Rheumatology Section at St. Luke's Medical Center (SLMC), Philippines.
Methods. This is a single center, case series of cancer patients who had immune related adverse event following ICI treatment.
Results. Therefore, we describe 8 cancer patients (see Table 1) who developed irAEs after receiving ICI (pembrolizumab n=7, Durvalumab n=1). Most of the patients who developed irAEs are of the older age group. Six out of the 8 patient were ages 60 and above. All of them were on their late stages of cancer (stage IV: n=7). Five of the eight patients developed rheumatic irAEs which include myositis (n=1), pneumonitis (n=2) and arthritis (n=2). The other 3 patients developed non rheumatic adverse events which include skin rash, bicytopenia, peripheral neuropathy and myelopathy. The most common presentation were arthritis and pneumonitis. Furthermore, arthritis was observed to have a non-severe presentation (n=2, Grade I). Most patients were treated with steroids while those with severe reactions also received intravenous immunoglobulin (n=4 IVIG treatment). In general, most of the them have improved condition after treatment. However, two patients died and 1 has unknown outcome.
Conclusions. Increasing utilization of ICI among cancer patients led to increase incidence of immune related adverse events. Thus, there is a need for more generalizable study with larger sample size in future research
Key words: cancer myositis, checkpoint inhibitors

OP-213

MALIGNANCY SCREENING AND PREVALENCE IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Katerina Jabbour[1,3], Charles Kassardjian[1,3], OPHIR Vinik[2,3]
[1]St Michael's Hospital, Division of Neurology, Toronto, Canada, [2]St Michael's Hospital, Division of Rheumatology, Toronto, Canada, [3]University of Toronto, Toronto, Canada

Background. Idiopathic inflammatory myopathies (IIM) are associated with an increased risk of cancer. The International Myositis Assessment and Clinical Studies Group (IMACS) published consensus-based guidelines to risk-stratify patients and guide cancer screening practices (1). Herein, we aim to identify malignancy prevalence and characterize clinical and serologic features of patients with IIM in a tertiary centre. We have also applied the IMACS consensus guideline criteria for cancer risk in IIM to our cohort to determine its utility in risk stratification.
Methods. A retrospective chart review was performed of 119 patients diagnosed with adult-onset IIM at St. Michael's Hospital, Toronto between 2010-2023. Key clinical data, including Myositis-specific antibody (MSA) profile, malignancy detected within 5 years of diagnosis, specific screening practices, and treatment responses were collected using a REDCap database. An analysis of all cases was performed, including retroactive risk stratification based on IMACS guidelines, using descriptive statistics.
Results. Malignancy was detected within 5 years of IIM diagnosis in 16.8% of this cohort. Prevalence varied within IIM subtypes with 15.2% in dermatomyositis, 19.0% in anti-synthetase syndrome, 12.0% in immune-mediated necrotizing myopathy (IMNM), 15.8% in overlap myositis, and 37.5% in MSA-negative inflammatory myopathy. Prevalence of cancer was highest for anti-PM/Scl (57.1%), anti-TIF1γ (50.0%) and anti-PL-7 (20.0%) antibodies. The most frequently detected malignancy was breast cancer (30.0%), and the most frequent investigations cited in the detection of malignancy in our cohort were CT chest (25.0%) and mammography (25.0%). Patients were stratified into "high risk" (55.5%), "intermediate risk" (36.1%), and "low risk" (8.4%) groups using the IMACS guidelines. Prevalence of malignancy was 18.2% in patients considered "high risk", 18.6% in patients considered "intermediate risk", with no cancer in patients considered "low risk". While for most subtypes of IIM, prevalence of malignancy was greatest in the "high risk" group, prevalence of malignancy in patients with anti-synthetase syndrome was 12.5% in the "high risk group" and 33.3% in the "intermediate risk" group.
Conclusions. We identified higher rates of malignancy than expected amongst certain subtypes of IIM as well as antibody profiles previously thought to confer lower risk (*e.g.* anti-synthetase syndrome, anti-PM/Scl and anti-PL-7). Patients stratified as "intermediate risk" as per IMACS guidelines had higher than expected rates of malignancy, particularly amongst those with anti-synthetase syndrome. These results suggest further work is needed to better characterize and identify IIM patients with high risk of malignancy.
Key words: myositis, cancer, risk, screening

OP-314

CHARACTERIZATION OF A SINGLE-CENTRE COHORT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: FOCUS ON CANCER-ASSOCIATED MYOSITIS AND ANTI-TIF1γ ANTIBODIES

Silvia Ebe Lucia Della Pina[1], Ilaria Cavazzana[1], Cesare Tomasi[1], Alessia Caproli[1], Roberta Ottaviani[1], Samantha Mazza[2], Franco Franceschini[1]
[1]Clinical and Experimental Sciences Department, Rheumatology and Clinical Immunology Unit, ASST Spedali Civili di Brescia, University of Brescia., Brescia, [2]University of Brescia, Brescia, Italy

Background. Idiopathic inflammatory myopathies (IIMs) are a heterogeneous group of systemic autoimmune diseases characterized by chronic muscle inflammation and variable extramuscular involvement. Among them, dermatomyositis (DM) displays the strongest association with malignancy, with approximately 10–20% of patients developing cancer within three years of disease onset. Autoantibodies play a crucial role in defining clinical phenotypes and cancer risk. In particular, anti-transcription intermediary factor 1γ (anti-TIF1γ) antibodies are strongly linked to cancer-associated myositis (CAM), while a subset of anti-TIF1γ-positive patients remain cancer-free, suggesting potential protective immunological mechanisms. Recently, anti-CCAR1 antibodies have been proposed as possible modulators of this association.
Methods. We conducted a retrospective monocentric study including 278 patients diagnosed with IIM (1977–2025). Demographic, clinical, serological, and oncological data were extracted from clinical records. Patients were stratified according to cancer history (N+ *vs*. N–) and timing of malignancy (concomitant [CC] *vs*. non-concomitant [NCC], defined by ±3 years from IIM onset). Subgroup analyses focused on anti-TIF1γ-positive patients and on the detection of anti-CCAR1 antibodies using ELISA on serum samples collected within ±1 year from diagnosis. Multivariable logistic regression and multilayer perceptron neural network analyses were performed to identify predictors of CAM.
Results. Among the 278 IIM patients, 70 (25.2%) had a malignancy, with 45,7% classified as CAM. DM was the predominant subtype among cancer patients (59%), characterized by older age, shorter follow-up, and more severe cutaneous involvement. No independent clinical predictors of CAM were identified at multivariable logistic regression, although age at diagnosis showed a trend toward increased risk. Anti-TIF1γ antibodies were present in 9.7% of the cohort, with 59.3% of these patients developing cancer. Anti-CCAR1 antibodies were detected in association with anti-TIF1γ positivity, showing lower cancer frequency and suggesting a potential protective role. Neural network analysis identified anti-TIF1γ positivity, low anti-CCAR1 levels, and older age at diagnosis as top predictors of CAM, with good performance, limited overfitting.
Conclusions. This study confirms the strong association between anti-TIF1γ antibodies and cancer in IIM, particularly in DM, and highlights the potential immunomodulatory role of anti-CCAR1 antibodies in reducing cancer risk. The findings support the use of personalized cancer surveillance strategies in anti-TIF1γ-positive and older DM patients. Further multicenter prospective studies are needed to validate anti-CCAR1 as a biomarker for refined risk stratification and to elucidate immune mechanisms underlying tumor-autoimmunity interplay.
Key words: idiopathic inflammatory myopathies, cancer-associated myositis, anti-TIF1γ antibodies

Classification of Inflammatory Myopathies

OP-17

BEYOND THE SKIN AND MUSCLE: A CASE OF NXP-2 DERMATOMYOSITIS WITH UNPRECEDENTED GASTROINTESTINAL CATASTROPHE

Alexandra Arges[1], Sathyabama Naidu[1], Amisha Mehta[1], Karen Clarke[1], Prateek Gandiga[2]
[1]Emory University School of Medicine, Department of Hospital Medicine, Atlanta, USA, [2]Emory University School of Medicine, Department of Rheumatology, Atlanta, USA

Background. Dermatomyositis (DM) encompasses a spectrum of subtypes that may present without the hallmark dermatological features, posing a diagnostic challenge. An astute clinician must consider dermatomyositis when they encounter a patient with significant dysphagia, especially with proximal muscle weakness. In addition, although abdominal involvement in adult DM is exceedingly rare, it should be considered in patients with gastrointestinal symptoms, given the potential for associated vasculitis, vasculopathy, and risk of perforation.
Case Description: Our case involves a 70-year-old female presenting with dysphagia, proximal muscle weakness, and abdominal pain, but without the classic dermatological features of dermatomyositis. She was found to have bowel perforation with peritonitis, requiring a total colectomy, and mesenteric vein thrombosis. Furthermore, she had pharyngeal dysphagia and thus required a percutaneous gastrostomy tube (PEG) tube. Testing done on hospital day 2 was notable for high titer antinuclear (ANA) antibody (1:2560, homogenous), and positive NXP antibody on myositis-specific antibodies (MSA) panel, without other positive myositis-associated antibodies (MAAs) and with a negative extractable nuclear antigens (ENA) panel. The patient was treated with monthly intravenous immunoglobulin therapy, since she was not a good candidate for steroid use due to her recent bowel surgery and concern for steroid-induced myopathy.
Following the initiation of IVIG treatments, the patient's ability to swallow improved, and she was able to tolerate a pureed diet. She was advised to complete evaluations for occult neoplasm (including routine follow-up evaluations over the next 3-5 years), given the association between NXP-2 dermatomyositis and malignancy.
Conclusions. Our patient presented with the core features of the anti-NXP2-

associated phenotype – profound muscle weakness and progressive dysphagia – but with the addition of a highly critical complication: life-threatening multisite colonic perforation, which has historically been attributed predominantly to the juvenile dermatomyositis population. The anti-NXP2 autoantibody in adult dermatomyositis is a known serological marker associated with severe myositis, peripheral edema, and an increased risk of calcinosis and malignancy. This case underscores the importance of recognizing atypical presentations of DM to guide timely diagnosis and prevent catastrophic complications.

Key words: NXP-2 dermatomyositis, dermatomyositis, bowel perforation, dysphagia

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OP-59

A FLARE UP OR AN OVERLAP, A CASE REPORT OF SUDDEN MUSCLE WEAKNESS IN SLE PATIENT WITH CHALLENGING DIAGNOSIS

Gantira Danasasmita[1,2], Abirianty Araminta[1,2,3], Anna Ariane[1,2,3], Luh Ari Indrawati[2,4]
[1]Indonesian Rheumatology Association, Central of Jakarta, Indonesia, [2]Faculty of Medicine, University of Indonesia, Jakarta, Indonesia, [3]Rheumatology Division, Departement of Internal Medicine, Cipto Mangunkusumo Hospital, Central of Jakarta, Indonesia, [4]Department of Neurology, Cipto Mangukusumo Hospital, Central of Jakarta, Indonesia

Background. Myopathy is one of rare symptoms in systemic lupus erythematosus, only about 5% in musculoskeletal manifestation. It can be otherwise manifest as overlap with idiopathic inflammatory myopathy. Difficulty in differentiating between the two conditions mostly affects the prognosis of the disease.
Case report. A 20-year-old woman with a history of SLE, with skin rash and joint pain, since 4 ago but no regular check-ups. Since the last 3 months she began to complain of swelling in the face and legs. When admitted there were complaints of recurrent seizures and followed by proximal body weakness. The myositis antibody examination panel showed high titers of anti-Ku, increasing of CK (255) and LDH (375), leukopenia (3680), weakly positive lupus anticoagulant (1.5), increase in qualitative proteinuria (3611) with normal eGFR 81.3. She also has normal anti-ds DNA and complement level. Cerebrospinal fluid analysis shows a normal protein and glucose ratio, negative gram and acid fast bacillus staining. NCS examination revealed axonal sensory and motor neuropathy, while EMG showed myogenic lesions with no denervation in the proximal and distal muscles. Other imaging studies were not performed. The patient was subsequently diagnosed with SLE-related myositis, along with transverse myelitis in NPSLE and lupus nephritis. During treatment, the patient received a 500 mg pulse dose of steroids for 3 days and cyclophosphamide. The patient was seizure-free, but motor weakness did not improve until discharge.
Discussion: Myositis as organ manifestation in SLE in several case reports manifests in early year of first diagnosis. Different with overlap IIM, it is typically milder and asymmetric with other SLE manifestations frequently malar rash and arthritis but rarely with nephritis. In laboratory findings, SLE myopathy is associated with high anti ds-DNA, anti-Ro/SSA, lupus anticoagulant, hypocomplementemia and lymphopenia. Autoantibodies specific myositis in SLE myopathy could be negative in pure SLE myopathy. Otherwise, anti-U1-RNP, anti-Jo-1, anti-PM-Scl, and anti-Ku can be present in overlapping IIM. Muscle biopsy in myopathy SLE is also not a gold standard and reported as necrotizing myopathy pattern or dermatomyositis pattern but have no correlation with the clinical symptoms.
Conclusions. Differentiating between these two conditions can lead to prognosis differences as 73% SLE myopathy regaining normal muscle strength with lower mortality rate than IIM overlap. Though the first line of treatment shares the same approaches using high dose corticosteroid. Immunosuppressant choices in these two conditions can be slightly different as in SLE we also need to consider the involvement of other organs.
Key words: myositis, myopathy SLE, overlapping myositis

Clinical Trials

OP-275

DESIGN AND RATIONALE FOR A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 2/3 STUDY OF DESCARTES-08, MRNA CAR T-CELL THERAPY, IN ADULTS WITH DERMATOMYOSITIS AND ANTISYNTHETASE SYNDROME

Tahseen Mozaffar[1], Adam Dore[2], Vera Sarkodie[3], Atanas Filev[3], Hafsa Kamboh[3], Andy Stewart[3], Milos Miljkovic[3], Mazen M. Dimachke[4]
[1]University of California Irvine School of Medicine, Irvine, USA, [2]Allegheny Health Network, Pittsburgh, USA, [3]Cartesian Therapeutics, Inc., Frederick, USA, [4]University of Kansas Medical Center, Kansas City, USA

Background. Idiopathic inflammatory myopathies (IIMs) are rare, chronic autoimmune muscle disorders associated with progressive weakness, functional impairment, and limited durable treatment options. Disease activity is driven by persistent activation of autoreactive immune cells, including long-lived plasma cells and plasmablasts that sustain production of pathogenic autoantibodies. These cells rely on B cell maturation antigen (BCMA) signaling for survival, making BCMA a compelling and biologically rational therapeutic target. Descartes-08 is an autologous mRNA CAR T-cell therapy engineered for transient expression of a BCMA-directed CAR and selective depletion of BCMA-expressing cells, designed to interrupt the autoimmune cascade. In patients with generalized myasthenia gravis, Descartes-08 demonstrated a well-tolerated safety profile and durable clinical responses lasting up to one year following a six once-weekly course of treatment. Here, we present the study design and scientific rationale for the first study evaluating the effects of Descartes-08 on disease activity in patients with IIMs.
Methods. This is a randomized, double-blind placebo-controlled phase 2/3 study in adults with active and refractory dermatomyositis (DM) and antisynthetase syndrome (ASyS). Up to 50 patients will be randomized 1:1 in Part 1 to receive Descartes-08 or placebo six weekly outpatient infusions without pre-treatment chemotherapy.
Safety assessments include number of adverse events and their severity. The primary efficacy endpoint is the proportion of patients achieving major improvement defined by a ≥60-point improvement on the 2016 ACR/EULAR Total Improvement Score (TIS) at Week 24. Secondary endpoints will include data on disease activity, quality of life, corticosteroid use, and biomarkers. Participants who continue to exhibit clinical symptoms (defined by a reduction in TIS score of <20 at Week 24) and meet pre-infusion criteria may be eligible to receive in the Part 2 open-label six weekly intravenous infusions of Descartes-08.
Conclusions. The study is currently being initiated with anticipated site activations in Q1 of 2026.
Acknowledgements. We acknowledge Aneta Kwiatkowska, PhD for editorial support
Key words: mRNA CAR-T Cell therapy, Descartes-08, autoimmune muscle disorders

OP-281

PHASE 1/2 DOSE-ESCALATION BASKET STUDY OF DESCARTES-08, MRNA CAR T-CELL THERAPY, IN JUVENILE AUTOIMMUNE DISEASES: DESIGN AND RATIONALE

Anant Vatsayan[1], Kaveh Ardalan[2,7], Stephen Balevic[2,7], Jessica Bloom[3,7], Eveline Wu[4,7], Yukiko Kimura[5,7], Vera Sarkodie[6], Theresa Pritchard[6], Hafsa Kamboh[6], Andy Stewart[6], Milos Miljkovic[6], Vincent Del Gaizo[7], Stacy Ardoin[7,8], Laura Schanberg[2,7], Hermine Brunner[9]
[1]Children's National Hospital, Washington , USA, [2]Duke University School of Medicine, Durham, USA, [3]Children's Hospital Colorado, Aurora, USA, [4]University of North Carolina at Chapel Hill, Chapel Hill, USA, [5]Joseph M. Sanzari Children's Hospital, Hackensack Meridian School of Medicine, Nutley, USA, [6]Cartesian Therapeutics, Inc, Frederick, USA, [7]Childhood Arthritis and Rheumatology Research Alliance, Washington, USA, [8]Nationwide Children's Hospital, Columbus, USA, [9]Cincinnati Children's Hospital Medical Center, Cincinnati , USA

Background. Pediatric-onset autoimmune diseases represent a diverse group of immune-mediated disorders, including juvenile dermatomyositis

(JDM), childhood-onset systemic lupus erythematosus (cSLE), antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), and juvenile myasthenia gravis (JMG). These conditions are driven by persistent activation of autoreactive immune cells, including long-lived plasma cells and plasmablasts producing pathogenic autoantibodies. These cells are fueled by B-cell maturation antigen (BCMA) signaling, a rational therapeutic target. We present the study design and rationale for evaluating Descartes-08, an autologous mRNA CAR T-cell therapy with transient expression and selective depletion of BCMA-expressing cells, in juvenile autoimmune diseases.

Methods. This is a Phase 1/2 dose-escalation, open-label basket study to evaluate the safety, tolerability and preliminary efficacy of Descartes-08, in children, adolescents, and young adults with autoimmune disorders. The study consists of two sequential parts, Part-1 (dose escalation) and Part-2 (early dose expansion), across four disease-specific baskets (JDM, cSLE, AAV, and JMG).

In Part 1, a minimum of 3 participants 12 years or older with cSLE, AAV, JDM, or JMG will undergo apheresis between Day -59 and Day -17, followed by staggered infusions of Descartes-08 on Day 1 (Dose Level 1), Day 8 (Dose Level 2), and Days 15, 22, 29, and 36 (Dose Level 3), following an intra-patient dose-escalation design. If any of the first three participants experience a dose-limiting toxicity, the study will transition to a classical 3 + 3 design where small groups of three patients are treated at each dose level, with subsequent dose levels determined per prespecified criteria. In Part 2, the Maximum Tolerated Dose (MTD) established in Part 1 will be administered as six once-weekly infusions in up to 10 participants within each of the four basket cohorts under open-label. No lymphodepleting chemotherapy is required.

The primary endpoints are MTD for Part 1 and the type and frequency of treatment-related Serious Adverse Events for Part 2. The secondary objectives of both parts are to assess the ability of Descartes-08 to (1) improve clinical symptoms as measured by validated disease-specific activity indices, and (2) reduce the level of circulating autoantibodies. Exploratory objectives are to characterize circulating Descartes-08; determine the impact of Descartes-08 on circulating cytokines, systemic soluble immune factors and BCMA levels; and test for immunogenicity of Descartes-08 after infusions.

Results. The study is being initiated, with ongoing site activation and patient enrollment through 2026.

Conclusions. Descartes-08 is a promising mRNA CAR T-cell therapy under investigation for juvenile autoimmune diseases.

Acknowledgements. Aneta Kwiatkowska, PhD: editorial support

Key words: cell therapy, Descartes-08, juvenile autoimmune diseases

Exercise & Rehabilitation

OP-202

ELEVATED SERUM CK ALONE IS INSUFFICIENT AS AN INDICATOR OF AKI IN PATIENTS WITH EXERTIONAL RHABDOMYOLYSIS

Amir Sabouri[1], Brian Yurgionas[1], Sara Khorasani[1], Edward Durant[1], Jafar Kafaie[2], Yunyi Hung[1], Jeffrey Klingman[1], Siamack Nemazie[1]
[1]Kaiser Permanente, Walnut Creek, USA, [2]Neurology Departmment, St Louis University, St Louis, USA

Background. Exertional rhabdomyolysis (ERM) may lead to acute kidney injury (AKI), yet the true incidence of AKI among hospitalized ERM patients and the contribution of additional risk factors remain insufficiently characterized. Although elevated serum creatine kinase (CK) is commonly used as a surrogate marker for muscle injury severity, its value in predicting AKI risk is uncertain.

Methods. We conducted a retrospective cohort study of adults (≥18 years) hospitalized with ERM across Kaiser Permanente Northern California from January 1, 2009, to December 31, 2019. ERM cases were initially identified through electronic screening of all-cause rhabdomyolysis admissions and subsequently confirmed via detailed medical record review. AKI and chronic kidney disease (CKD) were defined using KDIGO criteria and validated by chart review. Data were analyzed from October 1, 2023, to January 31, 2024. Exposures of interest included strenuous physical activity prior to admission, dehydration, and preadmission use of non-steroidal anti-inflammatory drugs (NSAIDs). Primary outcomes were development of AKI, CKD, compartment syndrome, and in-hospital mortality.

Results. Among 3,790 hospitalizations for rhabdomyolysis, 200 patients (mean [SD] age, 30.5 [8.5] years; 72.5% male) met diagnostic criteria for ERM. AKI occurred in 17 patients (8.5%). No cases of new CKD were observed; one patient (0.5%) developed compartment syndrome, and there were no deaths. Serum CK levels were not associated with AKI development. In contrast, preadmission NSAID exposure was significantly more common in those with AKI compared with those without (64.7% *vs*. 21.9%; p<0.001), as was clinical dehydration (52.9% *vs*. 4.9%; p<0.001). Modeling suggests that eliminating preadmission NSAID use, and dehydration could reduce AKI risk by 92.6% (95% CI, 85.7–96.1%) in this population.

Conclusions. In hospitalized ERM patients, serum CK elevation alone is not a reliable indicator of AKI risk. Modifiable co-factors – particularly NSAID use and dehydration – appear strongly associated with AKI development and should be prioritized in prevention strategies. Clinical evaluation of ERM should incorporate these risk factors rather than relying solely on CK thresholds when assessing hospitalization needs and AKI risk.

Key words: exertional rhabdomyolysis, acute kidney injury, creatine kinase, NSAIDs

Extra-Muscular Organ Involvement

OP-42

ANTI-SYNTHETASE SYNDROME: EXPERIENCE FROM A TERTIARY CENTER

Catarina Rua[1], Maria Oliveira[2], Tiago Beirão[1], Catarina Silva[1], Mariana Patela[1], Sara Braga[3], Patricia Pinto[1], Sofia Neves[2], Flávio Costa[1], Tiago Meirinhos[1]
[1]Rheumatology Department ULS Gaia Espinho, Vila Nova de Gaia, Portugal, [2]Pulmunology Departament ULS Gaia Espinho, Vila Nova de Gaia, Portugal, [3]Laboratory Medicine Department ULS Gaia Espinho, Vila Nova de Gaia, Portugal

Background. Anti-synthetase syndrome (ASSD) is a rare and heterogeneous autoimmune myopathy, characterized by a distinct set of clinical and serological features.

Methods. We conducted a retrospective study to describe the clinical profile and outcomes of ASSD patients, focusing on interstitial lung disease (ILD), including those followed in Rheumatology and Pulmonology between 2015 and the present.

Results. Most patients were female (65%, n=13), with median age at diagnosis of 63 years (45–82) and diagnostic delay of 11.1 months (1.4–242.1). Ninety percent (n=18) met Connors *et al*. (2010) and 50% (n=10) Solomon et al. (2011) criteria. All fulfilled 2024 CLASS classification: 20% (n=4) probable and 80% (n=16) definite. Presentation was pulmonary in 50% (n=10), articular in 40% (n=8), and muscular in 10% (n=2). Two patients (10%) had the triad of ILD, myositis, and arthritis. Main features: ILD (90%, n=18), inflammatory arthralgias (65%, n=13), arthritis (40%, n=8), mechanic's hands (35%, n=7), Raynaud's (35%, n=7), myositis (20%, n=4), dysphagia (20%, n=4). In 25% (n=5), ILD was the only manifestation. Elevated aldolase/creatine kinase in 8 patients (40%). Electromyography in 3 (15%) showed myopathy in 2; MRI was abnormal in 1, biopsy negative in 1. Three (15%) had overlapping connective tissue diseases. Anti-Jo1 was most frequent (75%, n=15), followed by anti-PL7 (20%, n=4), anti-PL12 (5%, n=1), and anti-OJ (5%, n=1). Anti-Ro52/SSa in 55% (n=11). Pulmonary hypertension in 2; cancer (ovary, breast, bladder, gastric) in 4 (20%). Corticosteroids in 65% (n=13). Other immunosuppressives: mycophenolate (40%, n=8), azathioprine (25%, n=5), cyclophosphamide (20%, n=4), rituximab (15%, n=3), tacrolimus (n=1), intravenous immunoglobulin (n=1). Antifibrotics in 4: nintedanib (n=3), pirfenidone (n=1). With median follow-up of 5.8 years (0.2–13.1), mortality was 20% (n=4), all from respiratory infections. Among 18 ILD patients, 1 had usual interstitial pneumonia, 1 respiratory bronchiolitis–ILD, 16 non-specific interstitial pneumonia. One underwent lung transplantation. Pulmonary function decline occurred in 16.7% (n=3) for forced vital capacity and 22.2% (n=4) for diffusing capacity for carbon monoxide. High-resolution computed tomography progression in 27.7% (n=5), consistent with functional worsening. ILD progression in 2 of 13 Jo1+ (15.4%) and 2 of 4 non-Jo1+ (50%).

Conclusions. This study confirms predominance of ILD and anti-Jo1 antibodies in ASSD. Pulmonary involvement was frequent at onset, often as the only manifestation, underscoring need for early respiratory evaluation. Despite small sample and possible selection bias, findings illustrate ASSD variability and highlight the need for multidisciplinary care and research on antibody-specific outcomes.

Key words: antisynthetase syndrome, interstitial lung disease, anti-Jo1 antibodies, autoantibodies, outcomes

OP-93

MYOSITIS AND CONSTIPATION: TIME-STRATIFIED RISKS OF LOWER GASTROINTESTINAL COMPLICATIONS IN IDIOPATHIC INFLAMMATORY MYOPATHIES

Chih-Wei Tseng[1,2], Yuan-Tsung Tseng[2,3]
[1]Taichung Veterans General Hospital, Taichung, Taiwan, [2]Department of Public Health, College of Medicine, National Cheng Kung University, Tainan, Taiwan., Tainan, Taiwan, [3]Department of Medical Research, Tainan Municipal Hospital, Tainan, Taiwan

Background. Constipation and anorectal disorders are under-recognized in idiopathic inflammatory myopathies (IIM). We quantified time-stratified risks for lower gastrointestinal outcomes in IIM versus matched comparators.
Methods. We conducted a retrospective cohort study in the TriNetX US Collaborative Network. Adults with IIM (dermatomyositis, polymyositis, or inflammatory/immune myopathy by validated ICD-10 codes) were compared 1:1 to adults with annual wellness encounters as healthy controls (HC). To assess incident outcomes, we applied a 30-day lag after index and excluded individuals with prior events. Outcomes included constipation or laxative use, hemorrhoids, fecal impaction, fecal incontinence, anal fissure, and a composite anorectal endpoint. Cox models estimated overall and time-window hazards (1, 3, 5 years post-index). Propensity score (PS) matching balanced demographics, comorbidities, body mass index (BMI), health-care utilization, and relevant medications (*e.g.* opioids, anticholinergics). Time-to-event analyses used Kaplan-Meier estimates and Cox models. We report overall hazard ratios (HRs) and time-stratified HRs within 1, 3, and 5 years post-index to align with planned forest plots.
Results. IIM showed higher lower-GI risk overall – constipation/laxatives 1.32 (1.24–1.40), fecal incontinence 1.82 (1.45–2.28), hemorrhoids 1.12 (1.06–1.18), composite 1.15 (1.09–1.21) – while impaction and fissure were imprecise. At 1 year, elevations appeared for fecal incontinence 1.25 (1.09–1.43), constipation 1.11 (1.07–1.16), and anal fissure 1.42 (1.04–1.94); by 3 years, constipation 1.07 (1.04–1.11) and fecal incontinence 1.17 (1.05–1.31) persisted, whereas hemorrhoids fell below null 0.95 (0.92–0.99) and the composite neared unity 0.98 (0.94–1.01). By 5 years, most effects attenuated, with sustained elevation for constipation/laxatives and fecal incontinence (Fig. 1). Time-stratified forest plots of HRs (95% CIs) comparing IIM to matched controls for lower-GI outcomes. Overall and 1-/3-/5-year estimates are shown; points = HRs, bars = 95% CIs, dashed line = HR = 1. Panels: constipation/laxatives, hemorrhoids, impaction, fecal incontinence, anal fissure, composite.
Conclusions. Adults with IIM exhibit sustained excess risks of constipation/laxative use and fecal incontinence, with smaller or null differences for hemorrhoids, fecal impaction, anal fissure, and the composite over time. Routine bowel-symptom screening and proactive management should be integrated into IIM care pathways.
Key words: idiopathic inflammatory myopathies, constipation, fecal incontinence

OP-118

CHARACTERISTICS OF LUNG TRANSPLANT LISTINGS IN THE US FOR IMMUNE INFLAMMATORY MYOPATHIES (IIM) IN COMPARISON TO LISTINGS FOR OTHER CONNECTIVE TISSUE DISEASES

Deepali Sen[1], Jisna Paul[2], Sambhawana Bhandari[1]
[1]Washington University St Louis, St Louis, USA, [2]Ohio State University, Wexner Medical Center, Columbus, USA

Background. Lung transplant for IIM interstitial lung disease (ILD) has been approached with hesitancy due to concerns of increased morbidity secondary to extra-pulmonary involvement. We looked at the Organ Procurement Transplant Network (OPTN) database to review all US listings for IIM-ILD from 2003- 2023 comparing them to listings for other connective tissue diseases (CTD) ILD
Methods. Data obtained from OPTN on lung transplant listings for patients ≥18 years for CTD-ILD. Patients classified into 2 groups, IIM and Non-IIM (including scleroderma, Sjögren's, rheumatoid arthritis, lupus, mixed connective tissue disease). We looked at differences in demographics, baseline lung function, functional scores, allosensitisation rates, and lung allocation scores (LAS) which is a metric used to prioritize patients for lung transplant. We compared listing outcomes in both groups, specifically percentage transplanted, death on wait list and days to transplant.
Results. Between 2003-2023, 1997 patients were listed for CTD-ILD, of which 221 (11%) were listed for IIM and 1776 (89%) for non-IIM diagnoses. IIIM listings increased over time, from 24 (2003-2008), 49 (2009-2013), 73 (2014-2018), to 75 (2019-2023). Demographics showed higher male predominance in IIM (43.7%) *vs*. non-IIM (32.9%). IIM had slightly higher prevalence of Asian and Black, lower prevalence of Latino population. Higher numbers of patients with IIM were classified overweight or obese (76%) *vs*. non-IIM (55%).
There was no difference in baseline FVC%, PA pressures or functional scores within groups. Mean 6-minute walk test was similar (IIM 715.2 ft v/s non-IIM 722 ft; p 0.82) in both groups despite potential for muscle weakness in IIM. Allosensitisation was seen in 19.6 % IIM and 16.5% in non-IIM group. LAS was significantly higher in IIM (48.1) *vs*. non-IIM (44.4), p0.002.
Transplant rates were similar IIM (76.47%) *vs*. non-IIM (75.74%). Average time from listing to transplantation were similar IIM (154 days) *vs*. non-IIM (161 days). Death while on wait list was lower in IIM (8.5%) *vs*. non-IIM (12.07 %) but did not meet significance p=0.13.
Conclusions. This observational study shows listings for IIM lung transplants are increasing and IIM patients are getting lung transplants at equitable rates to other CTDs in the US. Baseline lung function was similar in both groups. IIM patients had a slightly higher LAS reflecting urgency to transplant. Death on transplant list was lower for IIM although not statistically significant. Despite concerns for poor outcomes, our study suggest IIM patients have listing outcomes comparable to other CTD-ILD.
Key words: myositis, ILD, lung transplant

OP-167

INFLAMMATORY MYOPATHY WITH SEVERE CARDIAC INVOLVEMENT ASSOCIATED WITH ANTI-MITOCHONDRIAL ANTIBODIES TREATED WITH RITUXIMAB AND AZATHIOPRINE: A CASE REPORT

Silva Puksic[1], Christos Moulatzikos[1]
[1]Rheumatology Department, University Hospital Örebro, Örebro, Sweden

Background. A distinct inflammatory myopathy associated with anti-mitochondrial antibodies (AMA) and frequent cardiac involvement has recently been described (1). Diagnosis is often delayed as arrhythmias, cardiomyopathy, and myocarditis can precede the muscle disease by several years and are challenging to treat (1).
Methods. A 47-year-old woman without a family history of muscle disease was referred to rheumatologist due to progressive proximal muscle weakness over the past 6 months. She had a 4-year history of difficult-to-treat supraventricular and ventricular arrhythmias and underwent 2 radiofrequency ablation procedures.
The patient reported recent worsening of palpitations and dyspnea. The Manual Muscle Test 8 score was 42/80. She had no skin rash or thickening, arthritis, or dysphagia. Raynaud phenomenon was present but nailfold capillaroscopy was normal. Electromyoneurography and magnetic resonance of muscles were consistent with myositis. Muscle biopsy revealed fiber degeneration, necrosis, and atrophy predominantly in the perifascicular region without inflammatory infiltrate. MHC-1 was upregulated. Computed tomography showed no evidence of interstitial lung disease.
Laboratory investigation revealed elevated creatine kinase [53 (<3.5) μkat]. N-terminal-pro-B-type natriuretic peptide [4234 (<150) ng/l] and troponin I [2162 (<37) ng/l] levels were markedly elevated suggesting myocardial damage.
Antibody status revealed positive AMA (indirect immunofluorescence confirmed by immunoblot), Ro-52, and centromere antibodies. Other myositis-specific and associated antibodies were negative. Liver function tests were normal. Echocardiography showed globally reduced left ventricle (LV) contractility with an ejection fraction (EF) of 30%. Cardiac magnetic resonance showed subendocardial contrast enhancement in the LV anterior wall. Coronary angiography was normal.
Results. Patient was diagnosed with AMA-associated myositis and myocarditis. Treatment was initiated with intravenous methylprednisolone pulses 500 mgx3 followed by prednisolone 0.75 mg/kg, rituximab 1000 mg (day 0 and 14), azathioprine 2 mg/kg and standard heart failure medications. After 4 months, her LV EF had improved to 50% and troponin levels declined over following months, suggesting control of myocarditis. Rituximab (every 6 months) and azathioprine were continued and prednisolone gradually discontinued. Two years after diagnosis her muscle disease is in remission, but she continues to have bradyarrhythmia and is therefore planned for pacemaker insertion.

Conclusions. Timely diagnosis and optimal treatment of cardiac manifestations of this myopathy require further investigation. Early introduction of combination immunosuppressive therapy with rituximab might be beneficial in selective cases.
Acknowledgements. Written consent from the patient was obtained.
Key words: myocarditis, antimitochondrial antibody, rituximab

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OP-288

INTRAVENOUS IMMUNOGLOBULIN AS EFFECTIVE THERAPY FOR REFRACTORY CUTANEOUS ANTI-TIF1-γ DERMATOMYOSITIS

Jorge Lindo[1], Francisco Mano[1], Maria Manuel Xavier[1], Carolina Figueiredo[1], Margarida Gonçalo[1]
[1]Serviço de Dermatologia e Venereologia, Unidade Local de Saúde de Coimbra, Coimbra, Portugal

Background. Anti-transcription intermediary factor gamma (TIF1-γ) dermatomyositis (DM) is frequently associated with malignancy and can present as refractory cutaneous lesions, particularly in amyopathic or hypomyopathic variants. Although first-line therapy includes glucocorticoids, antimalarials, and immunosuppressants, treatment-resistant cases remain challenging. Intravenous immunoglobulin (IVIg) has emerged as a promising therapeutic option, particularly for refractory muscle disease.
Methods. This is a single-patient case report with clinical, serological, imaging and therapeutic data.
Results. We report a 53-year-old woman with anti-TIF1-γ-positive dermatomyositis. Initial management included hydroxychloroquine (400mg/day) and systemic corticosteroids, with partial response. From early 2024, methotrexate was introduced (20 mg/week), with tapering of corticosteroids and maintenance of hydroxychloroquine. Despite combination therapy, the patient developed persistent pruriginous heliotrope erythema, psoriasiform plaques on the scalp, hands and knees, Gottron's papules, and marked photosensitivity, later accompanied by mild muscle weakness. Electromyography demonstrated muscle fiber injury consistent with early myopathy. Comprehensive malignancy screening, including a PET/CT scan, was negative. Given therapeutic refractoriness, monthly IVIg therapy (2g/kg for 6 consecutive months) was initiated. After the second IVIg cycle, a progressive and sustained cutaneous improvement was observed, with resolution of erythema in photoexposed areas and regression of the other skin lesions. No new muscle or systemic symptoms developed. This allowed gradual tapering of methotrexate (7.5mg/week), prednisolone (2.5 mg on alternate days), and hydroxychloroquine (400/200 mg on alternate days), maintaining clinical cutaneous and muscular remission, now for 6 months. No adverse events occurred during or after IVIg infusions.
Conclusions. This case highlights the efficacy and safety of IVIg as an advanced therapeutic option for refractory cutaneous anti-TIF1-γ dermatomyositis. IVIg provided significant and durable cutaneous improvement, enabling corticosteroid and immunosuppressant reduction. Early consideration of IVIg may represent a valuable strategy in refractory cutaneous disease forms.
Key words: dermatomyosistis, anti-TIF1-γ antibody, intravenous immunoglobulin, cutaneous manifestations

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OP-289

PANNICULITIS IN ANTI-TIF1-γ DERMATOMYOSITIS

Jorge Lindo[1], Francisco Mano[1], Carolina Figueiredo[1], Margarida Gonçalo[1]
[1]Serviço de Dermatologia e Venereologia, Unidade Local de Saúde de Coimbra, Coimbra, Portugal

Background. Dermatomyositis is an inflammatory myopathy with characteristic cutaneous features. Panniculitis is a rare manifestation that may be under-recognized.
Methods. This is a single-patient case report with clinical, serological and imaging data.
Results. A 50-year-old woman presented with firm, painful subcutaneous plaques on the thighs and buttocks, which evolved for more than one year. Skin biopsies suggested lupus panniculitis but there were no criteria for systemic or cutaneous Lupus Erythematosus. At dermatologic consultation we could observe heliotrope rash, poikiloderma, Gottron's papules, telangiectasia of the nail cuticula associated with proximal muscle weakness. Laboratory evaluation revealed elevated muscle enzymes (CPK 226U/L, Aldolase 9.2U/L) and strongly positive anti-TIF1-γ antibodies. Age-appropriate malignancy screening with PET-CT scan and chest, abdomen and pelvis CT scan showed no evidence of malignancy but demonstrated subcutaneous calcifications corresponding to prior panniculitis lesions. Treatment with methylprednisolone (16mg), methotrexate (15mg/week), and hydroxychloroquine (400mg/day) resulted in substantial improvement in muscle strength and panniculitis lesions regressed with atrophy and calcified nodules.
Conclusions. This case highlights panniculitis as a prominent manifestation of anti-TIF1-γ dermatomyositis, which may mimic lupus panniculitis and complicate early diagnostic interpretation. Recognition of panniculitis in the appropriate setting should prompt evaluation for dermatomyositis.
Key words: dermatomyosistis, Anti-TIF1-γ antibody, panniculitis

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Genetic & Environmental Risk Factors

OP-248

SEASONAL PATTERN OF MYOSITIS RELAPSE AND TUMOR RECURRENCE IN CANCER-ASSOCIATED DERMATOMYOSITIS: A MULTICENTER CASE SERIES

Silvia Grazzini[1], Maria Rosa Pellico[2], Nicoletta Del Papa[2], Luca Cantarini[1], Bruno Frediani[1], Edoardo Conticini[1]
[1]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, Siena University Hospital, University of Siena, Siena, Italy, [2]Clinical Rheumatology Unit, ASST Gaetano Pini - CTO, University of Milan, Milan, Italy

Background. Seasonal variation has been reported in the onset and relapse of idiopathic inflammatory myopathies (IIM), possibly reflecting environmental or immunological triggers. Previous studies have shown seasonal clustering of disease flares and autoantibody detection, suggesting that external factors may modulate disease activity. In this regard, our case series aims to explore if a similar seasonal pattern exists in cancer recurrences among patients with myositis, a field not yet investigated
Methods. Patients were included if they had a clinically and serologically confirmed diagnosis of cancer-associated myositis, were regularly followed at the Siena or Milan Myositis Clinics, and had experienced a documented cancer recurrence.
Results. Nine patients (2 males), with a mean age of 54.44 years at the time of IIM diagnosis were enrolled: they were all affected by dermatomyositis and myositis specific antibodies were anti-TIF1γ (6), NXP2 (2) and anti-SAE (1). Involved organs at onset included skin (100%), muscle (89%) and esophagus (67%). Malignancies were detected concurrently of IIM in 4 pa-

tients, and from 6 to 29 months before or after diagnosis (mean 16 months). Cancer types were oropharyngeal (2), ovarian (2), breast (2), lung (2) and lymphoma. IIM relapsed with cutaneous (100%), esophageal (56%), muscular (56%) and articular (33.3%) involvement. At the time of flare, patients were receiving intravenous immunoglobulins (3), methotrexate (4), rituximab, mycophenolate mofetil, cyclosporine and subcutaneous immunoglobulins. Relapses occurred in April (7) and May (2) after a mean of 35 months from first cancer diagnosis: in 3 patients, a new primary malignancy was discovered (liver, different kind of lymphoma, contralateral breast).
Conclusions. To the best of our knowledge, our data are the first suggesting a seasonal pattern in the clinical relapse of myositis in a paraneoplastic setting, followed by evidence of tumor progression. This pattern does not imply a seasonality in tumor biology, but is consistent with the hypothesis that seasonal environmental triggers may modulate a residual autoimmune response, possibly anticipating the detection of an underlying ongoing oncologic progression.
Key words: seasonality, relapse, cancer-associated myositis

OP-372

WHEN COFFEE TURNS TOXIC: HMGCR IMMUNE-MEDIATED NECROTIZING MYOPATHY LINKED TO MUSHROOM SUPPLEMENTS

Nimisha Sinha[2], Matthew Means[1], Lakshmi Jayaram[1], Janice Lin[1]
[1]Stanford University, Palo Alto, USA, [2]JSS Medical College, JSS Medical Academy of Higher Education and Research, Mysore, India

Background. Immune-mediated necrotizing myopathy (IMNM) is a rare subtype of idiopathic inflammatory myopathy (IIM) characterized by proximal muscle weakness, markedly elevated creatine kinase (CK) levels, and minimal inflammatory infiltrates on biopsy. Among its variants, anti-3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR) myopathy involves antibodies directed against HMGCR, the pharmacologic target of statins (1-4). While statins are a recognized trigger, several statin-naïve cases, especially in Asians, suggest alternative environmental factors. Certain mushrooms, particularly Lentinula edodes (Shiitake), contain natural HMGCR inhibitors that act via mechanisms similar to statins – altering cholesterol biosynthesis and potentially initiating autoimmune responses in genetically predisposed individuals (5-7).
Methods. A 67-year-old man presented with six weeks of progressive proximal weakness, dysphagia, and exertional dyspnea. He consumed mushroom-based coffee twice daily for six months, containing extracts of Lentinula edodes, Cordyceps, Lion's Mane, Reishi, King Trumpet, and Turkey Tail mushrooms. His only prior statin exposure was a brief (<1 week) atorvastatin trial two years earlier. Examination revealed symmetric proximal weakness. Laboratory studies demonstrated elevated CK (9491 IU/L), AST (319 IU/L), and ALT (431 IU/L). Autoimmune testing was negative for anti-SRP and myositis-specific antibodies but strongly positive for anti-HMGCR antibodies (287.5 IU/mL; normal <1 IU/mL). MRI of the thighs showed symmetric intramuscular edema, and biopsy revealed necrotic fibers with minimal inflammation (3, 4).
Results. Based on the clinical findings, elevated anti-HMGCR titers, biopsy results, and temporal association with mushroom intake, the patient met 2017 European Neuromuscular Centre (ENMC) criteria for anti-HMGCR antibody-positive IMNM (3). He was treated with intravenous methylprednisolone (1 g daily for three days) and intravenous immunoglobulin for two days, followed by a prednisone taper starting at 60 mg daily. He demonstrated rapid symptomatic improvement and marked CK decline at discharge.
Conclusions. This case highlights a rare presentation of anti-HMGCR IMNM likely associated with prolonged mushroom supplement use in a patient with minimal statin exposure. Naturally occurring HMGCR inhibitors may represent underrecognized environmental triggers for autoimmune myopathy. Recognition and cessation of potential dietary exposures, coupled with prompt immunosuppressive therapy, are essential for optimal recovery and prevention of relapse. Clinicians should routinely assess supplement and dietary histories in patients with unexplained muscle weakness (6-9).
Key words: anti-HMGCR myopathy, mushroom supplements, statins, environmental triggers for autoimmunity

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Juvenile Myositis

OP-154

SEVERE JUVENILE POLYMYOSITIS TRIGGERED BY INFLUENZA A AND COVID-19: A CASE OF MULTI-ORGAN INVOLVEMENT AND THERAPEUTIC CHALLENGES

Joanna Lipińska[1], Elzbieta Smolewska[1]
[1]Department of Pediatric Cardiology & Rheumatology, Medical University of Lodz Poland, Lodz, Poland

Background. Juvenile polymyositis is a rare autoimmune inflammatory myopathy characterized by proximal muscle weakness and elevated muscle enzymes. Infectious triggers, including viral infections have been implicated in triggering autoimmune processes that lead to disease onset or exacerbation. The role of these infections in pathogenesis involves immune system activation and possible molecular mimicry that initiates a sustained autoimmune response.
A 9-year-old girl with recent influenza A and COVID-19 infections presented with acute polymyositis symptoms: muscle pain predominantly in the lower limbs, followed by tetraparesis, chest pain, and respiratory difficulties progressing to shock. Laboratory tests showed markedly elevated muscle enzymes (CK, LDH), elevated troponin, and features of multi-organ failure. Electromyography revealed no neurogenic changes, while whole-body MRI demonstrated inflammatory involvement across almost all muscle groups. Autoantibodies (anti-Mi and Ro52) were positive in serum, however measured after initiation of steroids and IV immunoglobulins. Intensive care treatment including mechanical ventilation and immunosuppressive therapy with methylprednisolone pulses, intravenous immunoglobulins, and later disease-modifying drugs (methotrexate switched to mycophenolate mofetil) was administered
The patient also received parenteral nutrition and high-dose diuretics. Rehabilitation and vocal cord therapy were part of supportive care. Due to severe infection-related complications, further immunosuppression with rituximab was contraindicated. Neverthless, the girl gradually stabilized, allowing extubation and improvement in muscle enzyme levels. Follow-up MRI revealed residual muscle inflammation and atrophic changes in paraspinal and pelvic muscles. Despite steroid therapy, macrocytic anemia and mild thrombocytopenia persisted but improved after adjustment of treatment. Endoscopy identified cricoarytenoid joint inflammation requiring continued speech therapy. One year after therapy, including tapered corticosteroids discontinued weeks prior, the patient reported weakness, difficulty rising from bed, and thoracic spine pain. Cushingoid features, skin striae, and lipid abnormalities persisted. Follow-up MRI showed no active muscle inflammation. Excessive rehabilitation and steroid side effects were considered. Lumbar-sacral MRI revealed compression fractures at L5, Th11, Th12, and L1 vertebrae. Bone densitometry was normal (total body T-score -1.0; spine -0.6). Pamidronate sodium treatment was started according to the Canadian protocol – 3-day intravenous infusions every 4 months – with good response after one year.
Conclusions. This case underscores viral infections' potential role in triggering severe juvenile polymyositis with multi-organ involvement. Early aggressive immunosuppression combined with multidisciplinary supportive care, including rehabilitation and endocrinologic management, can improve outcomes. Persistent complications like anemia and cushingoid features require ongoing management. Vigilance for steroid side effects, especially osteoporosis, is crucial. Furthermore, immunosuppressive therapy-related infections can limit treatment options.
Key words: juvenile myositis, severe course, viral infection

OP-196

EFFICACY AND SAFETY OF UP-FRONT ADD-ON IVIG IN JUVENILE DERMATOMYOSITIS: SINGLE-CENTER COHORT STUDY IN 21 PATIENTS

Renske Kamperman[1], Daniek Schinkel[2], Dieneke Schonenberg-Meinema[2], Mariken Gruppen[2], Amara Nassar - Sheikh Rashid[2,3], Giske Biesbroek[2], Taco Kuijpers[2], Anneke van der Kooi[1], Joost Raaphorst[1], Merlijn Van Den Berg[2]
[1]Department of Neurology, Amsterdam University Medical Center (AUMC), Amsterdam, The Netherlands, [2]Department of Paediatric Immunology, Rheumatology and Infectious Diseases, Emma Children's Hospital, Amsterdam University Medical Center (AUMC), Amsterdam, The Netherlands, [3]Department of Paediatrics, Zaans Medical Center, Zaandam, The Netherlands

Background. Juvenile dermatomyositis (JDM) is a rare and severe autoimmune disease of childhood characterized by inflammation of skin and muscles. Current treatment guidelines recommend the combination of up-front corticosteroids and methotrexate, based on expert-consensus. Historical evidence for add-on intravenous immunoglobulin (IVIG) is limited but positive. We examined the outcome and safety of up-front add-on IVIG treatment in JDM based on a single center cohort and reviewed the literature.
Methods. We did a retrospective chart review of all JDM patients diagnosed between 2003 and 2023 in our center (tertiary referral centre). Primary outcomes were attainment of inactive disease, disease remission, and (long-term) side effects. A systematic review was performed using PubMed and articles reporting IVIG treatment in JDM patients.
Results. A consecutive cohort of 21 newly diagnosed JDM patients (62% female, median age 10.0 years (range: 1.8–15.7 years)) received IVIG at diagnosis (2g/kg/4 weeks (max 60g)) for at least 6 months in addition to high-dosed glucocorticoids and methotrexate. Inactive disease was reached in 13/21 (62%) of the patients after a median time of 9.5 months. Disease remission, with no apparent sequelae, was achieved in 16/21 (76%) patients, after a median of 3.3 years (0.8-8.8 years); 3/21 (14%) had chronic fatigue, and 2/21 (10%) developed mild calcinosis. No serious adverse events were reported. The literature review retrieved 88 JDM patients treated with IVIG (of whom 38 up-front), 92% showed clinical improvement.
Conclusions. Up-front add-on IVIG therapy for at least six months in our cohort of JDM patients led to improvement and disease remission in the majority of patients. Our findings suggest superior long-term outcomes compared with JDM patients on standard treatment, especially considering the absence of severe calcinosis in all patients (1). With the lack of RCTs, further research is needed to corroborate the efficacy and safety of this therapy.
Key words: juvenile dermatomyositis, JDM, intravenous immunoglobulins, up-front IVIG

OP-251

INTERFERON SIGNALIZATION IN JUVENILE DERMATOMYOSITIS

Sara S. Kilic[1], Hulya Kose[1], Abdurrahman Simsek[2], Tugce Bozkurt[2], Ferah Genel[2], Hayriye Sarıcaoğlu[2]
[1]Department of Pediatric Immunology and Rheumatology Faculty of Medicine, Bursa Uludağ University, Bursa, Turkey, [2]Bursa Uludag University Department of Immunology, Bursa, Turkey

Background. Juvenile dermatomyositis (JDM) is an inflammatory myopathy characterized by skin involvement, vasculitis, and progressive muscle weakness. Increased interferon signaling is thought to play a role in the pathogenesis of JDM and is associated with disease severity and activation, as well as the development of calcinosis. The aim of this study is to measure the levels of cytokines and chemokines involved in interferon signaling in patients with JDM and JSc and to determine their correlation with disease severity.
Methods. 5 JDM, and 13 healthy controls were included in the study. Patients with morphea were scored according to the LoSCAT (activity index) and LoSDI (damage index) indices. Cytokines and chemokines involved in interferon gene signaling (IL-8, IL-1, IP-10, MCP1, TNF-α, CXCL-10, IFN-α, IFN-β, IFN-γ) were measured by ELISA. Interferon signaling genes were measured via the RT-PCR method.
The ratio of female to male patients was 3:2, the median age was 13 years (range: 5–17 years), and the median follow-up time was 36 months (range: 12–108 months).
IL-1, IL-6, IL-8, IFN-α, CXCL-10, TNF-α α and IFN-γ were significantly increased in patients with JDM compared with the healthy control group.
In RT-PCR analysis of the interferon signaling genes, including IFI27, IFI44, ISIG15, IFIT1, OAS1, and RSAD2, we found no statistically meaningful expression of the genes compared with the healthy group. However, we identified the fold changes in RSAD2, IFI27, and IFIT1 in JDM patients compared with the healthy controls in the related genes.
Conclusions. The results suggest that interferon signaling may be impaired in patients with JDM and that cytokines whose significant changes were observed in this study may play a key role in monitoring disease activity.
Key words: JDM, interferons, cytokines

Other

OP-28

PROCOAGULANT EXTRACELLULAR VESICLES IN PATIENTS WITH LIVEDO RETICULARIS

Avital Baniel[1,2,3], Cristina Ricco[3], Luca Musante[2], Victoria P. Werth[2,3]
[1]Dermatology, Tel Aviv Medical Center, Tel Aviv, Israel, [2]University of Pennsylvania, Philadelphia, USA, [3]VA Medical Center, Philadelphia, USA

Background. Procoagulant activity is a key property of extracellular vesicles (EVs). Connective tissue disease patients with livedo reticularis (LR) often exhibit procoagulant tendencies. This study aimed to investigate the role of EVs in LR
Methods. EVs were isolated from plasma of 12 LR patients and 7 healthy controls (HCs) using sequential ultracentrifugation and size-exclusion chromatography, followed by protein mass spectrometry. Tissue factor (TF) procoagulant activity and EV cellular origin were analyzed.
Results. TF activity was elevated in plasma of LR patients compared to HCs. Among EVs, TF activity was increased in small EVs (SEVs) but not in large EVs (LEVs). In the process of sequential centrifugation, we measured TF activity in supernatants after each step. The 1st supernatant represented plasma without LEVs and the 2nd represented plasma depleted of both LEVs and SEVs. LR supernatants demonstrated a decrease in TF activity with each step, supporting a role for both large and small EVs in TF activation. This pattern was seen only EVs derived from LR patients and absent in HCs or positive controls. EV concentrations were not elevated in LR, suggesting that procoagulant activity arises from vesicular cargo rather than abundance. Proteomic analysis revealed 274 differentially expressed proteins (DEPs): 5 upregulated and 269 downregulated. Most LR patients displayed distinct expression profiles relative to HCs, with remission cases resembling controls. A subset with profound vasculopathy showed a different pattern. Overrepresentation analysis identified enrichment of homeostasis, coagulation, and vascular endothelial growth factor (VEGF) signaling pathways. Notably, Krueppel-Like Factor 8 (KLF8), a vascular endothelial regulator of angiogenesis and vessel contractility, was markedly reduced (fold change 4.6, $p<0.001$). Cellular origin analysis showed increased leukocyte-derived EVs and decreased platelet-derived EVs in LR versus HCs, without significant change in endothelial EVs. This suggests a shift from homeostatic, platelet-driven EV release to an inflammatory, leukocyte-dominated EV profile in LR.
Conclusions. EVs exert a procoagulant effect in LR. Increased TF activity and a shift in EV release from primarily platelet-driven to those originating from inflammatory cells are possible mechanisms underlying this effect. Our findings suggest that a reduction in KLF8 within EVs may be a key regulatory factor in LR.
Key words: extracellular vesicles, livedo reticularis

OP-45

ADVERSE PERINATAL OUTCOMES AND RECURRENT PERIVILLOUS FIBRIN DEPOSITION IN ANTI-JO-1 ANTISYNTHETASE SYNDROME: A CASE REPORT

Ana Rita Lopes[1,2], Ana Teodósio Chícharo[3], Maria Pulido-Valente[4], Lucília Carvalho[5], Raquel Campanilho-Marques[1,2], Ana Rita Cruz-Machado[1,2], Luísa Pinto[2,4], Susana Capela[1,2]
[1]Rheumatology Department, ULS Santa Maria, Lisbon Academic Medical Center, Lisbon, Portugal, [2]Faculdade de Medicina, Universidade de Lisboa, Lisbon, Portugal, [3]Rheumatology Department, ULS Algarve, Faro, Portugal, [4]Obstetrics, Gynaecology, and Reproductive Medicine Department, ULS Santa Maria, Lisbon, Portugal., Lisbon, Portugal, [5]Anatomic Pathology Department, ULS Lisboa Ocidental, Lisbon, Portugal

Background. Pregnancy in women with antisynthetase syndrome (ASyS) is exceedingly rare, and maternal–fetal outcomes are poorly characterised. Available evidence is limited to isolated case reports suggesting increased risk of placental dysfunction, fetal growth restriction (FGR), and stillbirth, particularly in anti-Jo-1-positive patients. The mechanisms linking ASyS to placental injury remain largely unexplored.
Case report. We report a case of a 36-year-old woman with Anti-Jo-1-positive ASyS whose first pregnancy ended in intrauterine fetal death at term, with placental histology showing maternal floor infarction and massive perivillous fibrin deposition (MPVFD). In a subsequent pregnancy, she was

managed with tocilizumab, hydroxychloroquine, cyclosporine, and low-dose prednisolone, along with low-dose aspirin (also used in the first pregnancy) and prophylactic enoxaparin sodium (newly introduced in the second). Despite stable maternal disease, fetal growth restriction (FGR) was detected in the third trimester, leading to emergency caesarean section at 33+5 weeks for fetal distress. The neonate was healthy and discharged in good condition. Placental histology revealed extensive perivillous fibrin deposition not meeting MPVFD criteria.

Discussion. This case highlights the recurrence of perivillous fibrin deposition across two consecutive pregnancies in Anti-Jo-1 ASyS, associated with divergent perinatal outcomes. The findings suggest that immune-mediated placental injury may contribute to adverse events independently of maternal disease activity.

Placental dysfunction in ASyS may represent an organ-specific immune manifestation driven by persistent anti-Jo-1 activity. Recognition of this association is crucial for risk stratification, close fetal monitoring, and tailored antithrombotic-immunomodulatory therapy. This case highlights the need for systematic study of pregnancy outcomes and placental pathology in women with idiopathic inflammatory myopathies.

Key words: antisynthetase syndrome, anti-Jo-1 antibodies, fetal growth restriction, placental insufficiency, perivillous fibrin deposition

OP-107

A NEUROLOGICAL TWIST IN A PATIENT WITH INFLAMMATORY MYOPATHY: A RARE CASE REPORT

Tomás Stein Novais[1], Rodrigo Rei[1], Tatiana Correia[2], Isabel Pontes[3], Susana Matias[1], Catarina Abreu[1], Vanessa Fraga[1], Margarida Cunha[1], Pedro Manuel Pereira[4], Maria José Santos[1]

[1]Rheumatology Department, Hospital Garcia de Orta, Unidade Local de Saúde Almada-Seixal, Almada, Portugal, [2]Internal Medicine Department, Hospital Garcia de Orta, Unidade Local de Saúde Almada-Seixal, Almada, Portugal, [3]Physical Medicine and Rehabilitation department, Hospital Garcia de Orta, Unidade Local de Saúde Almada-Seixal, Almada, Portugal, [4]Neurology Department, Hospital Garcia de Orta, Unidade Local de Saúde Almada-Seixal, Almada, Portugal

Background. Inflammatory myopathies can be difficult to differentiate from other aetiologies of muscle weakness, namely of metabolic and neurological origin. Thus, identifying such mimickers requires careful clinical assessment and often a complex diagnostic workup.

Case presentation: We present a 76-year-old female patient attending our Rheumatology department with a recent diagnosis of anti-Mi2 antibody dermatomyositis with musculoskeletal (including oesophageal), cutaneous and systemic involvement under treatment with monthly intravenous immunoglobulin (IvIg) (2g/kg/month) and low-dose prednisolone (5mg/kg/day) – with no additional immunosuppression at the time due to an ongoing infection. Her remaining medical history was positive for asthma, hypertension and a 3rd degree atrioventricular block.

Before the 3rd IvIg cycle, the patient presented to the Emergency Department (ED) with a 1-week history of major relapse of muscle weakness and left ptosis. On ED observation, severe tetraparesis was recognized and a dermatomyositis flare was assumed, which led to her admission. Complete blood count, inflammatory markers and muscle, hepatobiliary, thyroid and renal parameters were uneventful, as were urinalysis and chest radiograph.

Upon joint observation by rheumatology and neurology, not only was a proximal-predominant quadriparesis evident but the patient also exhibited severe bilateral facial paresis, ophthalmoparesis and diplopia, severe hypoesthesia of the trunk and limbs, ataxia, pseudoathetosis and absent deep-tendon reflexes. So, what was believed to be a flare of her condition, had otherwise unexplained neurological features, namely, profound sensory impairment, areflexia, ataxia, and facial and extraocular musculature involvement.

Cerebrospinal fluid (CSF) revealed hyperproteinorrachia (63.8 (NR:15-45mg/dL), with albuminocytologic dissociation (leucocytes<2/µL). CSF culture and search for neurotropic viruses and autoantibodies were negative. Nerve conduction studies revealed new loss of F waves besides low amplitude motor responses (previously present). Blink reflex testing revealed absent responses bilaterally.

Encephalic and radicular lumbosacral magnetic resonance imaging were unremarkable.

Hence, the patient was instead diagnosed with Miller Fisher syndrome: an immune-mediated neuropathy represented by the triad of ataxia, areflexia, and ophthalmoparesis, along with ptosis, facial nerve palsy, hypoesthesia and paresis. IvIg therapy was resumed and in a month the patient displayed a major recovery of her deficits, regaining sensation and the ability to walk.

Conclusions. We describe two rare immune-mediated entities with overlapping presentations coexisting in the same patient. To our knowledge, this is the first case reported. This case underlines the need for a broad clinical reasoning and emphasizes the value of the clinician's observation in accurately interpreting signs and symptoms, not only when they align with the diagnosis but also when they do not.

Key words: dermatomyositis, differential diagnosis, Miller Fisher syndrome

OP-144

PATIENTS WITH MYOSITIS; THE JOURNEY FROM DIAGNOSIS IN INPATIENT CARE TO OUTPATIENT CLINIC CARE – HOW DO WE MEET PATIENT'S NEEDS IN EARLY DISEASE?

Ingrid Gerhardson[1], Heléne Sandlund[1], Annelie Dihkan[2], Ingrid E. Lundberg[3], Maryam Dastmalchi[1,3]

[1]Department of Gastro, Dermatology and Rheumatology, Theme Inflammation and Aging, Karolinska University Hospital, Solna, Sweden, [2]Swedish Rheumatism Association, Patient Research Partner, Sweden, [3]Division of Rheumatology, Department of Medicine, Karolinska Institutet, Solna, Sweden

Background. Myositis is a multiorgan disease with involvement of muscles, skin, lungs, joints and heart. Many patients with new onset myositis may present with acute symptoms and need hospitalization. In the hospital, an investigation and a plan for further care are initiated. These will look different according to the individual´s need. When the patient leaves the hospital an individualized plan for follow up for patient with myositis is created, but a specific time for an appointment is not always scheduled. In the myositis outpatient clinic the patient will meet a doctor, nurse, occupational therapist and a physiotherapist all specialized in myositis patients. The duration before the first follow up can be several weeks to a month. This can create anxiety and insecurity as the patient may feel "hanging in the air". In particular, when the illness occurs with sudden onset or with serious organ manifestations, the post hospitalization period is important, and the nurse becomes an important and safe point for the patient. With this project, we aimed to map the current structure for post-in-patient care to identify possibilities for improvement.

Methods. Structured interviews with doctors, nurses responsible for the schedules to the outpatient clinic and with patients, including a patient partner where done. The responsibilities of the different team members and what they do at different time points in hospital care were clarified. Interviews with patients including questions about their need after leaving hospital were undertaken. As a second step, new procedures will be discussed with the care team and the patient partner. After consensus the new procedures will be implemented. A checklist for follow up will be created for the discharging doctor and nurse.

Results. The project is ongoing. A binder with information of different subtypes of myositis disease and information about the outpatient clinic is in the ward. Information for the patient has been updated and communicated to doctors specialized in myositis. Evaluation of the changes in procedures is ongoing and a patient partner is consulted in the process.

Conclusions. We anticipate that a clear and individualized plan for follow-up of patients with myositis after in-patient care will improve knowledge on the disease and treatment, as well as adherence to treatment and over-all outcome for patients with myositis.

Acknowledgements. Funding have been received from Karolinska University Hospital for this project.

Key words: patient individualized myositis care, in-patient-care, out-patient-care

OP-214

MYOPREG: REGISTRY FOR PREGNANCY OUTCOMES IN IDIOPATHIC INFLAMMATORY MYOPATHIES – A CALL FOR COOPERATION

Melinda Nagy-Vincze[1,2], Dorottya Lujza Marien[1,2], Dorottya Szinay[1,2], Katalin Szabó[1,2], Zoltán Griger[1,2]
[1]University of Debrecen, Faculty of Medicine, Division of Clinical Immunology, Debrecen, Hungary, [2]University of Debrecen, Gyula Petrányi Doctoral School of Allergy and Clinical Immunology, Debrecen, Hungary

Background. There is increased evidence on the importance of preconception counselling in systemic autoimmune diseases including idiopathic inflammatory myopathies (IIM). Studies of the impact of IIM to pregnancy and vice versa have yielded controversial results. Planning or optimal timing of pregnancy to coincide with both disease quiescence and pregnancy-compatible medications increases the likelihood of pregnancy success. Former studies stated that maternal risk is low except hypertensive disorders during pregnancy and caesarean section at term. Meanwhile foetal risks seem higher. Some studies reported high miscarriage rate, others found increased frequency of preterm birth and growth restriction at birth. Besides maternal disease activity, antibody profile and internal organ involvements could distinguish a more vulnerable group considering pregnancy complications.
Objectives and Methods. The primary goal of this multicentre study is to collect well organised clinical data about IIM patients' pregnancy. We are planning 2 steps of data collection; between 2020 and 2025 retrospectively and from 2026 prospectively. We are collecting maternal data: epidemiology, disease onset, symptoms, antibody profile at diagnosis and before, during and after pregnancy. Therapeutic regimen will be collected before, during and after pregnancy including IIM specific and pregnancy specific drugs (aspirin, low-molecular weight heparin, etc.) Laboratory results, disease activity data will be registered from every trimester and post-partum. Pregnancy outcome, neonate parameters and lactation will also be recorded.
Results. Retrospective data will be analysed until and reported on next GCOM, prospective data collection will be ended on 31th Dec. 2030. Each colleague who registers for participation will get reminders regularly.
Conclusions. Based on our results open questions considering maternal and foetal risks during IIM patients' pregnancy could be answered. We could also identify high risk groups in our heterogeneous patient population and find differences in pregnancy risks between IIM subtypes.
Key words: myositis, pregnancy, registry

OP-222

REFRACTORY ANTI-HMGCR-NECROTIZING MYOPATHY WITH PROGRESSIVE HYPERCAPNIC RESPIRATORY FAILURE RESPONSIVE TO JAK INHIBITOR: A CASE REPORT

Nick Huang[1], Tissa Bijoy George[1], Lisa Christopher-Stine[2], Anthony Nicolas[1], Chester Oddis[1], Dana Ascherman[1], Vladimir Liarski[1]
[1]University of Pittsburgh, Pittsburgh, USA, [2]Johns Hopkins University School of Medicine, Baltimore, USA

Background/Objective: Immune-mediated necrotizing myopathy (IMNM) associated with 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) antibodies is a rare condition presenting with proximal weakness. Respiratory involvement is uncommon but can be life-threatening. We report a 58-year-old woman with long-standing anti-HMGCR-positive IMNM who developed progressive hypercapnic respiratory failure.
Methods. Retrospective single center single case report.
Results. A 58-year-old woman with history of gout, osteoporosis, diverticulitis, mixed hyperlipidemia, and hypertension, was diagnosed in May 2010 with anti-HMGCR-positive IMNM following atorvastatin exposure in 2004 (1, 2). Creatine phosphokinase (CPK) level was 1897 U/L. Autoantibody testing (ANA, SSA, SSB, Smith, Scl-70) was negative. MRI showed diffuse lower extremity muscle edema, and biopsy revealed necrosis and myophagocytosis consistent with necrotizing myopathy. The patient was later found to be anti-HMGCR antibody positive (3, 4).
She received glucocorticoids, methotrexate, azathioprine, IVIg, rituximab, and plasma exchange (PLEX). Refractory to most therapies, she was ultimately maintained on IVIg 2 g/kg every 2 weeks, normalizing her CPK (161 U/L) but with persistent weakness, pain, dyspnea, and dysphagia (Fig. 1). By October 2024, progressive orthopnea and reduced inspiratory capacity raised concern for diaphragmatic weakness.
In April 2025, she presented emergently with respiratory distress one week after IVIg. Examination showed proximal weakness (neck 4/5, hip 3/5, knee 3+/5), CPK 81 U/L, and negative inspiratory force (NIF) -40 cm H_2O. Arterial blood gas confirmed acute on chronic hypercarbia. Pulmonary embolism, infection, and myasthenia gravis were excluded. BiPAP and emergent PLEX (three sessions) were initiated. Repeat MRI showed diffuse fatty replacement with muscle edema. Despite therapy, NIF declined to –10 cm H_2O by hospital day (HD) 8, necessitating intubation for respiratory failure. Concurrent acute kidney injury (GFR 16 mL/min/1.73 m²) limited IVIg use.
Renally adjusted tofacitinib (5 mg daily, HD 12–35) was initiated as salvage therapy with methylprednisolone 100 mg daily (HD 9–20). Within one week, strength and inspiratory effort improved. Patient was extubated by HD 19, off oxygen by HD 25 (NIF -40 cm H_2O), and discharged to rehabilitation on HD 28 with prednisone 40 mg daily and NIF -60 cm H_2O. Her course is summarized in Figure 2.
Conclusions. This case suggests JAK inhibition may offer therapeutic benefit in IMNM when conventional therapies and PLEX fail.
Key words: immune mediated necrotizing myopathy, HMGCR, tofacitinib

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OP-260

ANCA-ASSOCIATED VASCULITIS PRESENTING WITH ISOLATED MYOSITIS: A DIAGNOSTIC CHALLENGE

Anita Cunha[1], Maria Pontes Ferreira[1], Susana Almeida[1], Francisca Guimarães[1], Ana Nascimento[2], Miguel Pinto[3], José Tavares-Costa[1], Daniela Peixoto[1]
[1]Rheumatology Department, Unidade Local de Saúde do Alto Minho, Ponte de Lima, Portugal, [2]Internal Medicine Department, Unidade Local de Saúde do Alto Minho, Viana do Castelo, Portugal, [3]Department of Neuropathology, Centro Hospitalar Universitário de Santo António, Porto, Portugal

Background. Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a rare systemic disease with highly variable clinical manifestations. Muscular involvement is uncommon, and myositis is not typically included among the classification criteria for systemic vasculitis. We present a case of AAV with isolated muscle involvement, illustrating the diagnostic complexity of this unusual presentation.
Methods. A previously independent 79-year-old female developed progressive asthenia and functional decline over four months. An infectious cause was initially suspected, but symptoms persisted despite antibiotic therapy, leading to her hospital admission in December 2023 for further evaluation. A comprehensive workup was undertaken to exclude common causes of generalized weakness, including metabolic, infectious, and neoplastic conditions
Results. On admission, she presented with generalized muscle weakness, complicated by recumbent posture and somnolence, which limited clinical assessment. Laboratory evaluation revealed new-onset anaemia, marked leucocytosis, and elevated inflammatory markers, with normal muscle enzyme levels. Positron emission tomography demonstrated diffuse bone marrow uptake; however, bone marrow biopsy and medullary studies excluded haematologic malignancy. Additional imaging, including temporal and axillary artery ultrasounds and thoracoabdominopelvic and spine computed tomography scans, showed no significant abnormalities. Electromyography revealed subacute myopathic changes, and whole-body MRI demonstrated bilateral, symmetrical muscle oedema involving the scapular girdle, forearms, and legs. After exclusion of neoplastic and infectious causes, immunologic testing identified positive myeloperoxidase (MPO)-ANCA. Given the atypical presentation, a muscle biopsy was performed, confirming small-vessel vasculitis with type 2 fibre atrophy, consistent with myeloperoxidase MPO-AVV.
Considering age, comorbidities, and infection risk, the patient was treated with high-dose prednisolone followed by methotrexate as a steroid-sparing agent. Rehabilitation therapy was initiated in parallel to optimize functional recovery. Clinical improvement was observed, with partial recovery of muscle strength and autonomy, stable haemoglobin and normalization of inflammatory markers, allowing prednisolone tappering. The patient maintai-

ned clinical stability until October 2025, when her condition deteriorated due to multiple infectious complications, ultimately resulting in death.
Conclusions. This case illustrates an exceptional presentation of MPO-AVV with isolated myositis, highlighting the importance of considering vasculitis in the differential diagnosis of atypical cases. Given the predominant muscle involvement, the main differential diagnoses included idiopathic inflammatory myopathies and paraneoplastic myositis. Histopathologic evidence of vasculitis was key to establishing the diagnosis. Further research is crucial for optimizing treatment strategies, in managing localized forms of vasculitis.
Key words: myositis, ANCA-associated vasculitis, MPO-ANCA

OP-323

LUNG DISEASE AS THE FIRST GLIMPSE OF AN INFLAMMATORY MYOPATHY: A CASE SERIES

Filipa Canhão André[1], João Oliveira[1], Fernando Albuquerque[1], André Saraiva[1,2], Margarida Coutinho[1,2], Tânia Santiago[1,2]
[1]Unidade Local De Saúde De Coimbra, Coimbra, Portugal, [2]Faculty of Medicine, University of Coimbra, Coimbra, Portugal

Introduction: Idiopathic inflammatory myopathies (IIM) typically present with proximal muscle weakness, but interstitial lung disease (ILD) can be a prominent initial manifestation.
Methods. Five illustrative cases of IIM with ILD as the initial manifestation were retrospectively identified and described.
Results. Case 1: A 48-year-old female presented with progressive dyspnea, cough and fatigue. Imaging revealed NSIP (Nonspecific interstitial pneumonia) and PFTs (pulmonary function tests) showed a restrictive pattern, with greatly decreased DLCO. After initial corticosteroid treatment symptoms progressed and, 3 months later, she developed myalgia and elevated muscle enzymes. Anti-Jo-1 antibodies were positive and a muscle biopsy confirmed myositis. She improved with high-dose corticosteroids and azathioprine.
Case 2: A 53-year-old male smoker presented with cough, arthralgia and edema. He had bibasilar crackles and mild arthritis, but no muscle weakness. Elevated muscle enzymes and a positive anti-SSA52 antibody were found. Imaging revealed UIP (Usual interstitial pneumonia) and PFTs showed a restrictive pattern, with greatly decreased DLCO. Despite normal EMG (eletromyogram) and ultrasound, a muscle biopsy confirmed IIM. Corticosteroids and mycophenolate mofetil were effective.
Case 3: A 66-year-old female with fibromyalgia presented with dyspnea, cough, asthenia and night sweats. Examination revealed bibasilar crackles. A NSIP pattern was confirmed, PFTs showed a restrictive pattern, with moderately decreased DLCO and muscle enzymes were elevated. Anti-PL7 and anti-SSA52 antibodies were positive. Despite no muscle weakness, EMG showed myopathic changes. Treatment with corticosteroids, mycophenolate mofetil and rituximab led to clinical stability.
Case 4: A 38-year-old male presented with acute respiratory failure and arthralgias. Imaging revealed NSIP and PFTs showed a restrictive pattern, with greatly decreased DLCO. He had elevated creatine kinase and positive anti-Jo-1 and anti-SSA52 antibodies. Antisynthetase syndrome was diagnosed. Initial treatment with corticosteroids and cyclophosphamide, followed by mycophenolate mofetil, resulted in stable disease.
Case 5: A 53-year-old female with known pulmonary fibrosis and restrictive PFTs developed polyarthralgias, Raynaud's phenomenon and fatigue. Although muscle enzymes were normal, strong positive anti-PL12 and anti-SSA52 antibodies suggested antisynthetase syndrome. Corticosteroids and cyclophosphamide had limited effect and she is being evaluated for lung transplantation
Conclusions. While not typical, ILD can be the initial presentation of IIM in 13-37.5% of cases. In patients with ILD, especially with elevated muscle enzymes or myositis-specific antibodies, prompt investigation for myopathy is warranted. Moreover, almost all the presented patients had not only myositis-specific antibodies but also myositis-associated antibodies, like anti-SSA52, which, as described in the literature, seems to predispose to a worse prognosis, with more severe ILD.
Key words: idiopathic inflammatory myopathies, Interstitial lung disease

OP-354

TOWARDS A NATIONWIDE MYOSITIS DATABASE – THE DUTCH MYOSITIS REGISTRY

Nienke Heida[1,2], Pinar Özkaynar[3], Marianne de Visser[3], Anneke van der Kooi[3], Ester van Leeuwen[4], Eleonora Aronica[5], Eric Voorn[1,2], Christiaan Saris[6], Marc Janssen[7], Annet van Royen[7], Umesh Badrising[8], Zana Brkic[9], Esther Brusse[10], Sander Tas[11], Dutch Myositis Network, Joost Raaphorst[3]
[1]Amsterdam UMC location University of Amsterdam, Department of Rehabilitation Medicine, Amsterdam, The Netherlands, [2]Amsterdam Movement Sciences, Rehabilitation & Development, Amsterdam, The Netherlands, [3]Department of Neurology, Amsterdam UMC, University of Amsterdam, Amsterdam Neuroscience, Amsterdam, The Netherlands, [4]Department of Laboratory Medicine, Laboratory Specialized Diagnostics and Research, Section Medical Immunology, Amsterdam University Medical Center, University of Amsterdam, Amsterdam, The Netherlands, [5]Department of Neuropathology, Academic Medical Center and Swammerdam Institute for Life Sciences, Center for Neuroscience, University of Amsterdam, Amsterdam, The Netherlands, [6]Department of Neurology, Donders Institute for Brain, Cognition, and Behavior, Radboud University Medical Center, Nijmegen, The Netherlands, [7]Department of Paediatric Rheumatology, Wilhelmina Children's Hospital, Utrecht, The Netherlands 8 Department of Neurology, Leiden University Medical Center, Leiden, The Netherlands, [8]Department of Neurology, Leiden University Medical Center, Leiden, The Netherlands, [9]Department of Internal Medicine, Division of Clinical Immunology and Allergology, Erasmus MC University Medical Center, Rotterdam, The Netherlands, [10]Department of Neurology, Erasmus MC, Rotterdam, The Netherlands, [11]Amsterdam Rheumatology and Immunology Center, Department of Rheumatology and Clinical Immunology, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands

Background. Idiopathic inflammatory myopathies (IIMs) often cause long-term muscle weakness, pain, and fatigue, resulting in substantial disability and reduced quality of life in up to 70% of patients. The clinical heterogeneity and incompletely understood disease mechanisms of IIM make clinical care and research challenging. A nationwide patient registry may improve disease insights, clinical care, data collection for research and it may contribute to international registry initiatives.
Methods. The Dutch Myositis Registry uses the Castor electronic data capture system for standardized data collection. Patients with a confirmed diagnosis of myositis (based on clinical features, muscle biopsy and/or myositis antibodies) are eligible. Patient data are collected, including demographics, clinical data including follow-up data (on treatments and outcomes using digital patient-reported outcome measures (PROMs) enabling standardized follow-up). The aim is to transfer data from multiple hospital electronic health records to the registry through automated and standardized data integration, reducing manual entry and improving data completeness. To achieve national coverage, which may be unique on a global level, the registry aims to connect to a nationwide network of laboratories performing either antibody testing or muscle biopsies enabling rapid and verifiable patient identification.
Results. Data collection is ongoing, with 278 patients with IIM included in the registry. All thirteen laboratories in the Netherlands that use the Euroimmun platform are connected, and provide nationwide coverage: we are preparing the forwarding of positive antibody test results to the registry. An automated nationwide pathology system in the Netherlands covers muscle biopsies with inflammatory myopathy (or similar) as conclusions; consensus has been reached on updates to the PALGA Thesaurus, including removal of outdated terms (e.g. polymyositis and the addition of terminology according to updated classifications. This framework enables alerts for newly diagnosed patients. A protocol for diagnosis verification is in progress. A standardized template for documenting clinical consultations is being developed for structured data capture and automated integration, including validated PROMs for IIM. Privacy and data-sharing agreements are being developed with participating hospitals and laboratories.
Conclusions. The Dutch Myositis Registry creates a national infrastructure that covers clinical, laboratory, and patient data to support better research and patient care. It promotes faster identification of patients for trials, and more consistent data collection to improve outcomes for people with myositis. Automated data integration from electronic health records is expected to improve data completeness.
Key words: idiopathic inflammatory myopathies, registry, trial readiness

Pathogenesis of Inflammatory Myopathy

OP-166

CLINICAL, IMMUNOLOGICAL AND METABOLOMIC RISK FACTORS ASSOCIATED WITH FYBROMIALGIA IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Samuel Govea-Peláez[1], Beatriz Alcalá-Carmona[1], Jennifer T. Balderas-Miranda[1], Yatzil Reyna-Juárez[1], María José Ostos-Prado[1], Nancy R. Mejía-Domínguez[2], Guillermo Juárez-Vega[2], Karina Santana-de Anda[1], Jiram Torres-Ruiz[1], Diana Gómez-Martin[1]
[1]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [2]Red de apoyo a la Investigación, Cordinación de Investigación Científica, Universidad Nacional Autónoma de México, Mexico City, Mexico

Background. Patients with idiopathic inflammatory myopathies (IIM) have reported chronic pain despite having normal serum muscular enzymes, physician global assessment (PhGA) and MMT8 scores, thus becoming a priority in treatment and research. The primary objective of this study was to analyze the clinical, immunological and metabolomic risk factors associated with fibromyalgia in patients with idiopathic inflammatory myopathies.
Methods. We performed a case-control study in a third-level referral center in Mexico City. We included patients who fulfilled EULAR/ACR 2017 criteria for IIM and had complete clinical response / remission for 6 months; patients with other autoimmune diseases were excluded. All subjects answered the PROMIS Pain Interference Short Form 8a; in case of a score >11, WPI and SSS were used for FM classification according to EULAR/ACR 2010 criteria. Activity and damage were evaluated by IMACS core set measurements. Peripheral blood mononuclear subsets were assessed by multiparametric flow cytometry; serum cytokines were measured by a multiplex luminometry assay, and an untargeted metabolomic analysis of the serum was conducted using gas chromatography coupled to mass spectrometry.
Results. We included 49 IMM patients in complete clinical response; the prevalence of FM was 40.1% (20/29) and female sex was predominant (95% *vs*. 68.9%, p=0.016). Dermatomyositis was the most prevalent subtype in both groups. Patients with IMM and FM displayed higher PtGA (3.5 *vs*. 0.50, p=0.001), as well as muscular damage (1.5 *vs*. 1.0, p=0.023); the percentage and doses of prednisone usage was more prevalent in IIM + FM (55% *vs*. 17.2%, p=0.005). Patients with IIM+ FM were characterized by lower amounts of T CD8+ cells (0.04 *vs*. 0.13, p=0.045), B cells (58.4 *vs*. 152, p=0.052), and non-classical monocytes (16.4 *vs*. 28.5, p=0.027). In the partial least squares discriminant analysis for metabolites, tryptophan, glyceric acid, pipecolic acid, cysteine, and alanine were the metabolites with the highest discriminative score (VIP). The binary logistic regression showed that the PtGA (OR 14.4, 95% CI 2.44-360.79) and the GA of muscle damage (OR 7.80, 95% CI 1.77-143.86) maintained a positive association with the presence of FM.
Conclusions. Our data suggests a high prevalence of FM in patients with IIM in complete clinical response. The main risks factors associated with FM in IIM are PtGA, muscular damage GA, lung damage score, as well as higher serum levels of pro-inflammatory cytokines MCP-1, whereas nonanoic acid levels were a protective factor for this association.
Key words: fibromyalgia, inflammatory myopathies, risk factors

Patient Perspectives

OP-279

EVALUATING GENERATIVE AI FOR PATIENT SELF-EDUCATION IN RARE DISEASES: A PILOT STUDY IN MYOSITIS

Pritikanta Paul[1], Rocio Vazquez Do Campo[2], Priya Dhawan[1]
[1]University of California San Francisco, San Francisco, USA, [2]University of Alabama at Birmingham, Birmingham, USA

Background. Patients with rare and complex diseases such as idiopathic inflammatory myopathies (myositis) often encounter limited and fragmented educational resources online. While traditional web searches have long served as the main avenue for patient self-education, the growing adoption of generative artificial intelligence (AI) tools such as ChatGPT is transforming how patients seek health information. Given the scarcity of authoritative resources for rare diseases, patients may increasingly depend on AI-generated materials. This study aims to evaluate the quality and reliability of ChatGPT's educational content related to myositis.
Methods. We reviewed literature on online health information-seeking behavior to identify commonly used search themes – disease overview, symptoms, causes and risk factors, diagnosis, and treatment and prognosis. Literature on myositis was used to identify the four most common adult-onset phenotypes: polymyositis, dermatomyositis, immune-mediated necrotizing myopathy, and inclusion body myositis. A total of 20 standardized prompts (4 diseases × 5 themes) were developed and submitted to ChatGPT (GPT-4, July 2025 release).
Responses will be systematically evaluated by two neuromuscular physicians with expertise in myositis care. Each response will be rated for accuracy, completeness, patient relevance, and overall satisfaction using a structured 5-point scale. In addition, qualitative contextualization will explore variations across disease subtypes and disagreements between reviewers. Quantitative grading and synthesis will be completed before the conference presentation.
Results. Preliminarily we expect that ChatGPT would provide broadly accurate and accessible summaries but varying in depth and disease-specific detail. Final analyses will be available at the time of presentation.
Conclusions. This pilot is anticipated to provide a framework for evaluating generative AI as an emerging source of patient education in rare neuromuscular diseases. Insights from this work may guide myositis foundations in developing evidence-based patient education strategies and help treating physicians counsel patients on the strengths and limitations of AI-generated materials.
Key words: generative AI, patient self-education, online health information seeking, medical internet research, digital health

Therapeutic Advances

OP-46

COULD TRIPLE THERAPY BE THE RIGHT TREATMENT FOR SEVERE IDIOPATHIC INFLAMMATORY MYOPATHIES?

Hugo Gonçalves[1], Paulo Pereira[1], Carla Campinho-Ferreira[1], Ana Margarida Correia[1], Emanuel Costa[1], Diogo Esperança-Almeida[1], Joana Leite-Silva[1]
[1]Unidade Local de Saúde de Braga, Braga, Portugal

Background. Idiopathic inflammatory myopathies are heterogeneous conditions, with different degrees of muscle involvement and extramuscular manifestations, lacking standardized treatment. Treatment relies on high-dose steroids, with evidence supporting intravascular immunoglobulins (IVIG), rituximab (RTX), and mycophenolate mofetil (MMF), including combined use of MMF with RTX or RTX with IVIG, while triple therapy remains scarcely studied (1, 2).
Methods. We report two cases of patients with severe proximal muscle weakness and dysphagia. Laboratory tests and electromyography confirmed inflammatory myopathy, and both were treated with steroids, IVIG, rituximab and MMF as well as intensive physiotherapy.
Results. Case 1: A 49-year-old woman was admitted with progressive proximal muscle weakness, dysphagia, and Raynaud phenomenon, without skin manifestations. Laboratory tests revealed elevated creatine kinase (CK), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). Electromyography was consistent with inflammatory myopathy. Myositis-specific antibodies (anti-PL7, Mi-2) were positive, suggestive of antisynthetase syndrome. During admission, she developed respiratory failure; submitted to thoracic computed tomography and cardiac magnetic resonance which were unremarkable. Treatment included intravenous methylprednisolone pulses, oral prednisone, IVIG (6 cycles), RTX, and MMF along with physiotherapy. One year later, she regained total autonomy. RTX and MMF were maintained. No infectious complications were recorded during hospitalization or during follow-up.
Case 2: An 86-year-old woman was admitted with progressive proximal muscle weakness and dysphagia, requiring nasogastric tube placement. Six months before, she developed heliotrope rash and Gottron papules. Laboratory tests showed elevated CK, elevated ESR and CRP; immunological testing revealed positive antinuclear antibodies (ANA) 1:2560, positive anti-Mi2 antibodies and electromyography suggested inflammatory myopathy,

which was consistent with the diagnosis of dermatomyositis. Treatment included oral prednisolone taper (from 60 mg of prednisolone to 5 mg), IVIG (3 cycles), RTX, and MMF, along with physiotherapy. Three months later, the patient was able to walk with assistance (being bedridden at the time of admission), having minor proximal muscle weakness in the arms and thighs and fully recovered of dysphagia and is currently regaining autonomy with physiotherapy. During admission, she developed an acute cystitis, successfully treated with cotrimoxazole guided by antibiogram and no other infectious complications were recorded.
Conclusions. In these cases, with severe muscle weakness and dysphagia, escalation of immunosuppressive therapy is required. There are limited reports on the use of triple therapy (Immunoglobulins, Rituximab, and MMF), which make those cases valuable, demonstrating efficacy and safety of this treatment, although prospective studies and controlled trials are needed to confirm these findings.
Key words: inflammatory myopathies, immunoglobulins, rituximab, mycophenolate mofetil

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2. doi: 10.1186/s42358-025-00450-x

OP-70

A SYSTEMATIC REVIEW OF NUTRITIONAL INTERVENTIONS IN MUSCLE DISEASES

Deepanjali Vedantam[1], Taanya Talreja[2], Pranathi Bandarupalli[3], Lakshmi Nagendra[4], Sheryl Salis[5], Karen Cheng[6], Teerin Liewluck[7], Debra Lupeika[8], Ashley Maclean[9], Latika Gupta[10,11,12]
[1]Shasta Regional Medical Centre, Redding, USA, [2]Seth GS Medical College and KEM Hospital, Mumbai, India, [3]Mercy Health, USA, [4]JSS Medical College, Mysore, India, [5]Nurture Health Solutions, India, [6]University Medical Center, Göttingen, Germany, [7]Mayo Clinic, Rochester, USA, [8]University of California, Davis, Davis, USA, [9]Stanford University, Stanford, USA, [10]University of Birmingham, Birmingham, UK, [11]Royal Wolverhampton Hospitals, UK, [12]Francis Crick Institute, UK

Background. Medical nutrition therapy significantly impacts cardiovascular risk and overall health, but effects on muscle diseases remain unclear. This systematic review evaluates nutritional interventions' safety and efficacy on muscle disease outcomes.
Methods. A multidisciplinary team conducted a PRISMA-guided systematic review registered on Prospero. Database searches yielded 107 full-text articles, with 52 meeting inclusion criteria after screening. Four reviewers assessed bias risk, with team review for appropriateness.
Results. For inflammatory myopathies, investigations primarily centered on creatine supplementation and branched-chain amino acids. The most notable finding demonstrated that creatine supplementation combined with exercise significantly improved aggregate functional performance time in patients with polymyositis and dermatomyositis, with a median decrease of 13% compared to only 3% in the placebo group (p=0.029) (1).
Studies involving congenital muscle disorders and muscular dystrophies examined a wider spectrum of interventions, including various dietary patterns, specific nutrients, supplements, and antioxidants. These studies assessed diverse outcomes from muscle strength and exercise capacity to body composition, functional tests, and quality of life measurements. Several interventions showed promising results, particularly creatine supplementation in Duchenne muscular dystrophy, which increased maximal voluntary contraction by 15% and doubled fatigue resistance ($p<0.05$) (2). Additionally, ketogenic diets demonstrated improvement in fatty acid oxidation by 60% and increased maximal exercise capacity by approximately 20% in patients with McArdle disease (3).
In critical illness myopathy, research investigating beta-hydroxy-beta-methylbutyrate (HMB)-enriched whey protein supplementation and high-protein dietary interventions generally showed positive trends in outcomes. However, several results did not reach statistical significance, highlighting the need for more robust studies.
Quality assessment revealed varying methodological rigor, with 32% of studies classified as low risk of bias, 45% raising some concerns, and 22% at high risk of bias, underscoring the need for more rigorously designed trials.
Conclusions. While nutrition therapy benefits other medical fields, evidence for muscle diseases remains limited. Promising interventions include physiologic creatine, high-protein diets, ketogenic diets, and supplements (coenzyme Q10, resveratrol, L-carnitine), which improved endurance and strength in some populations. Methodological concerns highlight the need for larger, better-designed multicenter trials with standardized outcomes. More research exists on non-inflammatory versus inflammatory myopathies. Given these uncertainties, dietary guidance should be tailored to specific disease features and comorbidities.
Figures: https://tinyurl.com/3ckbse3x
Key words: muscle diseases, nutritional interventions, creatine supplementation, inflammatory myopathies, muscular dystrophies, systematic review

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OP-359

CONCOMITANT INTRAVENOUS IMMUNOGLOBULIN AND ANIFROLUMAB IN LUPUS AND DERMATOMYOSITIS PATIENTS: REAL-WORLD DATA FROM A RETROSPECTIVE COHORT STUDY

Kathryn Rentfro[*1], Leila Shayegan[*2], Nikki Zangenah[1], Yoo Jung Kim[3], Joshua Prenner[1], Marissa Camillucci[1], Joseph Merola[4], Neda Shahriari[1], Ruth Ann Vleugels[1]
[*]Co-first authors
[1]Department of Dermatology, Brigham and Women's Hospital, Boston, USA, [2]Department of Dermatology, Lahey Hospital and Medical Center, Boston, USA, [3]Department of Dermatology, Mayo Clinic, Rochester, USA, [4]Department of Dermatology and Department of Medicine, UT Southwestern Medical Center, Dallas, USA

Background. Anifrolumab, a monthly infusion FDA-approved for systemic lupus erythematosus (SLE), is increasingly being utilized for cutaneous LE (CLE) and dermatomyositis (DM). Intravenous immunoglobulin (IVIG) is another infusion therapy used for these conditions, with several cases reporting patient improvement on concomitant treatment. However, the timing of IVIG (typically administered every 2 or 4 weeks) with respect to anifrolumab remains to be addressed.
Methods. We conducted a retrospective chart review of 9 patients who received anifrolumab and concomitant IVIG and examined real-world anifrolumab and IVIG administration to identify patterns in timing, associated adverse effects, and treatment response
Results. In a cohort of 80 patients receiving anifrolumab at two U.S.-based academic medical centers between January 2022 and April 2025, 9 patients received concomitant IVIG. Of these 9 patients, 89% were female with a mean age of 39 years. Indication for anifrolumab treatment was most commonly CLE (55%), followed by DM (33%), and SLE/systemic sclerosis overlap (11%). Six patients received IVIG every 4 weeks, while 3 received it every 2 weeks. IVIG timing after anifrolumab infusion was variable, ranging from the same day to 25 days later. IVIG was discontinued in one patient due to difficulty coordinating infusions, two were discontinued due to disease improvement, and another was discontinued due to a pulmonary embolism. The most common adverse effect of IVIG was headache in 6 patients (66%), all of whom had experienced these before starting anifrolumab. 8 of 9 patients experienced improvement in their skin disease. One patient reported worsening of headaches during the first IVIG infusion post-anifrolumab initiation (separated by 25 days), which did not recur on subsequent infusions. Rates of discontinuation of anifrolumab among patients on both IVIG and anifrolumab did not differ significantly from those on anifrolumab alone (33% *vs*. 32%).
Conclusions. This limited cohort indicates that in patients on both IVIG and anifrolumab, the relative timing of infusions varies widely but may not significantly impact adverse effects or efficacy.
Key words: anifrolumab, IVIG, dermatomyositis

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