XV. Mediterranean Congress of Rheumatology (MCR)

28-31 August 2014 – Istanbul, Turkey

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Abstracts

Oral Abstracts S-1–S-22

S-01

Impact of Disease Activity, Obesity and Depression on Lipid Status, Glycoregulation and Risk for Coronary Heart Disease in Patients with Rheumatoid Arthritis

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Background. The risk for cardiovascular disease is increased in rheumatoid arthritis (RA). Assessments based only on traditional risk factors are insufficient to capture the extent of cardiovascular risk in RA.
Objective. This study aims to estimate the impact of disease activity, obesity and depression on lipid status, glycoregulation and risk for coronary heart disease (CHD) in patients with RA.
Patients and Methods. Thirty six patients with RA (30 women and 6 men), mean age 54.9 years and mean disease duration 7.9 years, were included in this study. We estimated the impact of age, disease duration, body mass index (BMI), disease activity (assessed by DAS28 index and CRP value), functional ability (estimated using the HAQ disability index) and depression (assessed using the Beck's depression inventory-BDI) on glycoregulation, lipid status and risk for CHD. Glycoregulation was assessed by measuring insulin resistance, insulin and glucose in the blood. Lipids tested in the blood included total cholesterol, HDL- and LDL- cholesterol and triglycerides. Ten year risk for CHD was estimated using the Framingham risk score.
Results. Patients with high disease activity (DAS28>5.1) had lower HDL-cholesterol values than patients with mild or moderate disease activity (1.68 vs 1.35 mmol/l, p=0.04). Moreover, there was a statistically significant negative correlation between these two parameters (ϱ=-0.40, p=0.04). BMI correlated significantly with total cholesterol (r=0.46, p=0.02), LDL-cholesterol (ϱ=0.41, p=0.04) and triglycerides (ϱ=0.65, p<0.001) in the blood. Obese (BMI>=30) and overweight patients (25<BMI<30) had higher triglyceride values in the blood (p<0.05) compared to patients with normal BMI (2.3 and 1.9 vs 1.1 mmol/l, respectively). The BDI depression index correlated significantly with triglyceride value in the blood (ϱ=0.65, p=0.001). Other factors assessed in this study (age, disease duration, CRP and HAQ index) do not have impact on lipid status. We have noticed a significant correlation between CRP and insulin resistance (ϱ=0.57, p=0.003), and insulin resistance with glycaemia (ϱ=0.59, p=0.002) and function of beta-cells (ϱ=0.41, p=0.03). 11/36 (30.6%) of patients fulfilled criteria for metabolic syndrome (MS). 10/11 (90.1%) of patients with MS have a 10 year risk for CHD higher than 10%, compared to only 3/25 (12%) of patients without MS (p=0.0001).
Conclusion. Patients with RA and MS have a much greater risk for CHD than patients without MS. Higher disease activity is associated with increased insulin resistance and low level of HDL-cholesterol in the blood. On the other hand, depression and obesity are associated with higher values of total cholesterol, LDL-cholesterol and triglycerides. To reduce the overall cardiovascular risk in patients with RA, not only disease activity should be treated, but also obesity and depression.
Keywords. Rheumatoid arthritis, lipid status, glycoregulation, coronary heart disease.

S-02

Post-Menopausal Osteoporosis Risk Factors in a Mediterranean Population

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Rational osteoporosis affects 30% of postmenopausal women. It is essential to detect it in those subjects in order to treat them then to reduce the morbidity and mortality due to subsequent fractures.
The way to depict this condition is to perform a measurement of the bone mineral density (BMD) not in all women but in those with risk factors.
These risk factors vary from a population to an another because of the influence of genetics and environment.
The objective of this study is to determine post-menopausal osteoporosis risk factors in Algerian women.
Patients and Methods. This is a case-control study carried out in a 100.000 inhabitant town near Algiers.
Inclusion criteria: postmenopausal women for at least 2 years.
Non-inclusion criteria: other bone disease women taking an anti- osteoporotic drug impossibility to measure BMD subjects where randomly selected and invited to our bone unit where a questionnaire including risk factors was filled for each women and a BMD at the spine and hip (Hologic QDR 4500) was performed.
Subjects were classified as normal, osteopenic or osteoporotic according to WHO classification. The analysis consisted in a multivariate logistic regression to create a model which is a composite score. SPSS 13.0 was used for the statistical analysis.
Results. One Thousand two hundred and fifty five (1255) women were recruited. Their main characteristics are: age = 61.7±9.2, BMI = 27.5±5.2, average number of pregnancies = 6.4±3.9, age at menopause = 47.0±5.1, personal history fracture = 23.3%, family history of fracture = 05.30 %, tobacco intake = 2 women.
BMD Results: Normal = 292 (23.27%), osteopenia = 418 (33.30%) and Osteoporosis = 545 (43.43%). in uni- variate analysis 11 factors were statistically significant but only 5 factors remained significant in multivariate analysis: age, weight, body mass index, duration of menopause and personal history of fracture. Osteoarthritis seemed to be protective against the disease.
Discussion. This study of 1,255 subjects gave a minimal probability of error, the factors found to be significant are enough precise (power of the study >95%). risk Factors can be summarized in three main parameters: the duration of menopause >13 years, weight <62 kg and personal history fracture. The duration of menopause takes into account both the age and the age at menopause. the impact of the presence of a past history of fragility fracture is as well important. thinness is one of the most often found is in the literature but with different weight cut-off values. Secondary osteoporosis were excluded from this study because they should lead to screening easily.
Conclusion. The sample size offers a high power that gives an important significance for three factors: duration of menopause, low weight and personal history of fracture, these three factors appear to be in the most important determinants of bone mass population and may provide a basis for prevention.
Keywords. osteoporosis, risk factors, screening.

S-03

Survival on Treatment with Second-Third Biologic Therapy: Switching vs Swapping

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Background. The development of biological agents has significantly improved the management of Rheumatoid Arthritis. Anti-TNF drugs have been routinely used as first-line biotherapy for the treatment of RA patients who have failed DMARDs, in according to more recent international recommendations, Management of the first anti-TNF drugs failure may involve switching to a second anti-TNF or swapping of an alternative class of target agents with a different mechanism of action (MoA), but actually the optimal treatment approach has not yet defined.
Objective. The aim of this study was to evaluate the survival on treatment with second and third line biologic therapy in RA patient non responders to anti-TNF drugs by comparing treatments with a second or third anti-TNF or with agents with a different mechanism of action (MoA).
Methods. We evaluated 325 RA patients treated with biologics who stopped a first-line anti-TNF and started a second or third line biotherapy were included in this cohort of study. After adjusting for propensity scores, drug retention rates were calculated using the Kaplan-Meier method. The log-rank test was used to compare survival curves and hazard ratio was used to compare risk for discontinuation between two groups.
Results. 68 patients discontinued the first anti-TNF, switching to a second anti-TNF (n = 36 - 52,94%) or to abatacept (n = 18 – 26,47%), rituximab (n = 5 – 7,35%) or tocilizumab (n = 9 – 13,23%). Drug survival was not significantly different in two groups (p<0,27).
34 patients discontinued the second anti-TNF or MoA, switching to a third anti-TNF (n =14 – 41,18%) or to abatacept (n = 10 29,41%), rituximab (n = 4 – 11,76%) or tocilizumab (n = 6 – 17,65%). Drug survival was significantly higher in the swap group (p<0,029).
Etanercept retention rate (second line 84%, third line 80%) was significantly higher in the switching group, while in the swap group seems emerged a trend in favour to Abatacept (second line 83,33% - third line 80%) and Rituximab (second line 100% - third line 75%), even if we have few cases for the latter.

Conclusions. In the clinical practice, the best option for managing anti-TNF non-responders seems to be swapping to a different MoA, even if it is not completely clear. We consider that's important to focus on the search for specific biomarkers that can identify the most appropriate therapy for a particular type of patient.
Keywords. Rheumatoid arthritis, switch, swap, anti-TNF, management.

S-04

Administration of Multi-Epitope Citrullinated Peptide Attenuates Adjuvant Induced Arthritis in Rats via Induction of Immune Tolerance

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Background/Purpose. Antigen-induced peripheral tolerance is a potentially efficient and specific therapeutic approach to attenuate autoimmunity. Citrullinated peptides are major targets of disease-specific autoantibodies in Rheumatoid Arthritis (RA). Currently, citrullinated peptides serve primarily as biomarkers for the diagnosis of RA by measuring titers of anti-citrullinated protein antibodies. In an attempt to develop a citrullinated peptides-based specific immunotherapy for RA, we previously showed the potential of two citrullinated peptides (citrullinated-filaggrin and citrullinated-β-fibrinogen) to up-regulate TGF-β mRNA expression and concomitant expansion of regulatory T cell population. In addition, our citrullinated peptides reduced the expression of inflammatory cytokines (INF-γ, TNF-α and IL-17), reduced the percentage of pathogenic IL-17+ cells and increased the apoptosis rate of T cells following incubation with RA-derived peripheral blood mononuclear cells (PBMC). In view of the multiplicity of citrullinated target autoantigens in RA we tailored a multi-epitope citrullinated peptide (Cit-ME) derived from major prevalent citrullinated autoantigens (citrullinated filaggrin, fibrinogen, vimentin and collagen type II). The later was tested for treatment of adjuvant induced arthritis (AIA) via immune tolerance induction by attenuating the disease manifestations.
Methods. Seven days following induction of AIA in Lewis female rats we administrated Cit-ME (300μg/rat) by 8 subcutaneous injections given on alternate days. Clinical scoring was performed once a week during the experiment. At the end of the experiment rats spleens were analyzed for apoptosis of $CD4^+$ T cells by flow cytometer.
Results. Treatment with Cit-ME ameliorated the clinical score of the diseased arthritic rats.
Rats treated with the Cit-ME had significantly less arthritic symptoms compared to untreated rats at day 21 (Figure 1). Amelioration of disease manifestations was associated with increased apoptosis rate of T cells.
Conclusions. We demonstrated that citrullinated peptides induced immune tolerance in an experimental model of AIA.
Keywords. Rheumatoid Arthritis, ACPA, Citrullination, adjuvant arthritis

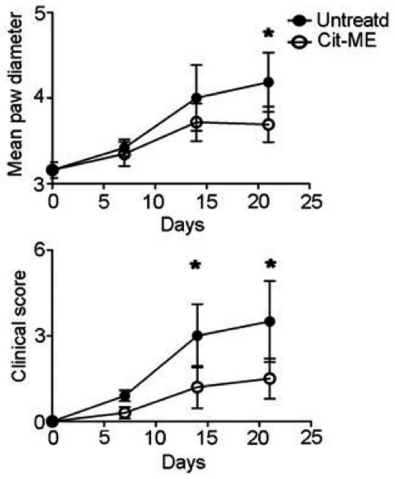

Fig. 1. Treatment with Cit-ME suppressed Adjuvant induced arthritis (AIA) clinical score in Lewis rats.

S-05

Evidence of Increased Expression and Function of NLRP3 Inflammasome in Rheumatoid Arthritis Patients

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Background. Interleukin-1β (IL-1β) is a major inflammatory cytokine, produced mainly upon NLRP3-inflammasome activation, expressed in cells of the innate immune system. Both intrinsic and extrinsic danger signals may activate NLRP3. Genetic variation of NLRP3-inflamassome components has been reported to influence rheumatoid arthritis susceptibility and severity.
Objective. To assess expression and function of NLRP3-inflammasome in patients with rheumatoid arthritis.
Methods. NLRP3-inflammasome related proteins (NLRP3, ASC, pro- and active caspase-1, pro- and active IL1β) intracellular expression at baseline and upon inflammasome activation was assessed by Western blotting. NLRP3 function (IL-1β secretion) was assessed upon stimulation of TLR2 (Pam(3)CysSK(4) or TLR3 (poly(I:C)) or TLR4 (LPS) and ATP sequential treatment for optimal NLRP3 activation. We also applied different caspases (casp-1, 3/7 & 8) inhibitors to assess their importance in IL-1β maturation. All the above experiments were performed in whole blood assays.
Results. Active RA patients (n=11) expressed higher intracellular levels of NLRP3 (p<0.008), ASC (p<0.003), active caspase-1 (p<0.02) and pro-IL1β (p<0.0001) while they expressed lower levels of active IL-1β (p<0.001) compared to controls. Accordingly, upon stimulation with LPS and ATP, RA-derived cell extracts (n=7) showed increased expression of NLRP3 (p<0.01) and active casp-1 (p<0.001), but comparable IL-1β. Secreted IL-1β in cultured supernatants upon TLR4 (LPS) or TLR3 agonist (poly(I:C)) and ATP sequential activation was higher in RA (n=20) versus controls (n=18) (p<0.02 for both) while TLR2 (Pam(3)CysSK(4) and ATP sequential activation resulted in comparable IL-1β secretion. Inhibition of casp-1, casp3/7 and casp-8 upon stimulation with the above triggers (TLRs and ATP), resulted in significant and comparable reduction in IL-1β secretion.
Conclusion. We found evidence of higher expression, activation of NLRP3 and eventually IL-1β secretion in rheumatoid arthritis patients, upon stimulation via TLR3 and TLR4 but not TLR2. Moreover, casp-1 but also casp-3/7 and casp-8 seems to be important in IL-1β production. These data support that targeting NLRP3 or different caspases could be of therapeutic benefit in down regulating IL-1β production in RA.
Keywords. NLRP3, inflammasome, rheumatoid arthritis.

S-06

The Characteristic Findings of Sacroiliitis Using Magnetic Resonance Imaging in Patients with Axial Spondylarthritis and Brucellosis

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Background. Axial spondylarthritis (AxSpA) is a chronic inflammatory disease affecting primarily the axial skeleton. Musculoskeletal involvement is seen as the most frequent complication of brucellosis in countries where the disease is endemic. The most commonly affected site is the sacroiliac joint. The main forms of this involvement are sacroiliitis that is important in view of the associated functional disability. In areas where brucellosis is endemic, the differential diagnosis of AxSpA and brucella is quite difficult in case of the presence of sacroiliitis especially when brucellosis and AxSpA occur at the same time. Magnetic resonance imaging (MRI) has proved especially useful for identification of sacroiliitis.
Objectives. The aim of the study was to determine the characteristic findings of sacroiliitis using by MRI in patients with AxSpA and brucellosis with sacroiliitis.
Methods. Fourteen patients with AxSpA and 13 patients with brucellosis were enrolled in the study. All the patients were examined by MRI. T1 pre-gadolinium and post-gadolinium and short tau inversion recovery (STIR) MRI sequences were performed.
Results. Unilateral sacroiliitis and soft tissue involvement were more frequent in brucellosis group than in AxSpA group. But, bilateral sacroiliitis was signifi-

cantly frequent in the patient with AxSpA. There was an abscess in only one of brucella patients. Moreover, chronic inflammatory lesions including sclerosis, erosions, fat deposition, and ankylosis were less frequent in patients with brucellosis than in AxSpA group (Table I). However, there was no significant difference between the AxSpA and brucellosis groups in terms of the presence of capsulitis, synovitis, enthesitis and fluid in the joint space (for all, $p>0.05$)

Conclusions. Unilateral sacroiliitis, soft tissue involvement, and abscess formation can be accepted as distinguishing MRI features of sacroiliitis of brucella. On the other hand, bilateral sacroiliitis and chronic inflammatory lesions including sclerosis and may be helpful in distinguishing AxSpA from brucellosis. MRI is a useful diagnostic modality in the differential diagnosis of sacroiliitis.

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Keywords. sacroiliitis, axial spondylarthritis, brucellosis.

Table I. MRI findings in the study groups.

	AxSpA (n=14)	Brucellosis (n=13)	*p*
Unilateral sacroiliitis, n(%)	4 (28.6)	11 (84.6)	0.003
Bilateral sacroiliitis, n(%)	10 (71.4)	2 (15.3)	0.003
Capsulitis, n(%)	5 (35.7)	5 (38.5)	>0.05
Synovitis, n(%)	9 (64.3)	9 (69.2)	>0.05
Effusion in joint space, n (%)	6 (42.9)	3 (23)	>0.05
Enthesitis, n(%)	6 (42.9)	6 (46.1)	>0.05
Sclerosis, n(%)	12 (85.7)	2 (15.4)	<0.001
Erosions, n(%)	10 (71.4)	1 (7.6)	0.001
Fat deposition, n(%)	11 (78.5)	1 (7.6)	<0.001
Bony bridges /ankylosis, n(%)	4 (28.6)	0 (0)	0.037
Joint space narrowing, n(%)	7 (50)	3 (23.1)	>0.05
Soft tissue involvement, n(%)	0 (0)	3 (23.1)	0.047
Abscess, n(%)	0 (0)	1 (7.6)	>0.05

S-07

Antı-Interleukın-1 Treatment In 19 Patıents with Famılıal Mediterranean Fever

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Background. Familial Mediterranean Fever (FMF) is the most common hereditary periodic fever syndrome. It has a quite heterogeneous patient profile with different clinical, epidemiological and genetic features. Colchicine, which is standardly used to control attacks and prevent amyloidosis, has a treatment failure in 5 to 10 % of patients and cannot be tolerated in 2-5 %. Interleukin-1 (IL-1) receptor antagonists (anakinra & canakinumab), which is the key enzyme converting pro-IL-1 to IL-1, are all the challenging molecules that inhibit the very specific pathogenetic pathway in patients resistant or intolerant to colchicine therapy.

Objective. We are report the effect of anti-interleukin1(IL-1) treatment in 19 cases resistant to or inability to tolerate in colchicine therapy.

Methods: We describe 19 patient followed up in our center. Clinical response was monitored through the number of attacks, whereas laboratory inflammation was monitored through erythrocyte sedimentation rate, C-reactive protein (CRP),and serum amyloid A (SAA) concentrations. Colchicine resistance was defined as at least 2 attacks/month along with CRP and SAA levels above normal range between attacks. The colchicine dose was increased to 2mg/day before they were considered colchicine-resistant.

Results. 19 of our FMF patients, using colchicine 4 months to 26 years, switched to anti-IL-1 treatment, 12 with resistance to colchicine, 1 with asthenozoospermia with colchicine, 3 with recurrent toxic hepatitis with colchicine, 2 with gastrointestinal intolerance and 1 with prolonged arthritis under colchicine. 17 patients used anakinra, 100 mg/day, and 2 used canakinumab, 150 mg/month, 2,5 to 19 months. 10 patients with colchicine resistance had no attack under anti-IL-1 treatment and 2 had decreased frequency and duration of attacks. 5 of 6 patients with intolerant to colchicine or who had side effects used anakinra, and all were attack-free under treatment, 1 using canakinumab had decreased frequency and duration of attacks. 1 patient with prolonged arthritis used canakinumab but arthritis showed progression and treatment switched to IL-6 inhibitor. 3 patients had injection site erythema and 1 had fatigue with anti-IL-1 treatment. Topical steroids with systemic antihistaminics were enough for symptom control in 2, but one switched to canakinumab treatment due to severe injection site erythema.

Conclusion. As a result, anti-IL-1 agents are rational treatment modalities in patients resistant or intolerant to colchicine. Anti-IL-1 agents can control FMF attacks quite effectively and they reveal a promising role in the treatment of FMF.

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Keywords. Familial Mediterranean Fever, Colchicine resistance, Antı Interleukın-1 Treatment.

S-09

Hellenic Registry for Biologic Therapies

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The Hellenic Registry for Biologic Therapies was founded in 2004 as an independent organization under the auspices of the Hellenic Rheumatology Society. Both University and state hospitals (8 in total) from Athens and four other major cities (Thessaloniki, Iraklio, Ioannina, Kavala) take part in this project. It is a prospective registration of all patients receiving biologic agents in their Rheumatology departments. The aim is to assess the long-term effectiveness and safety profile of these therapies. We collaborate with the University of Lund in Sweden (South Swedish Arthritis Treatment Group- SSATG). The center for data entry and analysis is at the University Hospital of Heraklion-Crete. Funding is through unrestricted grants from pharma industry.

Data are collected prospectively from all patients starting a biologic agent for inflammatory arthritis, most often rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and undifferentiated spondyloarthropathy (USp) but also for other less common diagnoses (juvenile chronic arthritis, Adult still's disease, enteropathic arthritis, Adamantiades-Behcet's disease, etc).

In this prospective study a standardized evaluation protocol is used according to which, data collection starts at baseline, every 6 months for the first 2 years of therapy and every year thereafter. DAS28, HAQ, ESR, CRP and EuroQol are registered in each of these timepoints. Additionally, all adverse events are recorded in every visit and are registered separately. They are graded as serious/life-threatening, moderate, or mild according to ICH (International Conference on Harmonization). If a biologic therapy is discontinued, the time and the reasons for discontinuation are registered.

Until March 2014, 2306 patients were included in the Registry: 1337 with a diagnosis of RA, 474 with AS, 305 PsA, 49 with USp and 141 with other diagnoses. These patients have received a total of 3536 biologic therapies: 1323 received Infliximab, 711 Adalimumab, 689 Etanercept, 255 Abatacept, 227 Rituximab, 174 Tocilizumab, 72 Anakinra, 70 Golimumab and 15 certolizumab pegol. The total follow up time for all the biologic cohorts in the Registry was 12802 years, while the mean follow-up time was 3.62 patient-years.

The total number of adverse events which occurred during this time was 5202, of which, 35 were lethal, 696 were graded serious or life threatening, 2230 moderate and 2241 were mild events. In 450 cases, these adverse events led to therapy discontinuation.

Results of this prospective study have been published recently (Semin Arthritis Rheum. 2014 Feb;43(4):447-57) and 14 presentations, 5 in Greek and 9 in International congresses.

Most of our results concern RA patients under anti-TNF-α therapy. In specific, it has been shown that disease activity is high in Greek patients starting anti-TNF-α agents (mean DAS28: 5.9) and biologic therapy leads to significant improvement (EULAR good and moderate response) in 72-78% of patients after one year. Response rates were comparable among anti-TNF agents. However, remission rates are low in clinical practice (10% according to ACR criteria after 12 months).

Drug retention rates were found to decline significantly after the third year of anti-TNF-α therapy and overall 5-year drug survival was below 50%, with infliximab demonstrating increased safety-related discontinuations compared with adalimumab and etanercept.

Factors predicting response to therapy and drug discontinuation were specified, while it was found that both response and survival of the 2nd anti-TNF-α agent are significantly lower than those of the first agent.

Regarding AS and PsA, improvement in disease activity with anti-TNF-α therapy is much more significant than that of RA (62% of AS patients have BASDAI50% improvement in the first 12 months) and drug survival is also higher (67% after 3 years of therapy).

S-10

Correlation of Different Disease Activity Indices During 24 Months Follow Up of 898 Patients with Rheumatoid Arthritis – Data from Serbian RA Registry

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Background. The three most commonly used indices of disease activity in rheumatoid arthritis (RA) are standard 28-joint Disease Activity Score (DAS28), Clinical Disease Activity Index (CDAI) and Simple Disease Activity Index (SDAI). Data about correlation of these indices during the follow up of patients with RA are insufficient.
Objectives. To evaluate the level of similarity between SDAI, CDAI, DASESR and DAS28CRP indices in the evaluation of disease activity in patients with RA.
Methods. Data from National registry of patients with rheumatoid arthritis in Serbia (NARRAS) were used. A total of 898 patients who fulfilled the ACR 87 criteria for the classification of RA, were followed up for a period of 24 months. The correlation between the DAS 28 (ESR), DAS 28 (CRP), SDAI and CDAI was assessed by the Pearson's correlation coefficient (r). The similarity between these composite indices was evaluated by Kendall's (K) „tau" similarity coefficient.
Results. The 742 female and 156 male (sex ratio 4.8F/1M) patents with RA, mean age 60.36±11.45 years (22-87), had RA for 13.66±8.32 years (2-43) at the beginning of the follow up period of 24 months. DAS28-ESR mean score was 5.59±1.37 [1.8-9.1]; DAS28-CRP mean score was 5.12±1.37 [1.3-8.8]; CDAI mean score was 26.42±14.79 [1.0-73.0] and SDAI mean score was 51.49±15.65 [2.0-96.3]. A positive, statistically significant correlation was noted between different indices of RA activity. The level of similarity between the different indices was good (K variation between 0.654 and 0.885). DAS28-ESR and DAS28-CRP classified 83% of patients in the same category of disease activity. DAS28-CRP and CDAI classified 79% of patients in the same category and DAS28-CRP and SDAI classified 83% of patients in the same category. Finally, CDAI and SDAI showed high level of similarity classifying 89% of patients in the same category.
Conclusion. CDAI and SDAI had good level of similarity with DAS28 during the follow up of 898 patients with RA. Similarity between SDAI and CDAI was high (89%).
Keywords. Rheumatoid arthritis, disease activity, DAS28, CDAI, SDAI

S-11

The Comparative One-Year Drug Survival Rate of Tumor Necrosis Factor Inhibitors in Patients with Rheumatoid Arthritis and Ankylosing Spondylitis; Results from Turkbio Registry

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Background. Three different anti–tumor necrosis factor α (anti-TNF-α) drugs (infliximab, etanercept, and adalimumab) are approved for patients with rheumatoid arthritis (RA) and particular ankylosing spondylitis (AS) in Turkey. Their efficacy has been well shown not only in randomized controlled clinical trials, but also in clinical practice setting. Comparative drug survival analyses across different diagnoses have been published in few studies. No data is yet available for the Turkish population.
Objective. The primary goal of this study was to compare the 1-year drug retention rates of TNF inhibitors in patients with AS and RA who were enrolled in the Turkish biologic registry, TURKBIO.
Methods. TURKBIO biological registry, which was established in October 2011, is a nationwide biological registry contributed by 10 different centers across Turkey. As of December 2013, 3380 patients who are receiving biologic treatment for RA (n=1355, 40.1%) or AS (n=2025, 59.9%) were enrolled in the database. However this analysis includes only 789 patients, who initiated biologic treatment after the participation of the individual centers in TURKBIO. Demographic and clinical data including age, sex, disease type, disease duration, and previous or current treatment with DMARDs and biological drug durations are stored in the database.
Results. Of the 789 patients included in this analysis, 386 patients (48.9%) were being treated for RA and 403 patients (51.1%) for AS. There were significant differences between the two groups in regard with age, gender distribution, DMARD use at baseline and DMARD use at last visit (Table). Preference for individual anti-TNF agents were also different between the RA and AS patients; infliximab, etanercept and adalimumab were used by 11.7%, 28.2% and 25.1% of the RA patients, respectively and 26.3%, 32.8% and 32.8 of the AS patients, respectively. AS patients had a shorter diagnosis duration than the RA patients. One year drug survival for the first anti-TNF agent was 60.8% for RA, and 78.3% for AS (p=0.0007).
Conclusion. The proportion of AS patients treated with biologic agents in the TURKBIO registry was slightly higher than that of RA. These results also suggest that the drug survival rate of anti-TNF agents in AS patients seems to be higher than in RA. This finding may explain the higher percentage of AS patients in the whole registry population, which included patients who had started biologics before the establishment of the TURKBIO registry.
Keywords. ankylosing spondylitis, rheumatoid arthritis, tumor necrosis factor inhibitors, registry

Table. Demographical and clinical features of rheumatoid arthritis (RA) and ankylosing spondylitis (AS) patients at baseline and one year drug survival data.

	RA (n=386)	AS (n=403)	P value
Age (years)	49 (38-58)	39 (30-46)	<0.00001
Female (%)	73.1	41.7	P>0.05
Disease duration (years)	7 (3-13)	7 (3-13)	0.09
Diagnosis Duration	4 (2-10)	2 (0.75-6)	<0.00001
Biological duration (months)	9 (5-13)	10 (5-13)	P>0.05
Number of biologic drugs used	1	1	P>0.05
Prior DMARD use (%)	82.4	73.9	0.005
Number of DMARD use	4 (2-6)	2 (1-3)	<0.00001
DMARD use at last visit (%)	67.4	21.6	<0.00001
1-year drug retention rate of TNFi (%)	60.7	78.3	0.0007

Continuous data are given as median with interquartile ranges.

S-12

Protracted Febrile Myalgia of Familial Mediterranean Fever Can Be Reliably Detected by Magnetic Resonance Imaging: A Comprehensive Analysis of 20 Cases

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Background. Protracted febrile myalgia (PFM) is a rare and least well recognized manifestation of familial Mediterranean fever (FMF), characterized by prolonged excruciating muscle pain, tenderness, fever, and elevated levels of acute phase reactants. While the diagnosis of PFM in the setting of previously diagnosed FMF is mostly clinical, diagnosis of PFM when it is the sole manifestation of FMF might be challenging.
Aim. To analyse clinical, laboratory, genetic, electrophysiological, histopathologic, and magnetic resonance imaging (MRI) findings in a series of patients who presented to our department with myalgia and diagnosed as having PFM secondary to FMF.
Methods. We describe a retrospective cohort PFM patients seen at our department between 2009 and 2012. Clinical, laboratory, and imaging data were obtained by medical record review.
Results. Study group consisted of 20 (19 male, mean age = 20 years, SD = 3.2) patients. Four (20%) of the patients had a previous diagnosis of FMF, while PFM occurred as the presenting symptom of FMF in 40%. Mean age of disease onset was 17 ± 2.6 years, characterized by severe muscle pain in lower extremities in all patients and affecting single extremity in 90% of the cases. M694V allelic involvement was noted in 80% of the patients. Muscle enzymes were in normal range in all patients, and EMGs were normal in all studied patients (n=13), but one. None of the patients in whom muscle biopsy was available (n=8) showed features compatible with myositis. All of the patients underwent MRI of the symptomatic extremity and showed different degrees of involvement on the MR images of the affected extremities. On MR images, the muscle involvement was either patchy or diffuse, displayed with the high signal intensity on fluid sensitive and gadolinium-enhanced fat saturated T1-weighted images. Extension of the inflammation around individual muscles and muscle groups (myofascial distribution) was observed, as well as subcutaneous tissue edema.
Discussion.
This series of patients with PFM, to our knowledge, is the largest one reported

in the literature. PFM can be the initial manifestation of FMF in some of the patients. Due to the lack of any specific abnormalities other than elevated acute phase response, diagnosis of such cases possess some difficulties. With the appropriate clinical history, detection of MRI findings compatible with myositis in the absence of other features suggestive of myositis (muscle enzymes, EMG, etc.) can help make or confirm the diagnosis of PFM, particularly in areas where the FMF is prevalent.

Keywords. FMF, febrile myalgia, magnetic resonance imaging

S-13

Echosonography of Skin Fingers in Patients with Systemic Sclerosis

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Background. skin thickening caused by excessive collagen accumulation is major clinical characteristic of systemic sclerosis, (SSc). High resolution ultrasound examination is non-invasive imagine procedure able to measure skin thickness.
Aim. To assess differences in skin thickness of patients with SSc and healthy subject at the level intermediary (IMF) and distal phalanges (DF) of II and IV finger of both hands by high resolution ultrasound.
Method. The cross-sectional clinical study enrolled 32 pts who fulfilled ACR criteria for classification of SSc and 13 healthy individuals. Ultrasound examination was performed using ESAOTE My Lab 70 machine equipped with 8-18 MHz linear probe. Skin thickness and appearance of Power Doppler skin signal of the second (II) and fourth (IV) finger of both hands were analyzed separately. The data were statistically analyzed in the SPS system, (Student t test, Fisher exact test).
Results. twenty nine pts (29/32) were females, mean age of pts was 56.3±10.1 yrs. The mean duration of Raynaud's phenomenon was 97.9 months. Twenty three (71.9 %) pts had pulmonary fibrosis as systemic manifestations of SSc (Table I). Average skin thickness was 3.31 mm for the SSc pts and 2.82 mm for healthy subject. Skin of SSc pts was significantly thicker then skin of healthy individuals, (p=0.01, Student t test). Power Doppler signal was present in skin of 15 (46.9 %) SSc patients while none of healthy had positive Power Doppler skin signal, (p=0.004, Fisher exact test). There was no statistically significant difference in skin thickness between SSc pts with and without pulmonary fibrosis, (p=0.203).
Conclusion. High resolution ultrasound measurement showed significantly thicker skin of II and IV finger in patients with SSc than healthy subject. SSc pts with pulmonary fibrosis did not have significantly thicker skin in comparison to SSc pts without pulmonary fibrosis. Power Doppler skin signal was present in 47% of SSc pts and in none of healthy subject.

Keywords. systemic sclerosis, ultrasonography, skin.

Table I. Ultrasound measurement of skin thickness (mm).

	Skin thickness of right hand (mm)	Skin thickness of right hand (mm)	Skin thickness of left hand (mm)	Skin thickness of left hand (mm)
	2nd falang	4th falang	2nd falang	4th falang
SSc patients	3.43 ± 0.56	3.38 ± 0.67	3.28 ± 0.66	3.16 ± 0.63
Healthy subject	2.83 ± 0.42	2.98 ± 0.53	2.76 ± 0.51	2.72 ± 0.50

S-14

Prevalence of Psoriatic Arthritis in Psoriasis Patients Attending Dermatological and Rheumatological Clinics According to PEST (Psoriasis Epidemiology Screening Tool) and Caspar Criteria

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Objective. Prevalence study of psoriatic arthritis (PsA) in patients with psoriasis (PsO) attending dermatological and rheumatological clinics.
Methods. 80 patients (pts) (male-35/female-45) with PSO mean age of 43.06±1.71 years (yrs.), duration, BSA 5.83±1.63 %, PASI 5.05±1.23, DQLI 8.57±0.94 were included. All pts completed the PEST questionnaire before being consulted by either a dermatologist or rheumatologist with no known diagnosis of inflammatory arthritis, then afterwards having a complete rheumatological evaluation. A total score PEST>=3 is indicative of PsA, PEST<3 is non-PsA. CASPAR criteria is considered the "gold standard" for the diagnosis of PsA. M±m, frequency characteristic (%), Fisher test, Person's correlation coefficient (r) were performed. All p<0.05 were considered to indicate statistical significance.
Results. 53 out of 80 pts (66.3%) had PEST>=3 but after rheumatological evaluation and according to CASPAR criteria PsA confirmed in significantly fewer cases - in 40 out of 80 pts (50 %) (Fisher test, p<0.04). 27 out of 80 pts (33.8%) had PEST<3 but 13 out of 27 pts (48.1%) were diagnosed with PsA after rheumatological evaluation and according to CASPAR criteria. 30 out of 80 pts (38.1%) were newly diagnosed PsA. After rheumatological evaluation PsA was found in 53 out of 80 pts (63%). In 13 out of 80 pts (16.3%) in pts with PsO were found one of the following rheumatic diseases (RhD) - Dermatomyositis, Fibromyalgia, Osteoarthritis (OA), Ankylosing Spondylitis, Reactive Arthritis, Rheumatoid Arthritis (RA) and Gout. In 3 out of 80 pts (3.8%) association of PsA+Gout and PsA+RA, OA+Gout were found. In 15 out of 80 pts (18.8%) no RhD were found. Nail disease was found in 56 out of 80 pts (70%). In comparison a greater number of pts with nail disease were found in PsO+PsA than in PsO alone – in 40 out of 56 pts (82.1%)/in 13 out of 56 pts (23.2%) accordingly (Fisher test, p<0.023). No significant correlations were observed between presence of PsA and PSO severity - BSA, PASI and DQLI.
Conclusion. PsA was observed in most cases (63%) of PsO pts but in the lesser cases other RhD could be found even though PEST categorizes the disease as PsA. Therefore pts should be consulted by both a dermatologist and a rheumatologist for a proper diagnosis. In this way we were able to newly diagnose 38.1% PsA pts

Keywords. psoriatic arthritis, psoriasis, pest, dermatologist, rheumatologist.

S-16

Effects of Smoking in Patients with Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis Receiving TNF Inhibitors

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Background. Ankylosing spondylitis (AS) is a systemic disease characterized by sacroiliitis and inflammatory back pain. The radiological findings of AS appear late causing delay in diagnosis, therefore axial spondyloarthritis (axSpA) which includes AS and nonradiographic axSpA (nr-axSpA) have been defined.
Objectives. The objective of this study is to identify the potential impacts of smoking on disease activity markers, physical examination and laboratory findings in severe AS and nr-axSpA receiving anti-TNF therapy.
Methods. In this study, 211 patients treated with anti-TNF agents and diagnosed as axSpA (142 AS according to modified New York criteria and 69 nr-axSpA based on ASAS criteria) between 2000 and 2013 were included. Patients were evaluated retrospectively. Smoking intensity has been evaluated as per pack-year. Patients were separated into groups according to smoking habits and intensity. Acute phase reactants and functional indexes - ESR, CRP, BASMI, BASFI, BASDAI and ASQoL were compared between groups. Physical examination including Schober's test (ST), chest expansion (CE), fingertip-to-floor distance (FFD), tragus wall distance (TWD), lateral lumbar flexion (LLF), cervical rotation (CR), occiput-to-wall distance (OWD), inter-malleolar distance (IMD), chin- sternum distance (CSD) was performed.
Results. Based on comparison between smokers (n:121) and non-smokers (n:90), physical mobility indicators ST (p:0.03), FFD (p<0.001) and LLF (p:0.035) were found significantly more restricted in smokers and BASDAI (p:0.011) values were significantly improved after anti-TNF-α treatment in non-smokers. If smoking period is >20 years, LLF (p:0.004), CR (p:0.004), CE (p:0.005), OWD (p:0.021), TWD (p:0.001), IMD (p:0.015), BASFI (p:0.019) and BASMI (p<0.001) were significantly deteriorated. When effects of smoking were evaluated between AS (n:142) and nr-axSpA (n: 69) groups, significant restriction of ST (p:0.04) and FFD (p<0.001) in AS group within smokers, restriction of FFD (p:0.02), CR(p:0.04), OWD (p:0.02), TWD (p:0.003), CSD (p:0.02) and LLF (p:0.002) in AS group among smokers >10 years or more and significant restriction of ST (p:0.04), FFD (p<0.001), LLF (p:0.01) in AS group who had quit smoking compared to non-smokers were found. Among currently smoking patients (n:46) comparison between who smoke >20 pack-year (n:23) and who smoke <20 pack-year (n:46) showed significant deterioration of ST (p:0.007), CR (p:0.01), CE (p:0.002), TWD (p:0.01), IMM (p:0.007), BASFI (p:0.004), BASDAI (p:0.005), BASMI (p:0.005) and ASQoL (p:0.04) only in nr-axSpA group (Table I).

Table I.

TABLE1		AS (n:142)	NrAxSpA (n:69)
		Mean±SD	Mean±SD
ST (cm)	<20 pack-year	2.92± 2.07	5.16 ± 1.43
	>20 pack-year	2.59 ± 0.97	1.16 ± 1.60
	p	0.61	0.007*
CR (°)	<20 pack-year	56.79 ± 24.40	69.11 ± 18.72
	>20 pack-year	47.50 ± 25.01	46.66 ± 23.04
	p	0.23	0.01*
CE (cm)	<20 pack-year	2.80 ± 1.95	4.17 ± 1.48
	>20 pack-year	2.32 ± 1.58	2.05 ± 1.37
	p	0.40	0.002*
TWD (cm)	<20 pack-year	18.0 ± 8.39	12.85 ± 5.33
	>20 pack-year	19.42 ± 4.86	20.44 ± 9.48
	p	0.55	0.01*
IMD (cm)	<20 pack-year	87.43 ± 25.78	99.30 ± 15.00
	>20 pack-year	87.57 ± 19.41	88.44 ± 17.04
	p	0.98	0.007*
BASFI	<20 pack-year	2.81 ± 2.29	1.78 ± 2.05
	>20 pack-year	3.30 ± 2.39	4.36 ± 1.88
	p	0.49	0.004*
BASDAI	<20 pack-year	3.27 ± 2.08	2.62 ± 2.08
	>20 pack-year	4.32 ± 2.85	4.60 ± 1.87
	p	0.15	0.02*
BASMI	<20 pack-year	3.79 ± 2.62	1.76 ± 1.98
	>20 pack-year	4.71 ± 1.85	4.44 ± 2.24
	p	0.23	0.005*
ASQoL	<20 pack-year	5.73 ± 4.53	4.29 ± 4.55
	>20 pack-year	8.35 ± 4.82	8.33 ± 447
	p	0.07	0.04*

Conclusions. Our study showed that smoking and especially heavy smoking had negative effects on all stages of axSpA. In nr-axSpA, considered as early axSpA, to quit smoking would be more important for significant differences were seen in spinal mobility, functional situation, disease activity and quality of life in this group of patients.
Keywords. Axial spondyloarthritis, Tumor necrosis factor-alpha, smoking.

S-17

Short Term Efficacy of Tumor Necrosis Factor Inhibitors in Patients with Non-Radiographic Axial Spondylarthritis and Ankylosing Spondylitis; Results From TURKBIO Registry

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Background. Axial spondylarthritis (AxSpA) has been proposed as an umbrella term for ankylosing spondylitis (AS) and non-radiographic (nr) AxSpA). This new concept makes diagnosis of AS possible at an early stage in the absence of radiographic sacroiliitis. Disease burden in AxSpA patients with or without radiographic sacroiliitis have been shown to be similar in different cohorts, which suggest that both diseases should be treated with the same approach. Recent randomized clinical trials showed that TNF inhibitors (TNFi) are effective also in treating signs and symptoms of nr-AxSpA. However, the efficacy of anti-TNF agents in patients with nr-AxSpA remains to be shown in daily rheumatology practice.
Objectives. To compare the efficacy of TNF inhibitors in patients with AS and nr-AXSpA in daily clinical setting.
Methods. A total of 174 patients with AxSpA (107 M; 40.8±10.0) from two centers, who contribute to TURKBIO, a biological database in Turkey, and who could provide detailed data on imaging for patients with AxSpA, were included in this study. Of these patients 115 had AS according to the modified New York criteria, 59 patients fulfilled the ASAS classification criteria for AxSpA (78 % fulfilling the imaging arm).
Results. Baseline demographics and clinical characteristics are summarized in the table below. Patients with nr-AxSpA were significantly younger, had a shorter disease duration and had a higher female predominance than patients with AS. After treatment with TNF inhibitors mean BASDAI score decreased significantly from 6.15±1.76 at baseline to 3.28±2.1 at 3 months (p=0.049) in patients with nr-AxSpA; from 5.99±1.69 to 3.05±1.7 (p:0.008) in patients with AS and from 6.05±1.71 to 3.12±1.85 (p=0.001) in the whole group. Minimal clinical response (a decrease of 2 units in BASDAI) was observed in 63% of the patients with nr-AxSpA and in 68% of the patients with AS. Major clinical response (BASDAI 50) was achieved in 49% and 51% of the patients with nr-AxSpA and AS, respectively. Other efficacy measures such as ASAS20 and ASAS40 response were also similar in both groups, but could be performed in only a small number of patients due to missing data.
Conclusion. The results of our study suggest that TNFi, which have been clearly shown to be effective in treating signs and symptoms of AS, seem to be equally effective in the treatment of nr-AxSPA.
Keywords. Ankylosing spondylitis, non-radiographic axial spondylarthritis, TNF inhibitors, efficacy.

Table. Demographics and clinical characteristics of the AxSpA and AS patients.

	Non-radiographic axial spondylarthritis (n=59)	Ankylosing spondylitis (n:115)	p value
Age	36 (± 10)	43 (± 11)	p<0.001
Disease Duration (years)	8.05 (±7.6)	14.15 (±8.8)	p<0.001
Diagnosis Duration (years)	3.6(±2.9)	8.6 (±7.3)	p<0.001
Female (%)	55.9	29.5	p<0.001
Elevated CRP (%)	68	85	p:0.013
Elevated ESR (%)	56	71	p:0.056
HLA B27 positivity, n1/n2 (%)	19/29 (66)	24/34 (71)	p:0.666
Sacroiliitis by MRI n1/n2 (%)	46/49 (94)	-	
DMARD use at last visit (%)	36	28	
Biologic drugs used			
Infliximab (%)	14	32	
Etanercept (%)	39	39	
Adalimumab (%)	37	19	
Golimumab (%)	10	10	

S-18

BAFF-R His159Tyr Mutation in Sjögren's Syndrome and Sjögren's Related Lymphomagenesis

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Background/Objective. A cardinal feature of SS is B-cell hyperactivity, manifested by the presence of various autoantibodies with B-cell activating factor (BAFF), a survival factor for B-cells, being a central contributor. Among all autoimmune diseases, SS has the highest risk for development of non-Hodgkin's lymphoma. The etiology of lymphoma development in the setting of SS is poorly understood. Of interest, the mutation His159Tyr of the BAFF receptor (BAFF-R) was found to confer increased risk in patients with NHL through activation of the NF-kB pathway. The aim of the current study is to evaluate the prevalence of the BAFF-R His159Tyr mutation in SS compared to other autoimmune disease and healthy controls and to explore any associations with certain disease characteristic and SS related lymphoma.
Methods. The BAFF-R His159Tyr mutation was evaluated in 247 SS patients (177 SS patients without lymphoma and 70 SS-lymphoma patients), 145 systemic lupus erythematosus (SLE) patients, 101 rheumatoid arthritis (RA) patients and 180 healthy controls (HC), all of Greek ancestry, by PCR-RFLP and PCR-sequencing.
Results. A significantly increased prevalence of the His159Tyr BAFF-R mutation in SS patients compared to HC was observed [17 out of 247 (6.9%) vs 3 out of 180 (1.7%), p=0.01)]. Among autoimmune diseases SS also exhibited the higher prevalence of the mutation (6.9% in SS vs 3.5% in SLE and 3% in RA respectively, p-values>0.05 in both comparisons). Both SS subgroups exhibited significantly higher frequencies of the His159Tyr BAFF-R mutation compared to HC (SS-lymphoma 8.6% and SS-non lymphoma 6.2% vs 1.7%, OR (95% CI): 5.53(1.34-21.77), p=0.02 and OR (95% CI): 3.91(1.07-14.26, p=0.04, respectively).When we stratified the SS lymphoma patients according to the age of SS onset (>=40 or <40 years) one third of patients with MALT lymphoma in the latter group were found to carry the mutation (31.3 % vs 1.9%, p-value: 0.0002). Of interest an extremely high prevalence (71.4%) of the mutation was noted in SS MALT lymphoma patients with SS onset in the 4th decade. In SS non lymphoma patients the presence of the BAFF-R His159Tyr mutation was associated with higher prevalence of hypergammaglobulinemia and RF positivity compared to their counterparts without the mutation (100% vs 56.6, p=0.04 and 87.5% vs 46.9, p=0.03, respectively).
Conclusion. In the present report, we identified an increased prevalence of BAFF-R His159Tyr mutation in SS patients and particularly in the younger onset subgroup complicated by MALT lymphoma, in association with B-cell activation markers.
Keywords. BAFF-R, Sjögren's syndrome, Lymphomagenesis.

S-19

Microvascular Worsening Associates with 2013 ACR/EULAR Systemic Sclerosis Classification Criteria Fulfillment in Very Early Systemic Sclerosis (VEDOSS) Patients

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Background. Nailfold videocapillaroscopy (NVC) is considered an important diagnostic tool in systemic sclerosis (SSc) and also a useful outcome measure to monitor disease response to treatment (1).
Objectives. a retrospective description of microvascular alterations detected by NVC in very early systemic sclerosis patients (VEDOSS) (2); an evaluation of microvascular evolution in time; an assessment of the possible correlation between microvascular changes between visits and fulfillment of the new 2013 ACR/EULAR classification criteria for SSc (3).
Methods. from March 2010 to March 2014, 167 patients affected by Raynaud's phenomenon were followed in our centre. NVC was performed at baseline and follow-up, with giant capillaries, micro-haemorrhages, capillary loss and ramified capillaries being recorded according to the semiquantitative scoring (4), as follows: score 0 if alteration was absent; score 1 if present from 0% to 33%; score 2 if present from 33% to 66%; score 3 if was present over 66%. The sum of the scores given to the four parameters was compared between baseline and next follow-up visit: a decrease of the score of at least 2 points was considered as improved, and increase of at least two points as worsened, otherwise as stable general microvascular assessment. Patients were evaluated retrospectively with the new ACR/EULAR criteria for SSc classification either at baseline and at follow-up.
Results. The fulfillment of the VEDOSS criteria was associated with both the presence of giant capillaries and haemorrhages at baseline(p<0.01), but also a trend to association with worsening of microvascular alterations at follow-up. At baseline, 28 VEDOSS patients (38.3%) fulfilled the 2013 ACR/EULAR classification criteria for SSc and, at follow-up, this number increased to 33 patients (44.3%). There was a significant association between new fulfillment of the classification criteria and worsening of NVC features(p=0.003).
Conclusions. Our data show the association between NVC worsening and new fulfillment of new SSc classification criteria, confirming the role of NVC as a capable tool to identify disease evolution.

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Keywords. very early systemic sclerosis, 2013 ACR/EULAR classification criteria, Nailfold Videocapillaroscopy.

Table I. Prevalence and statistical analysis of microvascular alteration in the study population at baseline and follow-up NVC assessment.

		A-ANA + ACA/ATA positive (n=58)		B=ANA positive (n=38)		C=ANA negative (n=71)		A vs (B+C)			B vs (A+C)			C vs (A+B)			Patient classified as VEDOSS (n=73)				
		n	%	n	&	n	%	*p**	*p***	corr**	*p**	*p***	corr**	*p**	*p***	corr**	n	%	p*	p**	corr**
Follow-up	Giant Capillares	36	62	18	47	8	11	<0.01	<0.01	+0.446	0.07	0.47	-0.040	<0.01	<0.01	-0.405	54	74	<0.01	<0.01	+0.595
	Hemorrages	32	55	21	55	19	27	<0.01	<0.01	+0.340	<0.05	0.35	-0.051	<0.01	<0.01	-0.289	46	62	<0.01	<0.01	+o.408
	Capillary Loss	0	0	2	5	0	0	0.09	0.16	+0.075	0.185	0.75	+0.017	0.16	0.10	-0.090	1	1	0.84	0.84	+0.016
	Ramified/busty capillares	3	5	5	13	2	3	0.44	0.05	+0.094	>0.99	0.48	-0.039	>0.99	0.29	-0.058	5	7	0.35	0.35	0.075
Baseline	Improved NVC	5	16	9	24	6	8	0.83		0.14		0.08		16	22	0.28					
	Stable NVC	36	62	28	74	54	76	0.11		0.70		0.22		44	60	<0.05					
	Worsened NVC	13	22	1	2	11	16	0.07		0.26		<0.99		13	18	<0.05					

*Chi-square test with Fisher exact test when appropriate. **Pearson correlation test.

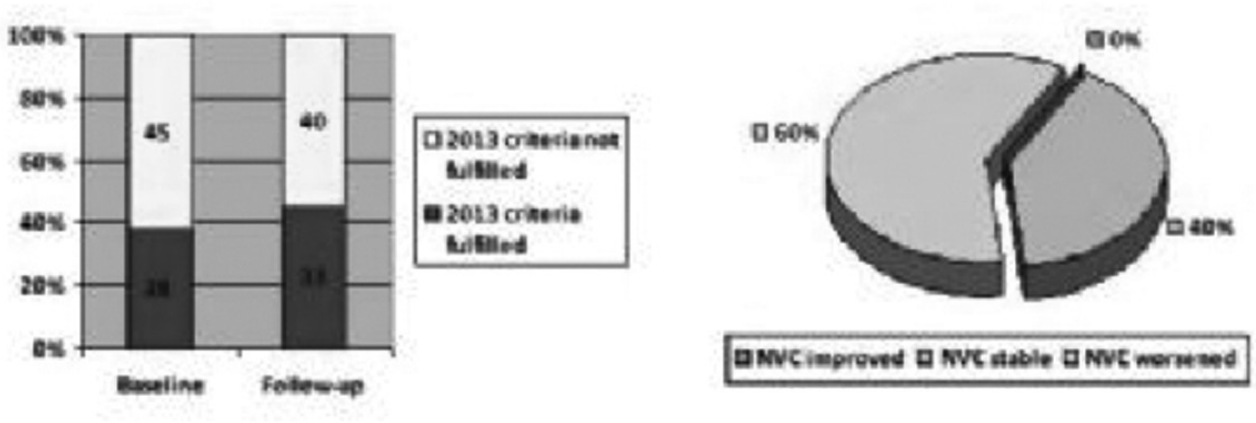

Fig. 1. Fulfillment of the 2013 ACR/EULAR criteria in the VEDOSS population study (A) and association with NVC.

S-20

Thrombospondin-1, An Antiangiogenic and Proapoptic Factor, Is Elevated in The Plasma of Patients with Antiphospholipid Syndrome and is Correlated with Soluble Fas Ligand and Free Active TGF-beta Levels

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Background. Antiphospholipid syndrome (APS) is an acquired thombophillia characterized by recurrent thromboembolism and pregnancy morbidity. Thrombospondin (TSP-1) is a matricellular glycoprotein secreted by platelets upon activation with antiangiogenic and proapoptotic properties. TSP-1 exerts its actions on endothelial cells through its receptors CD47 and CD36. TSP-1 moreover activates TGF-beta releasing it from the Latency Acossiated Peptide and has already been shown to induce apoptosis increasing the expression of Fas ligand on endothelial cell *in vitro* and in *vivo*.
Objectives. To investigate the involvement of Thrombospondin 1 in the Antiphospholipid syndrome.
Methods. The study involved 90 patients fulfilling the diagnostic criteria of APS, a healthy control (n=46) and a disease control group (SLE n=26). Plasma, serum and platelets were isolated from the above groups. Human Umbilical Vein Endothelial Cells were isolated from 3 patients with APS and 5 healthy donors and cultured with the presence of plasma from HC or APS patients. Plasma and platelet intracellular and cell culture supernatant TSP-1, soluble Fas ligand (sFas L) and active free TGF-β levels were determined using an ELISA.
Results. APS patients had higher plasma levels of TSP-1 than the healthy control group and the SLE patients (APS: mean 390.0 ng/ml intarquartile range 95.90-437.7 ng\ml versus HC: 185.3 [46.3-236.6 ng\ml], $p<0.0001$ and versus SLE: 153.0 [8.2-267.2 ng\ml], $p=0.029$). Moreover the plasma to intacellular levels ratio between APS and HC is not different suggesting not only platelet degranulation but overexpression as well. Patient plasma sFas L and free active TGF-β levels are highly correlated with TSP-1 (Spearman r=0,8785 and $p<0,0001$, Spearman r =0,6278 and $p=0,04$ respectively). Supernatants from HUVECs derived from APS patients and healthy donors' HUVECs cultured with APS plasma had higher levels of TSP 1 and sFasL than those from cultured with plasma from Healthy Control. (TSP-1:mean APS=500ng/ml vs HD=150ng/ml $p=0,02$).
Regarding the clinical aspects of APS there was no statistically significant difference between patients with thromboembosism and pregnancy morbidity or between venous and arterial events. However, there was significant difference between the patients who had experienced miscarriages only (403.2 ng\ml) and those had both miscarriages and thrombosis (130.1 ng/ml).
Conclusions. Preliminary results suggest that APS patients have higher levels of TSP-1 in plasma and platelets overexpress TSP-1 and are highly correlated with sFasL and free TGF-β suggesting a possible involvement in thrombus formation and inhibition of angiogenesis that needs to be clarified.
Keywords. APS Antiphospholipid Syndrome, TSP-1 Thrombospondin-1, sFas L soluble Fas ligand, SLE Systemic Lupus Erythymatosus, HC healthy control, HUVEC human umbilical vein endothelial cells, TGF-b transforming growth factor beta

S-21

Antiphospholipid Antibodies: Do They Contribute Atherosclerosis?

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Low grade inflammation may present in patients (pts) with antiphospholipid syndrome (APS) in relation to traditional and specific risk factors, such as C-reactive protein (CRP), cytokines or adhesion molecules. Antiphospholipid antibodies (aPL) can be involved in atherosclerotic process.
Objective. To investigate clinical and subclinical features of atherosclerotic in APS pts and the relationship between intimae media thickness (IMT) and immunological abnormalities and traditional risk factors of atherosclerosis.
Materials and methods. The total of 206 pts (58 with primary APS (PAPS), 76 with systemic lupus erythematosus (SLE) (29 aPL-positive and 47 – aPL-negative) 72 with SLE+APS) and 29 age– and sex–matched healthy controls (HC) were included. To evaluate atherosclerosis features we measured IMT of the common carotid (CCA), internal carotid (ICA) and femoral arteries (FA). Also IgG/M anticardiolipin antibodies (aCL), anti-beta2-glycoprotein I antibodies (aβ2GP1), lupus anticoagulant (LA), lipid profile of plasma and traditional risks factors of atherosclerosis were assessed in all pts.
Results. There were 56/206 (27,2%) pts with high positive aCL, 48/206 (23,3%) pts with mild positive aCL, 32/206 (15,5%) pts with low positive aCL and 70/206 (34,0%) with negative aCL. Elevated IMT was determined at 70/206 (34%) pts. Atherosclerotic plaques (AP) were detected in 25(12%) of these pts: 5/58 (9%) had PAPS, 10/72 (14%) - SLE+APS, 4/29 (14%) - SLE aPL+ and 6/47 (13%) - SLE aPL-. The presence of AP was strongly associated with age, ranging from 1% among those who were younger than 30 years to 11% among those who were 40 years or older ($p=0,01$). 14/206 pts developed myocardial infarction (MI). The IMT, plaque prevalence, frequency of MI, smoking, hypertension and dyslipidaemia did not differ between the groups of pts and HC. Elevated IMT and APs associated with combined arterial and venous thrombosis and occurred more frequently in pts with MI and stroke ($p<0.001$ in all cases). High positive levels of aCL associated with normal IMT of GCA ($p=0,05$) and with the absence of atherosclerotic plaques in all investigated vessels ($p=0,014$). High level of cholesterol was associated with negative aCL. There was not any association between aβ2GP1, LA and IMT.
Conclusion. Antiphospholipid antibodies did not associate with atherosclerosis, but associated with actual vascular complication. High levels of IgG-aCL had protective role for IMT in APS patients and other mechanisms were involved in thrombotic events in these patients.
Keywords. Antiphospholipid, antibodies, atherosclerosis, lupus

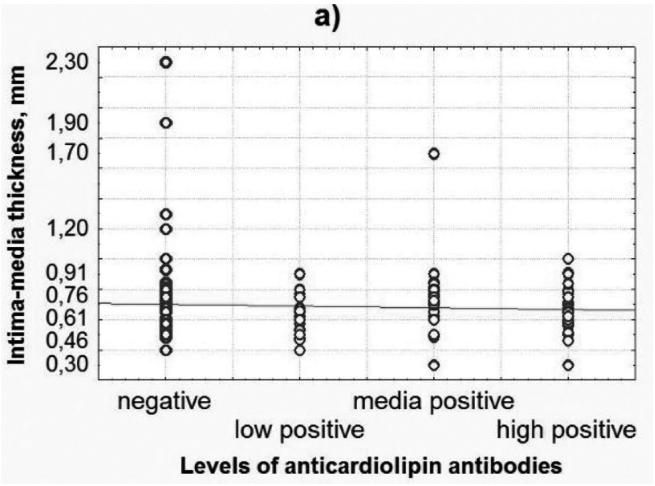

Fig. 1. Levels of aCL depending on intimae media thickness of the common carotid arteries High positive levels of aCL associated with normal IMT of GCA (p=0.05)

S-22

Efficacy of Kinesiotape Application on Pain, Cervical Range of Motion and Cervical Lordosis in Patients with Neck Pain: A Double Blind Randomized Placebo Controlled Clinical Trial

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Objectives. Cervical pain is one of the most common musculoskeletal symptoms. The aim of this study is to determine the therapeutic effects of Kinesio Taping, applied to the cervical spine, on neck pain, cervical range of motion and cervical lordosis.
Methods. A double blind randomized plasebo controlled trial is conducted in forty-four patients with neck pain. The participants were randomly assigned into 2 groups: the experimental group received Kinesio Taping to the cervical spine (applied with tension) and the placebo group received a sham Kinesio Taping application (applied without tension). Kinesio Tape was applied by the same investigator 3 times a week for 2 weeks. An investigator blinded to the treatment allocation of the patients collected the data of cervical range of motion (ROM) measurements, visual analogue scale (VAS), Neck Pain Disability

Index (NPDI) and SF-36 index at baseline and after the treatment. Baseline and first month lateral cervical roentgenograms were evaluated by a radiologist blinded to the clinical findings and treatment allocation of the patients. **Results.** The mean age of Kinesiotape group and sham group was 33.4±8.1 and 36.5±10.0 years respectively. There was statistically significant increase in ROM for all directions in the treatment group (p<0,05). Significant improvements in NPDI (p<0.0001) and SF-36 (p<0.0001) indices were achieved in the treatment group while only NPDI (p=0.013) significantly improved in sham group. Significant reductions in VAS score was achieved in the treatment group while there was no significant change in terms of VAS in the sham group. There was statistically significant increase in radiographic evaluation parameters in the treatment group in terms of cobbs angle (p=0.035) and tanjant angle (p=0.048) but no change was detected in the sham group in terms of these parameters. Although there was no statistically significant difference between the groups in terms of post treatment cervical lordosis, lordosis of 14% of patients in the treatment group was increased while this ratio was only 3% in the shamgroup. **Conclusions.** Patients receiving an application of Kinesio Taping applied with proper tension exhibited statistically significant improvements in pain, cervical range of motion and radiological measures of cervical lordosis. Future studies with larger groups should investigate if Kinesio Taping provides sustained improvements in long term follow ups.

Keywords. Cervical pain, cervical lodosis, kinesiotape.

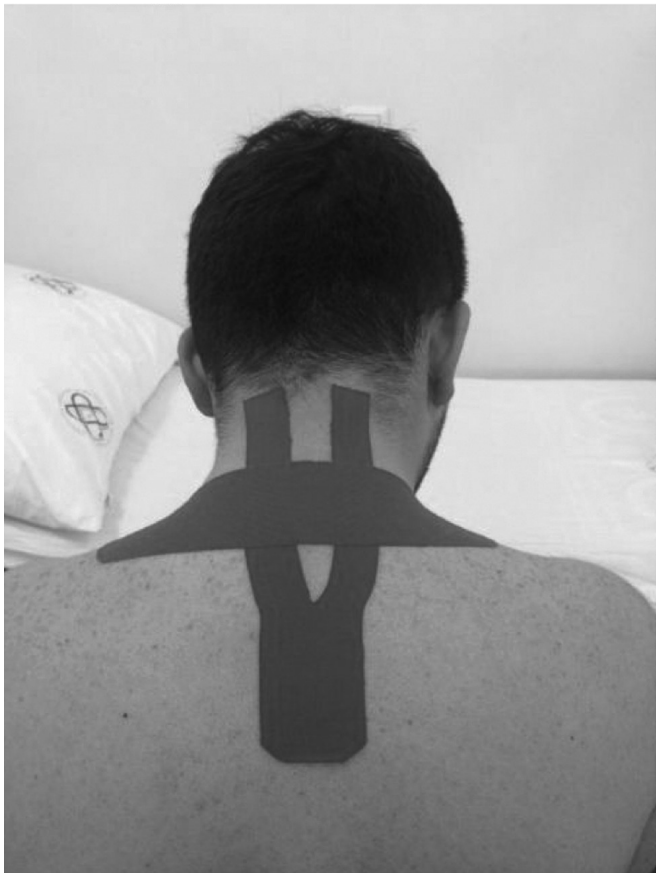

Fig. Kinesi Tape application (with tension).

S-23

Ultrasonographic Findings in Chronic Haemophilic Arthropathy in a Moroccan Children Population

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Objective. We aimed to describe the ultrasonographic findings in chronic haemophilic arthropathy.

Methods. Twenty-six children(mean age 11.3±3.8 years [4-18], all male, were included in this study; twenty-three of them (88.5%) had severe haemophilia. All patients have at least one joint affected by chronic haemophilic arthropathy. Sixty-one joints were sonographicaly examined with a high-frequency probe (7-14Mhz) in Doppler and B modes.

Following ultrasonographic parameters were analysed: synovitis, doppler activity, joint effusion, bone erosion, osteophytes and foreign bodies.

Results. Chronic haemophilic arthropathy affected knees elbows and ankles in respectively 49;31.1 and 19.6%. Chronic haemophilic arthropathy affectedmore than one joint in 87%. Below table summarizes ultrasonographic findings in joints examined.

Conclusion. Ultrasonography seems to be an interesting tool to individualize as well patterns of disease flare than joints status. This simple and practical examination should be integred in practice to monitoring children suffering from chronic hemophilic arthropathy especially in developing countries.

Keywords. Ultrasonography, joint, hemophilc arthropathy

Table. Ultrasonographic findings in 61 joints examined.

Ultrasonographic parameters	Knees (N=30)	Elbows (N=19)	Ankles (N=12)
Synovitis (%)	46.7	68.4	50
Doppler activity (%)	43.3	42.1	0
Effusion joint (%)	33.3	36.8	16.6
Bone erosion (%)	33.3	42.1	8.3
Osteophyte (%)	13.3	36.8	6.6
Foreign bodies (%)	20	21.1	8.3

Percentage of parameters found in ultrasonography.