Disease-specific quality indicators, outcome measures and guidelines in polymyositis and dermatomyositis

H. Alexanderson[1,2], I.E. Lundberg[2]

[1]Department of Physical Therapy, Rheumatology Unit and [2]Rheumatology Unit, Department of Medicine, Karolinska University Hospital, Solna, Stockholm, Sweden.

Helene Alexanderson, PhD, RPT; Ingrid E. Lundberg MD, PhD.

Please address correspondence to: Ingrid E. Lundberg, Rheumatology Unit, Karolinska University Hospital, SE-171 76 Stockholm, Sweden.
E-mail: Ingrid.Lundberg@ki.se

Received and accepted on August 3, 2007.

Clin Exp Rheumatol 2007; 25 (Suppl. 47): S153-S158.

Key words: Polymyositis, dermatomyositis, outcome measures, diagnostic tools, disease activity score, myositis activities profile (MAP), Functional Index (FI).

Competing interests: none declared.

ABSTRACT

Polymyositis and dermatomyositis are chronic inflammatory muscle disorders with frequent involvement of other organs hence outcome measures should include these different aspects of disease. Muscle strength and muscle endurance are the most specific clinical features that should be assessed during treatment and longitudinal follow-up. Extramuscular involvement should also be assessed. An international, interdisciplinary network, the International Myositis Assessment Clinical Study Group (IMACS) has proposed a core set of outcome measures to assess three dimensions of myositis disease; disease activity (MYOACT), disease damage (MYODAM) and health related quality of life (SF-36) to be used in clinical trials. These include scoring of extramuscular involvement (skin, lungs, articular, cardiac, gastro-intestinal tract) in both the disease activity and damage scores. In the disease activity score, muscle strength is measured by the manual muscle test (MMT)- 8, this could easily be used in clinical practice. Other myositis specific outcome measures are the Functional Index of myositis (FI) – 2 to measure muscle endurance and a questionnaire, the Myositis Activities Profile (MAP) to measure patient perspective. A close collaboration between physicians, physical and occupational therapists and specialized nurses is of great value in care and disease assessment of patients with polymyositis and dermatomyositis.

Introduction

Polymyositis and dermatomyositis are chronic inflammatory disorders whose predominating symptoms involve the striated muscles, although other organs may be affected as well, which underlines the fact that these are systemic inflammatory connective tissue diseases. In addition to skin involvement in dermatomyositis, organs that may become involved in both polymyositis and dermatomyositis are the lungs, joints, gastrointestinal system and heart. Therefore, like in systemic lupus erythematosus (SLE) and vasculitis, outcome measures should take into account these different aspects of the disease.

Pharmacological treatment is based on high doses of glucocorticoids in combination with other immunosuppressives, the most common being azathioprine or methotrexate (1). In recent years it has become evident that combining immunosuppressive treatment with exercise leads to additional positive effects on clinical outcome (2-7). Most patients respond at least partially to the current treatment regimens, but many are left with some degree of muscle impairment. Disease flares may occur while tapering or after stopping immunosuppressive treatment. Thus careful follow-up is important and should include outcome measures that can distinguish whether the clinical manifestations are the result of disease activity or damage, caused either by the disease or its treatment.

The diagnosis of polymyositis and dermatomyositis is based on clinical manifestations and laboratory variables that reflect muscle inflammation and muscle damage. Typical clinical manifestations are slowly progressive, symmetric weakness and reduced muscle endurance. The most frequently involved muscles are proximal muscle groups: neck, shoulder and pelvic muscle. Serum levels of muscle enzymes – including creatine phosphokinase (CK), lactate dehydrogenase (LD), aspartate and alanine aminotransferases (AST and ALT), and aldolase – are elevated in most cases, although normal enzymes do not exclude a diagnosis of myositis. However, high serum muscle enzymes are not specific, and other signs of my-

opathy are required for the diagnosis, such as a myopathic electromyogram (EMG) and/or positive muscle biopsy with inflammation and regenerating or degenerating fibers (8, 9). Expression of major histocompatibility complex (MHC) class I on muscle fibers has recently been demonstrated to be helpful in the diagnosis, although it is not specific for myositis (10) .

A muscle biopsy is important not only to demonstrate signs of inflammation but also to exclude other myopathies such as muscle dystrophies and metabolic myopathies. Magnetic resonance imaging (MRI) is useful, and in patients with skin rash typical of dermatomyositis may be sufficient to verify muscle inflammation. However, muscle inflammation on MRI is not specific for myositis and cannot replace the muscle biopsy in patients with polymyositis. Furthermore, the sensitivity of MRI compared to muscle biopsies has not been clarified. Nonetheless, MRI can serve as a useful guide to site(s) for muscle biopsy (11, 12).

Autoantibodies may be helpful in the differential diagnosis from other, non-autoimmune myopathies, and are present in approximately 70% of patients with polymyositis or dermatomyositis (13, 14). Some are specific for myositis, the so-called myositis-specific autoantibodies (MSA) of which anti-Jo-1 autoantibodies are the most frequent, being present in 20-35% of myositis patients (13, 15). Anti-Jo-1 autoantibodies are directed against histidyl-tRNA synthetase, a tRNA-synthetase. Other MSAs include autoantibodies directed against other tRNA-synthetases [threonine (anti-PL-7), alanine (anti-PL-12), glycine (anti-EJ), asparagine (KS) and isoleucine (anti-OJ)] as well as anti-Mi-2, anti-SRP and the recently reported anti-p155 kD autoantibodies (16). Routine clinical tests for the most recent MSAs are lacking at the present time, but may prove to be of value in advancing our understanding of the pathogenesis of the diseases and the development of new treatments.

Some of the diagnostic tools for polymyositis and dermatomyositis could also be useful as outcome measures, beginning with the instruments designed to measure muscle strength and endurance (see below). Serum levels of muscle enzymes can be easily measured, but are not always helpful as outcome measures because they may not always correlate with disease activity or muscle performance. EMG may not be readily available, is often painful, and its sensitivity to change is unclear. Repeat muscle biopsies may be of value to re-evaluate the diagnosis in patients who fail to respond to treatment, but otherwise are not needed, nor are they appropriate for use in clinical practice due to their invasiveness. Some autoantibodies correlate with disease activity, such as anti-DNA in SLE. Among the autoantibodies found in patients with myositis, the anti-Jo-1 autoantibodies may be of special interest as occasional case reports suggest that anti-Jo-1 may fluctuate with disease activity, although this remains to be confirmed. Finally, MRI signals in muscle tissue fluctuate over time and seem to follow disease activity, but have several limitations that are discussed below. Therefore, the tools used to confirm the diagnosis of polymyositis or dermatomyositis are not ideal as outcome measures. Furthermore, they do not take into account patient preferences.

Disease-specific quality indicators

Muscle strength and muscle endurance are the most specific clinical features that should be assessed during treatment and longitudinal follow-up (Table I). Furthermore, extra-muscular involvement, including skin changes (17), should be evaluated. Interstitial lung disease (ILD) is frequently seen in both polymyositis and dermatomyositis, and may have profound effects on a patient's physical activities and quality of life (18). As the presence of ILD could influence the prognosis and choice of immunosuppressive treatment, ILD should be screened for by means of pulmonary function tests and high resolution computerized tomography (HRCT). These tools should also be used as outcome measures of ILD during treatment.

Table I. Disease-specific quality indicators for inflammatory myopathies.

A. Impairment
Muscle endurance (FI, FI-2) (30, 33)
Muscle strength (MMT) (19)
Serum levels of muscle enzymes CK, LD
Skin score (17)
Pulmonary function tests
Myositis disease activity core set (19, 20)
Myositis disease damage score (MYODAM) (19, 20)
Magnetic resonance imaging (MRI) of skeletal muscle
B. Activity limitation and participation restriction
Myositis Activities Profile (MAP) (37)

Table II. Myositis Disease Activity Core Set (19, 20).

Physician's overall assessment of disease activity on a visual analogue scale (VAS)
Patient/parent overall assessment of disease activity (VAS)
Functional assessment [Health assessment questionnaire (HAQ)]
Muscle strength testing [Manual muscle test (MMT)]
Serum levels of at least 2 of 4 muscle enzymes (CK, LD, AST, ALT)
Extra-muscular score [visual analogue scales to assess myositis disease activity (MYOACT) or the Myositis Intention to Treat Activity Index (MITAX)] in which disease activity in seven organ systems is recorded by the physician (general symptoms, skin, joints, gastrointestinal tract, pulmonary, heart and skeletal muscles)

CK: creatine kinase; LD: lactate dehydrogenase; AST: aspartate aminotransferase; ALT: alanine aminotransferase.

Outcome measures

Clinical and laboratory manifestations in polymyositis and dermatomyositis may be caused either by active inflammation or organ damage. This was taken into account when outcome measures for myositis were developed recently by an international, interdisciplinary network – the International Myositis Assessment Clinical Study (IMACS) Group (19, 20). Consensus was achieved by this group on a core set of outcome measures designed to assess three dimensions of myositis disease – disease activity, disease damage, and health-related quality of life – for use in clinical trials (19).

The myositis disease activity score is a composite made up of six dimensions (Table II). It was developed to include basic, readily available measures for

Table III. Clinical outcome measures for polymyositis and dermatomyositis based on the International Classification of Functioning Disability and Health (ICF).

Impairment	Activity limitation/participation restriction
Muscle biopsy	HAQ
MRI	MAP
MR-spect	MACTAR
Ultrasound	SF-36
Laboratory parameters (CK, LD, AST, ALD, CRP, ESR)	
Myositis: disease activity 6-item core set	
MMT	
FI	
FI-2	

MRI: Magnetic resonance imaging; MR-spect: Magnetic resonance spectroscopy; 6-item core set: Patient's and physician's assessment of disease activity, MMT, HAQ, laboratory analysis and extra-muscular involvement using the MITAX, MYOACT; MMT: Manual Muscle Test; FI: Functional Index; FI-2: Functional Index-2; HAQ: Health Assessment Questionnaire; MAP: Myositis Activities Profile; MACTAR: MacMAster Toronto Arthritis Patients Preference Questionnaire; SF-36: Short Form 36-item questionnaire.

use in clinical trials. A definition of "improvement" was also proposed – improvement of 20% or more in 3 of 6 outcome measures, with no more than 2 variables worsening that cannot include the manual muscle test (MMT) (21).

The myositis damage score, MYODAM, is based on the SLE disease damage score and covers possible damage caused either by disease or by treatment and that has been present for more than 6 months. Extra-muscular dimensions (skin, lungs, articular, cardiac, gastrointestinal tract) are all included in the IMACS disease activity and damage scores. The muscle score in the IMACS disease activity measure is the MMT. The generic SF-36 was recommended to measure health-related quality of life.

These outcome measures have been partially validated, but their sensitivity to change still needs to be tested in longitudinal studies (22). Additional outcome measures of muscle performance have been developed for myositis and are presented below. These may be useful in clinical trials and some of them also in clinical practice.

Clinical outcome measures

The International Classification of Functioning Disability and Health (ICF) was presented by the World Health Organization (WHO) as a unified language and framework to describe health and health-related conditions (23). In the ICF, health is described in terms of bodily functions and structures, and activity/participation under the umbrella category "Functioning." A health-related condition is described in terms of impaired bodily functions and structure (*e.g.*, inflammatory infiltrates in muscle and reduced muscle function) and activity limitation/participation restriction (*e.g.*, walking limitations and restricted ability to participate in society) under the umbrella term "Disability." In this review, clinical outcome measures will be defined using ICF Disability terminology (Table III).

The most frequently used outcome measure of muscle performance in clinical trials to date has been the MMT. There are many versions, but the one suggested for use in the disease activity core set for myositis is the MMT subdivided into eight muscle groups (MMT-8). However, MMT-8 has been validated only for juvenile dermatomyositis (JDM), and not for adult myositis. A hand-held dynamometer and a computerized test device to measure muscle strength have also been used to assess muscle function, *i.e.*, isometric muscle strength in patients with inflammatory myopathies (24). There is a dearth of information on the measuring properties of these instruments in the adult inflammatory myopathy population, however. The MMT and the hand-held dynamometer are both easy to use in the clinic, whereas the computerized device is very expensive and requires trained personnel. Several clinical trials have shown that these tools are able to detect statistically significant changes in muscle strength in patients with inflammatory myopathies (2, 3, 6, 25-28). As many of our daily activities involve dynamic muscle action, it could also be of interest to assess isokinetic muscle strength using a computerized device. However, this has been undertaken in only one exercise study involving a small number of patients with inclusion body myositis, and did not show significant changes in muscle strength (29).

One limitation of the MMT and dynamic strength testing during an office visit is that it does not fully evaluate the effects that can accumulate over the course of time, in which both fatigue and weakness may contribute to create significant problems in the activities of daily life. This is partially addressed in the first disease-specific impairment measure for patients with polymyositis and dermatomyositis, the Functional Index (FI), which was designed to assess muscle endurance with inter- and intra-rater reliability (30). It was discovered, however, that although the FI was sensitive to change when measuring outcome after exercise or medical treatment (4, 5, 31, 32), it had some floor and ceiling effects when evaluating patients with mild to moderate impairment (4, 5). Therefore, the FI was further refined into the Functional Index 2 (FI-2) (33). Tasks with the most obvious ceiling effects were removed and the number of repetitions was increased for the remaining tasks, leading to a 7-muscle group functional test for muscle endurance. A 7-week intensive exercise study showed the FI-2 to be sensitive to change with good inter- and intra-rater reliability (7).

In a study that compared isometric muscle strength as measured by the MMT-8 with muscle endurance as measured by the FI-2 in 60 adults with inflammatory myopathies, patients overall showed reduced muscle endurance, as demonstrated by a mean maximal score of 23% on the FI-2 compared to a mean maximal score of 96% on the MMT-8 (34). These results indicate the impor-

tance of measuring both strength and endurance when either screening for myositis or assessing muscle impairment following different interventions (as outcome measures). One limitation to the use of FI-2 in clinical practice is that it may take up to 33 minutes to complete depending on the patient. It could therefore be performed instead by a physical therapist before the patient sees the treating physician. To save time in clinical trials or in clinical practice, the FI-2 could also be measured on the dominant side of the body only, thus reducing the time needed to complete the test to a maximum of 20 minutes. In clinical practice the time could be further reduced by testing a specific combination of tasks depending on the distribution of muscle impairment in the patient.

The Stanford Health Assessment Questionnaire Disability Index (HAQ-DI) (35) has been in use for many years to assess patients with inflammatory myopathies. The HAQ examines 20 activities divided into eight categories and offers many advantages. It is a simple questionnaire that does not take more than 10 minutes to complete, and translated versions, culturally adapted and duly validated, exist in many languages. However, the HAQ was designed for arthritis patients and while it has been validated for juvenile dermatomyositis [using the Childhood Health Assessment Questionnaire (CHAQ) (36)], such is not the case for adult myositis. The HAQ has been used in studies on the effect of exercise on adult myositis patients and was found to be sensitive to change following different interventions (2, 3, 6), but its other measurement properties for adult myositis are unknown.

To fill this gap the Myositis Activities Profile (MAP) was developed (37). Patients with adult polymyositis and dermatomyositis (22) were asked to rate the difficulty and the importance of a vast number of activities from the International Classification of Impairments, Disabilities, and Handicaps (ICIDH)-2 beta-2 draft (38), the previous version of the WHO ICF. An analysis of internal redundancy and consistency was then performed, and a 31-item questionnaire was generated. Activities from all relevant domains of the ICIDH were represented in one of the four subscales or in one of the four single items of the MAP. The correlation of this instrument with the HAQ was found to be moderate to good; it correlated less well with measures of impairment (muscle endurance and disease activity) and participation restriction (global disease impact on general well-being).

The MAP has been used in one exercise study and was found to have limited sensitivity to change following a 7-week intensive exercise regimen, similar to the sensitivity of the HAQ. The MAP was originally developed in Swedish; it has since been translated into American English and is currently undergoing cultural adaptation for myositis patients in the USA. The MAP has introduced a significant new feature – when completing the questionnaire, the patient is asked to estimate not only how difficult a given activity is to perform, but also the importance of this activity in his or her daily life. The MAP must be tested in future clinical trials and exercise studies to further establish its sensitivity to change and evaluate to what extent patients are able to estimate the difficulty and importance of the activities included in the MAP.

Recently international collaborations in the field of rheumatology (CARE III and OMERACT) have identified the need to include the patient's perspective when assessing the clinical outcome in arthritis care and valid clinical measures of participation restriction (39, 40). In our opinion, this is equally important in myositis care. The McMaster Toronto Arthritis Patient Preference Questionnaire (MACTAR) was originally developed in Canada as an arthritis-specific questionnaire (41). It was later translated into Dutch and modified into a semi-structured interview (42). The MACTAR baseline and MACTAR follow-up consist of questions divided into six different categories, including general health, quality of life, physical function, and social function, as well as the most important daily activities requiring improvement, where patients are encouraged to identify spontaneously at least five activities that they want to improve. The MACTAR has been translated into Swedish and validated for patients with adult polymyositis and dermatomyositis by our research group (43). It was found to have good content validity, correlating best to a participation restriction measure and less with the measures of other constructs, and showing good test-retest reliability. The Swedish MACTAR is now being used in an extensive exercise study with myositis patients conducted at the Karolinska University Hospital, Stockholm, Sweden.

The generic SF-36 questionnaire (44) has proven to be a valid and sensitive tool for the assessment of perceived health in patients with inflammatory myopathies. In one study patients with adult polymyositis and dermatomyositis were rated as having significantly poorer health in all eight domains of the SF-36 (45). The SF-36 was able to detect significant improvement in several domains following a 12-week home exercise program in patients with chronic as well as recent-onset disease (4, 5).

Laboratory outcome measures

Muscle enzymes. Serum levels of muscle enzymes – in particular, creatine kinase (CK) and lactate dehydrogenase (LD) – are often used as outcome measures. CK and LD are included as one of the six variables in the IMACS disease activity core set. Alone they have limited value as outcome measures, because their levels do not necessarily reflect muscle function or disease activity; *i.e.*, a normal value does not exclude persisting muscle inflammation and conversely some patients may have persisting elevated levels despite clinical improvement. However, in some patients muscle enzymes may be a useful indicator of disease activity and ongoing muscle damage.

Magnetic resonance imaging (MRI). MRI of the skeletal muscles, using short tau inversion recovery (STIR), is a non-invasive tool that could be useful in clinical practice. It can, for example, help to guide biopsy sampling in the diagnostic evaluation (11, 12). MRI may also be used to monitor the effects of treatment;

Table IV. General guidelines for outcome measures in patients with polymyositis or dermatolmyositis.

Our recommendations are that:

- Patients with recent onset disease should be assessed using measures covering all levels of the ICF, impairment and activity limitation and participation restriction, and this should be done at disease onset, at 3, 6 and 12 months, and then at least once a year.
- The goal should be to use only valid and reliable clinical outcome measures for this group of patients.
- The ability of the 6-item core set (including MMT-8 and HAQ) and FI-2 to assess disease activity in adult inflammatory myopathies needs to be further validated
- The MAP and the MACTAR are promising new outcome measures for activity limitation and participation restriction in patients with polymyositis and dermatomyositis. These need to be further validated and further translation and cultural adaptation is required.

A close collaboration between physicians, physical therapists, occupational therapists and specialized nurses is of great value in patient care and in the disease assessment of patients with inflammatory myopathies.

ICF: International Classification of Functioning, Disability and Health; MMT-8: Manual muscle test in eight muscle groups; HAQ: Health Assessment Questionnaire; FI-2: Functional index 2; MAP: Myositis Activities Profile; MACTAR: MacMaster Toronto Arthritis Patients Preference Questionnaire.

although its sensitivity to change has not been clarified, in a few longitudinal reports decreased signals were recorded in patients with clinical improvement (46). Another limitation to the use of MRI is its high cost and limited availability in some hospitals and outpatient clinics that follow myositis patients.

Magnetic resonance spectroscopy. MR spectroscopy and phosphorus-31 proton MR spectroscopy constitute promising, non-invasive tools that could provide information pertinent to outcome measures in terms of metabolic changes in the muscle tissue. A few limited studies demonstrated biochemical changes that were correlated with clinical improvement during treatment (46, 47). Major drawbacks to the use of MR spectroscopy as an outcome measure today are its limited availability (particularly with regard to proton MR spectroscopy, which requires another, more powerful magnet), and the fact that it has only been validated to a limited extent against other outcome measures.

Ultrasound. Ultrasound machines are widely available and are being increasingly used by rheumatologists to investigate synovial tissue inflammation. To date, there is only limited data on the use of ultrasound studies of muscle tissue as an outcome measure in patients with inflammatory myopathies. The recent introduction of contrast-enhanced ultrasound makes it possible to determine blood flow in muscle vessels. Ultrasound therefore could be used as an outcome measure to determine the degree of inflammation. Reduced blood flow was seen on ultrasound after immunosuppressive treatment in patients with polymyositis or dermatomyositis who had improved muscle strength and decreased CK (48). This interesting observation must be confirmed in larger cohorts.

Guidelines

Our recommendations concerning guidelines for outcome measures in patients with myositis are summarized in Table IV. We suggest using IMACS's proposed Clinical Outcome Measures in clinical trials on patients with inflammatory myopathies (Table IV). The feasibility of outcome measures in clinical practice needs to be tested, but we propose their use until simpler outcome measures have been developed and validated. In addition, the FI-2 could be helpful when screening new patients with signs and symptoms of myositis, and as an outcome measure during follow-up. MAP and MACTAR are promising activity limitation/participation restriction measures, both of which take into account the patient's perspective. However, all of these instruments require further validation, and the goal should be to use only valid and reliable clinical outcome measures.

Conclusion

In clinical practice, patients with suspected myositis should undergo thorough investigations before a diagnosis is made. When the diagnosis is confirmed, measures of disease activity, performance and health-related quality of life should be applied. We also believe that during follow-up patients should be monitored systematically, using clinical outcome measures as proposed by IMACS, preferably after 3, 6 and 12 months and yearly thereafter, until simpler tests have been developed and validated. In addition, based on our clinical experience it is of great importance that patients with inflammatory myopathies be followed by a professional, multi-disciplinary team to measure and minimize disability on all ICF levels.

References

1. CORDEIRO AC, ISENBERG DA: Treatment of inflammatory myopathies. *Postgrad Med J* 2006; 82: 417-24.
2. WIESINGER GF, QUITTAN M, ARINGER M *et al*.: Improvement of physical fitness and muscle strength in polymyositis/dermatomyositis patients by a training programme. *Br J Rheumatol* 1998; 37: 196-200.
3. WIESINGER GF, QUITTAN M, GRANINGER M *et al*.: Benefit of 6 months long-term physical training in polymyositis/dermatomyositis patients. *Br J Rheumatol* 1998; 37: 1338-42.
4. ALEXANDERSON H, STENSTROM CH, LUNDBERG I: Safety of a home exercise programme in patients with polymyositis and dermatomyositis: a pilot study. *Rheumatology (Oxford)* 1999; 38: 608-11.
5. ALEXANDERSON H, STENSTROM CH, JENNER G, LUNDBERG I: The safety of a resistive home exercise program in patients with recent onset active polymyositis or dermatomyositis. *Scand J Rheumatol* 2000; 29: 295-301.
6. VARJU C, PETHO E, KUTAS R, CZIRJAK L: The effect of physical exercise following acute disease exacerbation in patients with dermato/polymyositis. *Clin Rehabil* 2003; 17: 83-7.
7. ALEXANDERSON H, DASTMALCHI M, ESBJORNSSON-LILJEDAHL M, OPAVA CH, LUNDBERG IE: Benefits of intensive resistance training in patients with chronic polymyositis or dermatomyositis. *Arthritis Rheum* 2007; 57: 768-77.
8. BOHAN A, PETER JB: Polymyositis and dermatomyositis (first of two parts). *N Engl J Med* 1975; 292: 344-7.
9. BOHAN A, PETER JB: Polymyositis and der-

matomyositis (second of two parts). *N Engl J Med* 1975; 292: 403-7.
10. VAN DER PAS J, HENGSTMAN GJ, TER LAAK HJ, BORM GF, VAN ENGELEN BG: Diagnostic value of MHC class I staining in idiopathic inflammatory myopathies. *J Neurol Neurosurg Psychiatry* 2004; 75: 136-9.
11. LAMPA J, NENNESMO I, EINARSDOTTIR H, LUNDBERG I: MRI guided muscle biopsy confirmed polymyositis diagnosis in a patient with interstitial lung disease. *Ann Rheum Dis* 2001; 60: 423-6.
12. TOMASOVA STUDYNKOVA J, CHARVAT F, JAROSOVA K, VENCOVSKY J: The role of MRI in the assessment of polymyositis and dermatomyositis. *Rheumatology (Oxford)* 2007; 46: 1174-9 (E-pub 2007 May 10).
13. BROUWER R, HENGSTMAN GJ, VREE EGBERTS W *et al*.: Autoantibody profiles in the sera of European patients with myositis. *Ann Rheum Dis* 2001; 60: 116-23.
14. HENGSTMAN GJ, BROUWER R, EGBERTS WT *et al*.: Clinical and serological characteristics of 125 Dutch myositis patients. Myositis-specific autoantibodies aid in the differential diagnosis of the idiopathic inflammatory myopathies. *J Neurol* 2002; 249: 69-75.
15. LOVE LA, LEFF RL, FRASER DD *et al*.: A new approach to the classification of idiopathic inflammatory myopathy: Myositis-specific autoantibodies define useful homogeneous patient groups. *Medicine* 1991; 70: 360-74.
16. TARGOFF IN, MAMYROVA G, TRIEU EP *et al*. and the Childhood Myositis Heterogeneity Study Group; International Myositis Collaborative Study Group: A novel autoantibody to a 155-kd protein is associated with dermatomyositis. *Arthritis Rheum* 2006; 54: 3682-9.
17. RIDER LG, FELDMAN BM, PEREZ MD *et al*.: Development of validated disease activity and damage indices for the juvenile idiopathic inflammatory myopathies. I. Physician, parent, and patient global assessments. Juvenile Dermatomyositis Disease Activity Collaborative Study Group. *Arthritis Rheum* 1997; 40: 1976-83.
18. FATHI M, DASTMALCHI M, RASMUSSEN E, LUNDBERG IE, TORNLING G: Interstitial lung disease, a common manifestation of newly diagnosed polymyositis and dermatomyositis. *Ann Rheum Dis* 2004; 63: 297-301.
19. MILLER FW, RIDER LG, CHUNG YL *et al*. for the International Myositis Outcome Assessment Collaborative Study Group: Proposed preliminary core set measures for disease outcome assessment in adult and juvenile idiopathic inflammatory myopathies. *Rheumatology (Oxford)* 2001; 40: 1262-73.
20. IMACS website. Available at: https://dir-apps.niehs.nih.gov/imacs /
21. RIDER LG, GIANNINI EH, BRUNNER HI *et al*. and the International Myositis Assessment and Clinical Studies Group: International consensus on preliminary definitions of improvement in adult and juvenile myositis. *Arthritis Rheum* 2004; 50: 2281-90.
22. ISENBERG DA, ALLEN E, FAREWELL V *et al*.: International consensus outcome measures for patients with idiopathic inflammatory myopathies. Development and initial validation of myositis activity and damage indices in patients with adult-onset disease. *Rheumatology* 2004; 43: 49-54.
23. WORLD HEALTH ORGANIZATION: *The International Classification of Functioning, Disability and Health*. Geneva, World Health Organization, 2001.
24. RIDER LG: Outcome assessment in the adult and juvenile idiopathic myopathies. *Rheum Dis Clin North Am* 2002; 28: 935-77.
25. CHERIN P, PELLETIER S, TEIXEIRA A *et al*.: Results and long-term follow-up of intravenous immunoglobulin infusions in chronic, refractory polymyositis: An open study with thirty-five adult patients. *Arthritis Rheum* 2002; 46: 467-74.
26. DANIELI MG, MALCANGI G, PALMIERI C *et al*.: Cyclosporin A and intravenous immunoglobulin treatment in polymyositis/dermatomyositis. *Ann Rheum Dis* 2002; 61: 37-41.
27. HENGSTMAN GJD, VAN DEN HOOGEN FHJ, BARRERA P *et al*.: Successful treatment of dermatomyositis and polymyositis with anti-tumor-necrosis-factor-alpha: Preliminary observations. *Eur Neurol* 2003; 50: 10-5.
28. BADRISING UA, MAAT-SCHIEMAN ML, FERRARI MD *et al*.: Comparison of weakness progression in inclusion body myositis during treatment with methotrexate or placebo. *Ann Neurol* 2002; 51: 369-72.
29. ARNARDOTTIR S, ALEXANDERSON H, LUNDBERG IE, BORG K: Sporadic inclusion body myositis: Pilot study on the effects of a home exercise program on muscle function, histopathology and inflammatory reaction. *J Rehabil Med* 2003; 35: 31-5.
30. JOSEFSON A, ROMANUS E, CARLSSON J: A functional index in myositis. *J Rheumatol* 1996; 23: 1380-4.
31. VENCOVSKY J, JAROSOVA K, MACHACEK S *et al*.: Cyclosporine A versus methotrexate in the treatment of polymyositis and dermatomyositis. *Scand J Rheumatol* 2000; 29: 95-102.
32. HEIKKILÄ S, VIITANEN JV, KAUTIAINEN H, RAJAMAKI T, MANTYVUO P, HARJU T: Rehabilitation in myositis. *Physiotherapy* 2001; 87: 301-9.
33. ALEXANDERSON H, BROMAN L, TOLLBACK A, JOSEFSON A, LUNDBERG IE, STENSTROM CH: Functional index-2: Validity and reliability of a disease-specific measure of impairment in patients with polymyositis and dermatomyositis. *Arthritis Rheum* 2006; 55: 114-22.
34. ALEXANDERSON H, DASTMALCHI M, LUNDBERG IE: Patients with chronic inflammatory myopathies have reduced muscle endurance rather than reduced muscle strength. *Arthritis Rheum* 2006; 54 (Suppl.): 1639: S658.
35. FRIES JF, SPITZ P, KRAINES RG, HOLMAN HR: Measurement of patient outcome in arthritis. *Arthritis Rheum* 1980; 23: 137-45.
36. HUBER AM, HICKS JE, LACHENBRUCH PA *et al*.: for the Juvenile Dermatomyositis Disease Activity Collaborative Study Group: Validation of the Childhood Health Assessment Questionnaire in the juvenile idiopathic myopathies. Juvenile Dermatomyositis Disease Activity Collaborative Study Group. *J Rheumatol* 2001; 28: 1106-11.
37. ALEXANDERSON H, LUNDBERG IE, STENSTRÖM CH: Development of the myositis activities profile – validity and reliability of a self-administered questionnaire to assess activity limitations in patients with polymyositis/dermatomyositis. *J Rheumatol* 2002; 29: 2386-92.
38. WORLD HEALTH ORGANIZATION: *International Classification of Impairment, Disability and Handicap, Beta-2 Draft*, full version. Geneva, World Health Organization, 1999.
39. KIRWAN JR, HEWLETT SE, HEIBERG T *et al*.: Incorporating the patient perspective into outcome assessment in rheumatoid arthritis – progress at OMERACT 7. *J Rheumatol* 2005; 32: 2250-6.
40. BACKMAN CL: Outcome measures for arthritis care research: Recommendations from the CARE III conference. *J Rheumatol* 2006; 33: 1908-11.
41. TUGWELL P, BOMBARDIER C, BUCHANAN WW, GOLDSMITH CH, GRACE E, HANNA B: The MACTAR Patient Preference Disability Questionnaire – an individualized functional priority approach for assessing improvement in physical disability in clinical trials in rheumatoid arthritis. *J Rheumatol* 1987; 14: 446-51.
42. VERHOEVEN AC, BOERS M, VAN DER LIDEN S: Validity of the MACTAR questionnaire as a functional index in a rheumatoid arthritis clinical trial. The McMaster Toronto Arthritis. *J Rheumatol* 2000; 27: 2801-9.
43. ALEMO-MUNTERS L, VAN VOLLENHOVEN R, ALEXANDERSON H: Measurement properties of the Swedish MACTAR. *Arthritis Rheum* 2006; 54 (Suppl.): S503.
44. WARE JE, SHERBOURNE CD: The MOS 36-item short-form health survey: Conceptual framework and item selection. *Med Care* 1992; 30: 473-83.
45. SULTAN SM, IOANNOU Y, MOSS K, ISENBERG DA: Outcome in patients with idiopathic inflammatory myositis: Morbidity and mortality. *Rheumatology (Oxford)* 2002; 41: 22-6.
46. PARK JH, VITAL TL, RYDER NM *et al*.: Magnetic resonance imaging and p-31 magnetic resonance spectroscopy provide unique quantitative data useful in the longitudinal management of patients with dermatomyositis. *Arthritis Rheum* 1994; 37: 736-46.
47. PFLEIDERER B, LANGE J, LOSKE KD, SUNDERKOTTER C: Metabolic disturbances during short exercises in dermatomyositis revealed by real-time functional 31P magnetic resonance spectroscopy. *Rheumatology (Oxford)* 2004; 43: 696-703.
48. WEBER MA, WEBER MA, JAPPE U *et al*.: Contrast-enhanced ultrasound in dermatomyositis and polymyositis. *J Neurol* 2006; 253: 1625-32.