ARTHRITIS & RHEUMATOLOGY
Vol. 69, No. 12, December 2017, pp 2271–2282
DOI 10.1002/art.40320

2017 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies and Their Major Subgroups

Ingrid E. Lundberg,[1] Anna Tjärnlund,[1] Matteo Bottai,[2] Victoria P. Werth,[3] Clarissa Pilkington,[4] Marianne de Visser,[5] Lars Alfredsson,[2] Anthony A. Amato,[6] Richard J. Barohn,[7] Matthew H. Liang,[8] Jasvinder A. Singh,[9] Rohit Aggarwal,[10] Snjolaug Arnardottir,[2] Hector Chinoy,[11] Robert G. Cooper,[12] Katalin Dankó,[13] Mazen M. Dimachkie,[7] Brian M. Feldman,[14] Ignacio Garcia-De La Torre,[15] Patrick Gordon,[16] Taichi Hayashi,[17] James D. Katz,[18] Hitoshi Kohsaka,[19] Peter A. Lachenbruch,[20] Bianca A. Lang,[21] Yuhui Li,[22] Chester V. Oddis,[10] Marzena Olesinska,[23] Ann M. Reed,[24] Lidia Rutkowska-Sak,[25] Helga Sanner,[26] Albert Selva-O'Callaghan,[27] Yeong-Wook Song,[28] Jiri Vencovsky,[29] Steven R. Ytterberg,[30] Frederick W. Miller,[31] Lisa G. Rider,[31] and the International Myositis Classification Criteria Project Consortium, the Euromyositis Register, and the Juvenile Dermatomyositis Cohort Biomarker Study and Repository (UK and Ireland)

This criteria set has been approved by the American College of Rheumatology (ACR) Board of Directors and the European League Against Rheumatism (EULAR) Executive Committee. This signifies that the criteria set has been quantitatively validated using patient data, and it has undergone validation based on an independent data set. All ACR/EULAR-approved criteria sets are expected to undergo intermittent updates.

The ACR is an independent, professional, medical and scientific society that does not guarantee, warrant, or endorse any commercial product or service.

This article is published simultaneously in the December 2017 issue of *Annals of the Rheumatic Diseases*.

The views expressed herein are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government, or the NHS, the National Institute for Health Research, or the Department of Health (UK).

Supported by the European League Against Rheumatism, the American College of Rheumatology, The Myositis Association, and in part by the NIH (Intramural Research Program and the National Institute of Environmental Health Sciences), the European Science Foundation for the Euromyositis Register, the Swedish Research Council (grant K2014-52X-14045-14-3), and the regional agreement on medical training and clinical research between the Stockholm County Council and the Karolinska Institutet. The project also received support (not financial support/funding) from different associations: the American Academy of Neurology, the Childhood Arthritis and Rheumatology Research Alliance (CARRA; CARRA Inc. is funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH), Friends of CARRA, the Arthritis Foundation, the European Neuromuscular Centre, the International Myositis Assessment and Clinical Studies Group, the Muscle Study Group, the Rheumatologic Dermatology Society, the Pediatric Rheumatology European Society network for juvenile dermatomysitis, and the Pediatric Rheumatology International Trials Organization. Drs. Chinoy and Cooper's work in myositis is supported in part by Arthritis Research UK (grant 18474) and the Medical Research Council (grant MR/N003322/1). Dr. Vencovsky's work in myositis is supported by the Ministry of Health, Czech Republic (Project for Conceptual Development of Research Organization grant 00023728).

[1]Ingrid E. Lundberg, MD, PhD, Anna Tjärnlund, MSc, PhD: Karolinska University Hospital, and Karolinska Institutet, Stockholm, Sweden; [2]Matteo Bottai, PhD, Lars Alfredsson, PhD, Snjolaug Arnardottir, MD, PhD: Karolinska Institutet, Stockholm, Sweden; [3]Victoria P. Werth, MD: Philadelphia VA Medical Center and Hospital of the University of Pennsylvania, Philadelphia; [4]Clarissa Pilkington, MBBS, MRCP: Great Ormond Street Hospital for Children NHS Trust, London, UK; [5]Marianne de Visser, MD, PhD: Academic Medical Centre, Amsterdam, The Netherlands; [6]Anthony A. Amato, MD: Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; [7]Richard J. Barohn, MD, PhD, Mazen M. Dimachkie, MD: University of Kansas Medical Center, Kansas City; [8]Matthew H. Liang, MD, MPH: Brigham and Women's Hospital and Boston VA

Objective. **To develop and validate new classification criteria for adult and juvenile idiopathic inflammatory myopathies (IIM) and their major subgroups.**

Methods. **Candidate variables were assembled from published criteria and expert opinion using consensus methodology. Data were collected from 47 rheumatology, dermatology, neurology, and pediatric clinics worldwide. Several statistical methods were utilized to derive the classification criteria.**

Results. **Based on data from 976 IIM patients (74% adults; 26% children) and 624 non-IIM patients with mimicking conditions (82% adults; 18% children), new criteria were derived. Each item is assigned a weighted score. The total score corresponds to a probability of having IIM. Subclassification is performed using a classification tree. A probability cutoff of 55%, corresponding to a score of 5.5 (6.7 with muscle biopsy) "probable IIM," had best sensitivity/specificity (87%/82% without biopsies, 93%/88% with biopsies) and is recommended as a minimum to classify a patient as having IIM. A probability of ≥90%, corresponding to a score of ≥7.5 (≥8.7 with muscle biopsy), corresponds to "definite IIM." A probability of <50%, corresponding to a score of <5.3 (<6.5 with muscle biopsy), rules out IIM, leaving a probability of ≥50–<55% as "possible IIM."**

Conclusion. **The European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for IIM have been endorsed by international rheumatology, dermatology, neurology, and pediatric groups. They employ easily accessible and operationally defined elements, and have been partially validated. They allow classification of "definite," "probable," and "possible" IIM, in addition to the major subgroups of IIM, including juvenile IIM. They generally perform better than existing criteria.**

Introduction

Idiopathic inflammatory myopathies (IIMs), collectively known as myositis, are heterogeneous disorders characterized by muscle weakness and muscle inflammation (1). The most common subgroups in adults are dermatomyositis (DM), polymyositis (PM), and inclusion body myositis (IBM) (2), and in children, juvenile DM (JDM).

The International Myositis Assessment and Clinical Studies group (IMACS) has developed consensus on outcome measures and definitions of improvement to be used in clinical trials for myositis (3,4). A prerequisite for clinical trials and other clinical studies is the inclusion of well-defined patient groups. A wide variety of diagnostic or classification criteria for myositis are used (2,5–16), but are generally derived empirically and not validated. The criteria of Bohan and Peter (7,8) are most widely used, but have limitations. Because they do not clearly specify how to exclude other forms of myopathy, they may misclassify IBM patients as having PM (13,17–19), and muscular dystrophies with inflammation as myositis, and each criterion is not defined explicitly. New discoveries in the last decade, such as myositis-specific autoantibodies, that are associated with distinct clinical phenotypes (2,20–22), may provide opportunities to

Healthcare, Boston, Massachusetts; [9]Jasvinder A. Singh, MD, MPH: Mayo Clinic College of Medicine, Rochester, Minnesota, and University of Alabama and Birmingham VA Medical Center, Birmingham, Alabama; [10]Rohit Aggarwal, MD, Chester V. Oddis, MD: University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; [11]Hector Chinoy, BMBS, MSc, PhD, FRCP: Central Manchester University Hospitals NHS Foundation Trust, University of Manchester, Manchester, UK; [12]Robert G. Cooper, MD, FRCP: University of Liverpool, Liverpool, UK; [13]Katalin Dankó, MD: University of Debrecen, Debrecen, Hungary; [14]Brian M. Feldman, MD, MSc, FRCPC: University of Toronto and The Hospital for Sick Children, Toronto, Ontario, Canada; [15]Ignacio Garcia-De La Torre, MD: Hospital General de Occidente, Secretaría de Salud and University of Guadalajara, Guadalajara, Mexico; [16]Patrick Gordon, PhD, MBBS, FRCP: King's College Hospital NHS Foundation Trust, London, UK; [17]Taichi Hayashi, MD: University of Tsukuba, Tsukuba, Japan; [18]James D. Katz, MD: National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH, Bethesda, Maryland; [19]Hitoshi Kohsaka, MD: Tokyo Medical and Dental University, Tokyo, Japan; [20]Peter A. Lachenbruch, PhD: Oregon State University, Corvallis; [21]Bianca A. Lang, MD: IWK Health Centre and Dalhousie University, Halifax, Nova Scotia, Canada; [22]Yuhui Li, MD: People's Hospital of Beijing University, Beijing, China; [23]Marzena Olesinska, MD: National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw, Poland; [24]Ann M. Reed, MD: Duke University, Durham, North Carolina; [25]Lidia Rutkowska-Sak, MD: Institute of Rheumatology, Warsaw, Poland; [26]Helga Sanner, MD, PhD: Oslo University Hospital–Rikshospitalet, Oslo, Norway; [27]Albert Selva-O'Callaghan, MD, PhD: Vall d'Hebron General Hospital, Barcelona, Spain; [28]Yeong-Wook Song, MD: Seoul National University College of Medicine, Seoul, Republic of Korea; [29]Jiri Vencovsky, MD, PhD: Charles University, Prague, Czech Republic; [30]Steven R. Ytterberg, MD: Mayo Clinic College of Medicine, Rochester, Minnesota; [31]Frederick W. Miller, MD, PhD, Lisa G. Rider, MD: National Institute of Environmental Health Sciences, NIH, Bethesda, Maryland.

Dr. Singh has received consulting fees from Savient, Regeneron, Merz, Iroko, Bioiberica, Crealta/Horizon, Allergan, WebMD, UBM (less than $10,000 each), and Takeda (more than $10,000) and research grants from Takeda and Savient; he also serves as the principal investigator for an investigator-initiated study funded by Horizon Pharmaceuticals through a grant to DINORA, Inc., a 501 (c)(3) entity, and is a member of the executive committee of OMERACT, an organization that develops outcome measures in rheumatology and receives arms-length funding from 36 companies.

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

Submitted for publication March 14, 2017; accepted in revised form July 26, 2017.

improve the precision of classification, but have not been tested adequately (11,23).

The aim of this project was to develop classification criteria for adult and juvenile IIM. The specific goal was to define the minimum essential, easily available clinical and laboratory features to 1) distinguish IIM from mimicking conditions with high sensitivity and specificity, and 2) distinguish the major subgroups of IIM.

Methods

Study design. The International Myositis Classification Criteria Project (IMCCP), an international collaboration with experts from adult and pediatric rheumatology, neurology, dermatology, epidemiology, and biostatistics, was established in 2004 and followed at our best the European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) recommendations for development of classification criteria from that time or published soon thereafter (24,25). A steering committee and a larger working committee with experts in IIM were formed (see Supplementary Table 1 and Supplementary Appendix, available online on the *Arthritis & Rheumatology* web site at http://onlinelibrary.wiley.com/doi/10.1002/art.40320/abstract).

Using the nominal group technique, experts in IIM from the steering committee and the working committee (26–29) designed the study and validation experiments, assembled and defined candidate criteria from published myositis criteria (2,5–16) and other characteristics of myositis, and determined and assembled the IIM subgroup diagnoses and comparator conditions that were studied. A pilot study to assess the practicality of capturing the items showed a fair agreement of data availability from IIM and non-IIM cases (Supplementary Table 2, http://onlinelibrary.wiley.com/doi/10.1002/art.40320/abstract). Input was obtained from myositis experts, by email to the IMACS network, and requesting comments on the items, to maximize face and content validity (24,25). The steering committee revised the list of variables based on the comments and further suggestions from the IMACS network, and 93 variables (Supplementary Table 3, http://onlinelibrary.wiley.com/doi/10.1002/art.40320/abstract) were selected by the steering committee for study in cases and comparators. A glossary and definitions were developed according to an ACR glossary (30,31) (Supplementary Table 4, http://onlinelibrary.wiley.com/doi/10.1002/art.40320/abstract). Data were abstracted from patients' records and entered into a web-based database.

Inclusion criteria for cases and comparators were 1) diagnosis for at least 6 months prior to study inclusion; 2) physician certainty of diagnosis—either known IIM or, as comparators, known non-IIM cases where myositis was considered in the initial differential diagnosis; and 3) patients with the most recent and complete data were prioritized to acquire the most complete data in a consistent manner. A maximum of 40 cases and an equal number of comparators were collected from each center.

The study was approved by the ethics committees at each site.

Data analysis and candidate criteria selection. The association of each variable with the diagnosis (IIM, non-IIM) was assessed by odds ratios and tested with the Fisher's exact test. The treating physician diagnosis was considered the gold standard for analysis. Three classification techniques were explored: 1) a sum-of-items model in which a patient was classified as a case if the patient had a specified number of items from a set of item; 2) a probability-score model; and 3) a classification tree. The ensuing candidate criteria were examined with respect to statistical performance and clinical relevance. Due to the observed superior discriminating performance of the probability-score model, the other models were set aside.

Criteria development. The probability-score model summed score points associated with the signs and symptoms present. The score points were obtained as coefficients of a logistic regression model used to combine multiple variables for predicting IIM. The statistical significance of the resulting increase in the goodness-of-fit of the model was assessed using the Wald test. The improvement in predictive ability was measured by the increment in specificity and sensitivity and summarized by the area under the receiver operating characteristic curve (AUC).

Pediatric experts are using fewer muscle biopsies for classification of JDM in clinical practice than adult rheumatologists. Thus, a second model not including biopsy variables was developed. Assessment of statistical performance for each score/probability cutoff value provided the basis for a recommendation of a cutoff value for IIM classification by the steering committee. The proposed cutoffs were then defined as possible, probable, and definite IIM. To facilitate use of the new criteria, a web-based calculator for the probability-score model was developed.

The new classification criteria were compared with previous IIM criteria. Their statistical performance, and number of patients per IIM subdiagnosis classified as IIM by the different criteria sets, were calculated.

To distinguish subgroups of patients classified with IIM according to the new criteria, a classification tree was developed. The tree was based on the variables in the new classification criteria, statistical analyses as described in a separate methodology paper, and on expert opinion.

Validation. The new criteria were internally cross-validated. Samples of equal size to the original sample were drawn from the entire population at random with replacement, so-called "bootstrap" samples (32). The bootstrap sample represented the training sample, and the remaining subjects not contained in the bootstrap sample constituted the validation sample. The probability score was applied to each bootstrap training sample separately and then utilized to predict IIM in the validation sample. The procedure was repeated in over 200 bootstrap samples, and the average AUC was calculated.

The performance of the new criteria for IIM including the subgroups was tested for sensitivity in 2 independent cohorts, the Euromyositis Register (https://euromyositis.eu/) and the Juvenile Dermatomyositis Cohort Biomarker Study and Repository (JDRG) (UK and Ireland) (https://www.juveniledermatomyositis.org.uk/).

The program Stata V.13 (StataCorp) was used for data management and statistical analyses. The statistical program R (R Core Team [2014]. R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/) was used for some analyses.

A report detailing the methodology will be submitted as a separate publication (manuscript submitted).

Results

Study population. Data from 976 IIM patients (74.5% adults; 25.5% children) (Table 1) were collected between 2008 and 2011 from 23 European, 17 North American, 1 South American, and 6 Asian sites, representing IIM subgroups of JDM (n = 248), PM (n = 245), DM (n = 239), IBM (n = 176), amyopathic DM (ADM) (n = 44), hypomyopathic DM (n = 12), immune-mediated necrotizing myopathy (IMNM) (n = 11), and juvenile PM (n = 1). A total of 624 comparators (81.6% adults; 18.4% children) (Table 1) representing a broad spectrum of conditions that can mimic IIM were included, comprising systemic inflammatory diseases (36.5%), muscle dystrophies (16.0%), drug-associated or toxin-associated myopathies (7.9%), motor neuron diseases/neuropathies (7.7%), metabolic myopathies (6.9%), myalgias (4.5%), dermatologic diseases (3.7%), endocrine myopathies (3.7%), infectious myopathies (4.5%), mitochondrial myopathies (2.4%), neuromuscular diseases (2.6%), other myopathies (1.9%), immune-mediated skin conditions (0.5%), as well as other diagnoses (1.3%) (see Supplementary Tables 5 and 6, available online on the *Arthritis & Rheumatology* web site at http://onlinelibrary.wiley.com/doi/10.1002/art.40320/abstract).

Candidate criteria selection and criteria development. Based on statistical models, 16 variables from 6 categories best distinguished IIM cases from comparators (Table 2), and each variable was assigned a weight (score) based on its influence to discriminate IIM from non-IIM. A total score was computed by adding score points corresponding to each criterion being present. The score can be converted into a probability of IIM (Figures A and B), by:

$$\text{Probability of IIM including muscle biopsy} = 1/[1 + \text{exponential}\ (5.33\ -\ \text{score})]$$

$$\text{Probability of IIM without muscle biopsy} = 1/[1 + \text{exponential}\ (6.49\ -\ \text{score})]$$

or by using the online web calculator (www.imm.ki.se/biostatistics/calculators/iim). Sensitivity and specificity for varying probability cutoffs are shown in Figures 1C and D.

Cutpoints for classification. The best balance between sensitivity and specificity was found for a probability of 55–60% for the criteria not including muscle biopsy data, and 55–75% when including muscle biopsies, or a total aggregated score of score of ≥5.5 and ≤5.7 (≥6.7 and ≤7.6 if biopsy is available).

Table 1. Demographic data of the International Myositis Classification Criteria Project cohort*

	IIM (n = 976)	Comparators (n = 624)
Sex, no. (%)		
Female	652 (66.8)	369 (59.1)
Male	324 (33.2)	255 (40.9)
Adult onset disease, no. (%)†	727 (74.5)	509 (81.6)
Childhood onset disease, no. (%)†	249 (25.5)	115 (18.4)
Age at onset of symptoms, median (IQR) years	44.0 (14.7–57.0)	41.0 (20.0–56.0)
Age at diagnosis, median (IQR) years	45.5 (16.2–59.3)	45.0 (25.8–58.0)
Disease duration from time of first symptom, median (IQR) years‡	4.0 (2.0–8.0)	4.0 (1.0–9.0)
Disease duration from time of diagnosis, median (IQR) years§	3.0 (1.0–6.0)	1.8 (0.0–4.5)
Ethnicity, no. (%)		
Caucasian	611 (62.6)	360 (57.7)
Asian	177 (18.1)	156 (25.0)
Hispanic	51 (5.2)	25 (4.0)
African	40 (4.1)	28 (4.5)
Native American	18 (1.8)	4 (0.6)
Pacific Islander	3 (0.3)	1 (0.2)
Mixed	37 (3.8)	22 (3.5)
Unknown	54 (5.5)	32 (5.1)
Disease onset, no. (%)¶		
Acute (days to 2 weeks)	45 (4.6)	64 (10.3)
Subacute (>2 weeks to ≤2 months)	237 (24.3)	88 (14.1)
Insidious (>2 months to years)	648 (66.4)	444 (71.2)
NA	46 (4.7)	28 (4.5)

* IIM = idiopathic inflammatory myopathies; IQR = interquartile range; NA = information not available.
† Onset of first symptoms assumed to be related to the disease.
‡ Time from first symptom to last clinical evaluation.
§ Time from diagnosis to last clinical evaluation.
¶ Onset and progression of the first symptoms of the syndrome to the full disease presentation.

Table 2. The European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for adult and juvenile idiopathic inflammatory myopathies (IIMs)

When no better explanation for the symptoms and signs exists, these classification criteria can be used			
	Score points		
Variable	Without muscle biopsy	With muscle biopsy	Definition
Age of onset			
Age of onset of first symptom assumed to be related to the disease ≥18 years and <40 years	1.3	1.5	18 ≤ age (years) at onset of first symptom assumed to be related to the disease <40
Age of onset of first symptom assumed to be related to the disease ≥40 years	2.1	2.2	Age (years) at onset of first symptom assumed to be related to the disease ≥40
Muscle weakness			
Objective symmetric weakness, usually progressive, of the proximal upper extremities	0.7	0.7	Weakness of proximal upper extremities as defined by manual muscle testing or other objective strength testing, which is present on both sides and is usually progressive over time
Objective symmetric weakness, usually progressive, of the proximal lower extremities	0.8	0.5	Weakness of proximal lower extremities as defined by manual muscle testing or other objective strength testing, which is present on both sides and is usually progressive over time
Neck flexors are relatively weaker than neck extensors	1.9	1.6	Muscle grades for neck flexors are relatively lower than neck extensors as defined by manual muscle testing or other objective strength testing
In the legs, proximal muscles are relatively weaker than distal muscles	0.9	1.2	Muscle grades for proximal muscles in the legs are relatively lower than distal muscles in the legs as defined by manual muscle testing or other objective strength testing
Skin manifestations			
Heliotrope rash	3.1	3.2	Purple, lilac-colored, or erythematous patches over the eyelids or in a periorbital distribution, often associated with periorbital edema
Gottron's papules	2.1	2.7	Erythematous to violaceous papules over the extensor surfaces of joints, which are sometimes scaly. May occur over the finger joints, elbows, knees, malleoli, and toes
Gottron's sign	3.3	3.7	Erythematous to violaceous macules over the extensor surfaces of joints, which are not palpable
Other clinical manifestations			
Dysphagia or esophageal dysmotility	0.7	0.6	Difficulty in swallowing or objective evidence of abnormal motility of the esophagus
Laboratory measurements			
Anti–Jo-1 (anti–histidyl–transfer RNA synthetase) autoantibody present	3.9	3.8	Autoantibody testing in serum performed with standardized and validated test, showing positive result
Elevated serum levels of creatine kinase (CK)* *or* lactate dehydrogenase (LDH)* *or* aspartate aminotransferase (ASAT/AST/SGOT)* *or* alanine aminotransferase (ALAT/ALT/SGPT)*	1.3	1.4	The most abnormal test values during the disease course (highest absolute level of enzyme) above the relevant upper limit of normal
Muscle biopsy features—presence of:			
Endomysial infiltration of mononuclear cells surrounding, but not invading, myofibers		1.7	Muscle biopsy reveals endomysial mononuclear cells abutting the sarcolemma of otherwise healthy, non-necrotic muscle fibers, but there is no clear invasion of the muscle fibers
Perimysial and/or perivascular infiltration of mononuclear cells		1.2	Mononuclear cells are located in the perimysium and/or located around blood vessels (in either perimysial or endomysial vessels)
Perifascicular atrophy		1.9	Muscle biopsy reveals several rows of muscle fibers, which are smaller in the perifascicular region than fibers more centrally located
Rimmed vacuoles		3.1	Rimmed vacuoles are bluish by hematoxylin and eosin staining and reddish by modified Gomori trichrome stain

* Serum levels above the upper limit of normal.

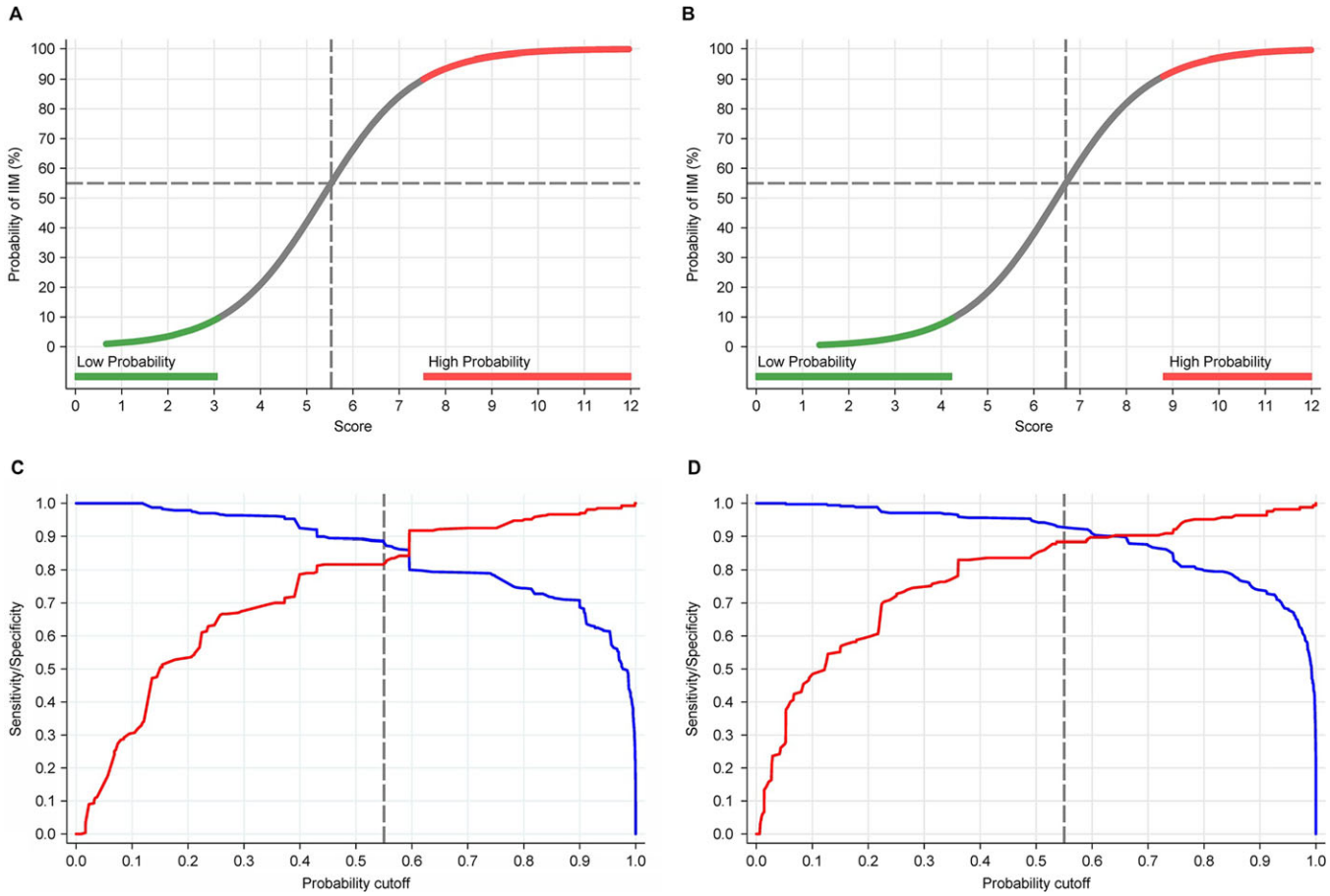

Figure 1. Probability of having idiopathic inflammatory myopathies (IIMs) based on the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for IIM. Each score obtained from the classification criteria corresponds to a probability of having the disease, without muscle biopsy data (**A**) or with muscle biopsy data (**B**). Each score and probability of disease display a unique set of sensitivity (blue line) and specificity (red line) measurements for the classification criteria not including muscle biopsy data (**C**) or including muscle biopsy data (**D**). The most optimal point of accuracy should be stated in publications and be appropriate to the intended purpose, with the recommendation of using a minimum of 55% probability (score of 5.5 without biopsies; 6.7 with biopsies) for classifying a case as IIM ("probable IIM") (dotted line). "Definite IIM" corresponds to a probability of at least 90% (score of ≥7.5 without biopsies; ≥8.7 with biopsies).

The IMCCP proposes that a patient may be classified as IIM if the probability exceeds a predetermined cutoff of at least 55% (corresponding to a score of ≥5.5, or ≥6.7 if biopsies are included) based on maximization of statistical performance and best balance between sensitivity and specificity. The level of probability ≥55% and <90% was defined as "probable IIM." The steering committee recommends, based on expert opinion, that "definite IIM" should equal a probability of ≥90%, corresponding to having total aggregate score of ≥7.5 without muscle biopsy and ≥8.7 with muscle biopsy.

Patients falling in the probability range ≥50% and <55% will be classified as "possible IIM." For a patient to be classified as a non-IIM patient, the probability would have to be <50% (score of <5.3 without biopsies; <6.5 with biopsies).

As suggested by pediatric experts and dermatologists, for patients with pathognomonic skin rashes of DM or JDM, classification criteria were developed, which did not include muscle biopsy data (Table 2). However, where no skin rash is present, a muscle biopsy is required for classification, as determined by a consensus of expert opinion within the IMCCP steering and working committees. Both sets apply equally well to adult IIM patients and to juvenile DM patients and should be used when IIM is suspected and no better explanation for the symptoms exists, as agreed on by expert opinion. Definitions for the criteria items are presented in Table 2.

Identification of subgroups. A patient classified with IIM by the EULAR/ACR classification criteria (probability of IIM ≥55%) can be further subclassified

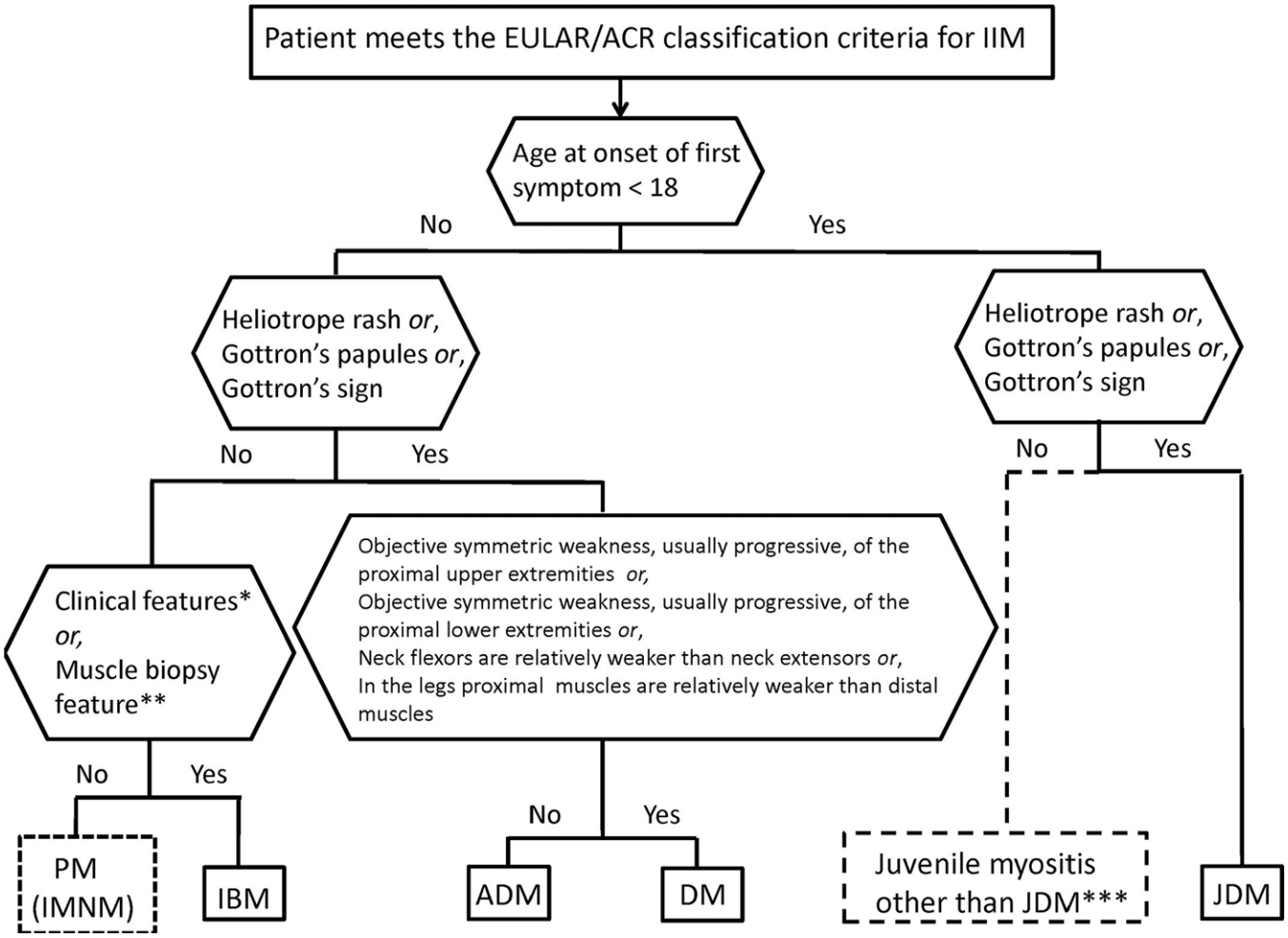

Figure 2. Classification tree for subgroups of idiopathic inflammatory myopathies (IIMs). A patient must first meet the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for IIM (probability of IIM ≥55%). The patient can then be subclassified using the classification tree. The subgroup of polymyositis (PM) patients includes patients with immune-mediated necrotizing myopathy (IMNM). For inclusion body myositis (IBM) classification, one of the following is required for classification: finger flexor weakness and response to treatment: not improved (*), or muscle biopsy: rimmed vacuoles (**). *** = Juvenile myositis other than juvenile dermatomyositis (JDM) was developed based on expert opinion. IMNM and hypomyopathic dermatomyositis were too few to allow subclassification. ADM = amyopathic dermatomyositis; DM = dermatomyositis.

with a classification tree (Figure 2). Age at onset of first symptom (≥18 years of age) distinguishes adult from juvenile IIM. Thereafter, clinical findings and muscle biopsy features subclassify adult IIM patients into PM, IBM, ADM, or DM. Based on our data set, juvenile patients with skin rash can be classified into JDM. Three subgroups cannot be further separated using our criteria because of small sample sizes: juvenile PM, IMNM, and hypomyopathic DM.

Among patients with IIM by the EULAR/ACR classification criteria (probability of IIM ≥55%), and with sufficient data to allow subclassification (n = 703), the number of cases in the subgroups as defined according to the classification tree was enumerated (Table 3). The agreement between the classification tree subgroups and the physician-diagnosed subgroups in the data set was high (92.6% agreement; $\kappa = 0.90$, $P < 0.00001$). The agreement proportions, with a probability of 55%, were 1.00 for JDM, 0.89 for DM, 0.94 for ADM, 0.92 for IBM, and 0.93 for PM. Raising the probability cutoff of IIM to 90% yielded 94.9% agreement ($\kappa = 0.93$, $P < 0.00001$). With a probability cutoff of 90%, the agreement proportions were 1.00 for JDM, 0.96 for DM, 0.95 for ADM, 0.93 for IBM, and 0.88 for PM.

Performance of EULAR/ACR criteria compared with published criteria. Performance of the EULAR/ACR criteria was compared with published criteria for

Table 3. Comparison of physician-diagnosed idiopathic inflammatory myopathy (IIM) subgroups with IIM subgroups defined according to the classification tree among patients meeting the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for IIM*

	Classification tree subgroups†					
	JDM	DM	ADM	IBM	PM	Total
JDM	235	0	0	0	0	235
DM	0	191	6	2	15	214
ADM	1	1	30	0	0	32
IBM	0	0	0	66	5	71
PM	0	7	0	3	131	141
IMNM	0	0	0	0	10	10
Total	236	199	36	71	161	703
% of all IIM	33.6	28.3	5.1	10.1	22.9	–
% of adult IIM	–	42.6	7.7	15.2	34.5	–

* JDM = juvenile dermatomyositis; DM = dermatomyositis; ADM = amyopathic dermatomyositis; IBM = inclusion body myositis; PM = polymyositis; IMNM = immune-mediated necrotizing myopathy.
† Classification of IIM by the EULAR/ACR classification criteria for IIM, using a 55% probability cutofff for classification, followed by the classification tree for subclassification.

IIM (7,8,10,11,14,15) using the IMCCP data set (Table 4). The new criteria including muscle biopsy features displayed high sensitivity (93%) and specificity (88%). There was slightly lower performance without biopsy variables (sensitivity and specificity 87% and 82%, respectively). Among the assessed criteria, the Targoff criteria (11) showed the highest sensitivity (93%) and specificity (89%). Other criteria had either high sensitivity and low specificity (Bohan and Peter [7,8] and Tanimoto criteria [10]), or low sensitivity and high specificity (Dalakas and Hohlfeld [14] and European Neuromuscular Centre [ENMC] criteria [15]).

We studied how different criteria could classify patients with diverse IIM subdiagnoses in the IMCCP data set (Table 4). The EULAR/ACR classification criteria correctly classified most patients with all IIM subdiagnoses. When biopsy data were used, the performance improved for IBM (94% with biopsy data versus 58% without biopsy data) and PM (86% with biopsy data versus 79% without biopsy data). The Bohan and Peter (7,8), Tanimoto (10), and Targoff (11) criteria correctly classified all IIM subdiagnoses except ADM, a diagnosis not included in those criteria. The Dalakas and Hohlfeld criteria (14) could not classify any subdiagnoses. The ENMC criteria (15) correctly classified DM and JDM cases but no other subdiagnoses.

A comparison between the EULAR/ACR classification criteria (55% probability cutoff) and the Bohan and Peter criteria (7,8) showed 89% agreement ($\kappa = 0.71$, $P < 0.00001$) without including muscle biopsy data, and 93% agreement ($\kappa = 0.73$, $P < 0.00001$) using muscle biopsy findings. Comparison between the newly developed criteria and the Targoff criteria (11) demonstrated that the agreement was 89% ($\kappa = 0.74$, $P < 0.00001$) and 93% ($\kappa = 0.82$, $P < 0.00001$) without or with inclusion of muscle biopsy data, respectively.

Validation. *Internal validation.* Using the criteria without muscle biopsy data, 733 observations were used,

Table 4. Performance of the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for idiopathic inflammatory myopathies (IIMs) and existing classification and diagnostic criteria for IIM*

	The EULAR/ACR classification criteria for IIM†						
Performance	Without muscle biopsy	With muscle biopsy	Bohan and Peter (7,8)‡	Tanimoto et al (10)	Targoff et al (11)	Dalakas and Hohlfeld (14)‡	ENMC: Hoogendijk et al (15)‡
Sensitivity, mean (95% CI) %	87 (84–90)	93 (89–95)	98 (96–99)	96 (94–97)	93 (90–95)	6 (5–8)	52 (48–55)
Specificity, mean (95% CI) %	82 (77–87)	88 (83–93)	55 (50–61)	31 (25–37)	89 (84–92)	99 (98–100)	97 (95–98)
Positive predictive value, mean %	90	94	85	80	95	92	96
Negative predictive value, mean %	79	85	90	73	85	43	57
Correctly classified, mean %	86	91	86	79	91	45	70
Correct classification of IIM per subgroup, %§							
Amyopathic dermatomyositis	94	60	25	14	0	0	0
Dermatomyositis	96	98	100	96	99	7	83
Hypomyopathic dermatomyositis	83	100	80	40	67	0	20
Immune-mediated necrotizing myopathy	100	100	100	100	100	0	10
Inclusion body myositis	58	94	97	97	91	1	1
Juvenile dermatomyositis	97	96	100	96	98	5	86
Polymyositis	79	86	95	100	85	11	9

* ENMC = European Neuromuscular Centre; 95% CI = 95% confidence interval.
† Cutoff for probability: 55%.
‡ Definite and probable polymyositis and dermatomyositis.
§ Classification as idiopathic inflammatory myopathy per subgroup out of total number of cases per subgroup, expressed as the mean.

resulting in AUC = 0.942 and cross-validated area = 0.933. Using the criteria with muscle biopsy data, 507 observations were included, resulting in AUC = 0.962 and cross-validated area = 0.942.

External validation for sensitivity. Data from 592 cases (PM = 281, DM = 256, IBM = 33, JDM = 18, and ADM = 4) in the Euromyositis register were used where clinical, laboratory, and muscle biopsy data were available (Karolinska University Hospital, Stockholm, Sweden; Prague Hospital, Prague, Czech Republic; Oslo University Hospital, Oslo, Norway) (Supplementary Table 7, http://onlinelibrary.wiley.com/doi/10.1002/art.40320/abstract). When there was sufficient information available, the EULAR/ACR classification criteria confirmed IIM diagnosis using a 55% probability cutoff for classification of IIM with no misclassification, yielding 100% sensitivity. Using the criteria without muscle biopsies, 489 patients (83%) were classified as IIM, and 103 patients (17%) could not be classified due to missing data. For the criteria with biopsies, 204 (34%) were classified as IIM and 388 (66%) could not be classified due to missing muscle biopsy data in the register. Results for the IBM and PM subgroups improved when biopsy data were included: 97% of IBM cases could be classified, compared with 73% when biopsy data were not included. For PM, 80% and 76%, respectively, could be classified. Raising the IIM classification cutoff from 55% to 90% decreased the total number of cases that could be classified to only 63% (not including muscle biopsies) or 28% (including muscle biopsies) due to absence of some muscle biopsy variables in the Euromyositis registry database.

The Juvenile Dermatomyositis Biomarker Study and Repository (UK and Ireland). The JDRG register included 332 juvenile IIM cases in the study (definite JDM = 292, probable JDM = 20, definite juvenile PM = 4, probable juvenile PM = 2, focal myositis = 6, and other IIM = 8) (Supplementary Table 8, http://onlinelibrary.wiley.com/doi/10.1002/art.40320/abstract). Muscle biopsy data were not available for all; thus the EULAR/ACR classification criteria without muscle biopsy data were used to test sensitivity in this data set. Three hundred seven cases (92%) could be classified using the 55% cutoff and no case was misclassified, yielding 100% sensitivity. The remaining 25 cases (8%) could not be classified due to missing data. Raising the cutoff stepwise to 60%, 70%, 80%, or 90% yielded classification of 92%, 88%, 87%, or 64% cases, respectively, where classification was possible.

Web-calculator. A web-calculator was developed (www.imm.ki.se/biostatistics/calculators/iim) as an aid to use the EULAR/ACR classification criteria. A probability range of classification can be obtained, providing the minimum and maximum probability. In addition to the probabilities acquired, the aggregated scores will be displayed. Whenever sufficient data are entered, the subclassification will be displayed.

Discussion

Classification criteria are essential for inclusion of comparable patients in studies. No validated classification criteria for IIM currently exist. The EULAR/ACR classification criteria for IIM offer advantages that previous criteria lack. They are data-driven, exhibit high sensitivity and specificity, and use a limited number of accessible, defined clinical and laboratory variables. Internal validation and testing in external cohorts confirmed excellent performance. Importantly, the new criteria capture the most frequent IIM subgroups and can be used for both adults and children for research studies and clinical trials.

The new EULAR/ACR classification criteria provide a score with a corresponding probability of having IIM. This provides investigators flexibility in inclusion criteria for different types of studies, for example, clinical trials requiring high specificity would warrant a high probability of IIM in the inclusion criteria, whereas epidemiologic studies requiring high sensitivity would need inclusion criteria with lower probability of IIM.

The new criteria are based on data from children and adults with different ethnicities from centers in Europe, America, and Asia, and use symptoms, signs, and other measures that are routinely assessed. A limitation is still that a majority of the patients were Caucasian, and even though we included data from 298 patients from Asia, we cannot exclude that there can be differences in manifestations between different ethnic groups; hence we still need to validate the criteria in Asian and African populations. Importantly, in patients with a typical DM skin rash, the criteria can be used without muscle biopsy data. For JDM, 97% of patients were correctly classified using the new criteria without muscle biopsy data. The new criteria also offer practical advantages in the number of variables needed to be tested. If a sufficient probability is reached, there is no requirement to test all items. Each criterion is well-defined, lessening the opportunities for ad hoc interpretation. The skin rash typical of DM contributed with high weights in the probability score. Skin biopsy is recommended in the absence of muscle symptoms (33,34). The EULAR/ACR classification criteria are the first myositis criteria to be validated and tested for sensitivity in other cohorts and revealed no misclassification.

Compared with most previous criteria, the new criteria are superior in sensitivity, specificity, and classifi-

cation accuracy. Classification criteria should have high sensitivity and specificity. The EULAR/ACR criteria demonstrated sensitivity and specificity of 87% and 82%, respectively, with even higher accuracy when muscle biopsies were included: 93% and 88%, respectively. Correctly classified patients were 86% and 91%, respectively, with and without inclusion of biopsies, and the criteria performed equally well for adult and juvenile cases. The Targoff criteria (11) also showed good statistical properties, but were not able to capture all subgroups of IIM as ADM patients were not included. Furthermore, the variables were not clearly defined in the Targoff criteria, and testing of more variables is required, including electromyography, which is not always easily accessible and may be painful for patients. Importantly, the EULAR/ACR criteria can be applied to myositis patients with overlap diagnoses, such as mixed connective tissue disease or systemic lupus erythematosus with myositis, since these patients were included among IIM cases.

There are limitations of the study; no controls or comparators were included in the external validation cohort, since the IMCCP study was designed before those recommendations from ACR/EULAR were in place, requiring future validation. A validation study using comparators is underway, but we encourage additional validation studies in different populations. Another limitation largely unavoidable in observational data is the high frequency of missing data in the derivation data set and validation samples, reflecting differences in practice patterns in evaluating patients. Nevertheless, 80% of cases and comparators had muscle biopsy data available, whereas magnetic resonance imaging (MRI) data and electromyography were only available for 38% and 29% of cases, respectively, reflecting their limited usage in clinical diagnosis. However, MRI data and electromyography examination are still important for diagnostic purposes of IIM. Patients studied had to have their disease for at least 6 months, which did not allow us to study new-onset patients. Importantly, these criteria are proposed as classification criteria in research and in clinical trials, not as diagnostic criteria (35).There is also some possibility that the cut points established for probable and definite myositis will need adjustment when tested with new populations of patients.

It took almost 10 years to assemble sufficient numbers of patients with these rare diseases, and 3 subgroups did not have enough subjects to study adequately. During this period, a new IIM subgroup became recognized, IMNM (36), of which only a few cases were included in the study. IMNM cases could thus not be distinguished from PM in the subclassification tree. Another subgroup with few cases was juvenile PM, making a data-derived distinction from JDM impossible. However, pediatric rheumatology experts in the IMCCP recommended that the adult subclassification of IIM could be used for juvenile PM by extrapolation (Figure 2). IBM cases were identified in the subclassification tree by the clinical features of finger flexor weakness and no response to treatment, or by the presence of rimmed vacuoles in muscle biopsies (37).

Another limitation was the low frequency of myositis-specific autoantibodies documented. Five myositis-specific autoantibodies were included: anti–Jo-1, anti–Mi-2, anti–signal recognition particle, anti–PL-7, and anti–PL-12 antibodies, and all were strongly associated with IIM. However, only anti–Jo-1 autoantibody had a significant number of observations (n = 1,062) to permit analyses and inclusion in the classification criteria. A future update of the EULAR/ACR classification criteria should include the more recently-identified myositis-specific autoantibodies (21,22), in addition to more patients with IMNM, ADM, hypomyopathic DM, and juvenile cases other than JDM.

Recommendations

- Patients with pathognomonic skin rashes (heliotrope rash, Gottron's papules, and/or Gottron's sign) of JDM or DM are accurately classified with the EULAR/ACR classification criteria without including muscle biopsy data. For patients without these skin manifestations, muscle biopsy is recommended. For DM patients without muscle involvement, a skin biopsy is recommended.
- The EULAR/ACR classification criteria provide a score and a corresponding probability of having IIM. Each probability displays a unique sensitivity and specificity. The best balance between sensitivity and specificity can be found for a probability of 55–60% (total aggregated score of ≥5.5 and ≤5.7) for the criteria not including muscle biopsy data, and 55–75% (total aggregated score ≥6.7 and ≤7.6) when including muscle biopsies. These cases are designated "probable IIM." The recommended cutoff needed for classifying a patient as having IIM is ≥55%.
- "Definite IIM" corresponds to a probability of ≥90% or a total aggregate score of 7.5 or more without muscle biopsy and 8.7 with muscle biopsy, and is recommended in studies where a high specificity is required.
- A patient is termed "possible IIM" if the probability is ≥50% and <55% (a minimum score of 5.3 without biopsies and 6.5 with biopsies).
- For clarity and transparency, both the descriptive term ("possible," "probable," or "definite") and the probability and the aggregated score should be reported in studies.

Conclusions

New classification criteria for IIM and the major IIM subgroups have been developed. These data-driven criteria have a good feasibility, high sensitivity and specificity, have been partly validated in external cohorts, and are superior to previous criteria in capturing different subgroups of IIM. Revision of the criteria in the future will be important when additional validated myositis autoantibody tests, imaging, and other tests are available in more IIM cases and comparator cases without IIM.

ACKNOWLEDGMENTS

We thank Elin Forslund for assistance with data registration. We thank Dr. Andrew Mammen and Dr. Mike Ward for critical reading of the manuscript. We are grateful for contribution of clinical data from investigators and for participants contributing with valuable input at IMCCP meetings.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Lundberg had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Lundberg, Tjärnlund, Bottai, Werth, Pilkington, de Visser, Alfredsson, Amato, Barohn, Liang, Singh, Dankó, Feldman, Kohsaka, Lachenbruch, Lang, Miller, Rider.

Acquisition of data. Lundberg, Tjärnlund, Bottai, Werth, Pilkington, de Visser, Alfredsson, Amato, Barohn, Liang, Singh, Aggarwal, Arnardottir, Chinoy, Cooper, Dankó, Dimachkie, Feldman, Garcia-De La Torre, Gordon, Hayashi, Katz, Kohsaka, Lachenbruch, Lang, Li, Oddis, Olesinska, Reed, Rutkowska-Sak, Sanner, Selva-O'Callaghan, Song, Vencovsky, Ytterberg, Miller, Rider, International Myositis Criteria Consortium working committee members.

Analysis and interpretation of data. Lundberg, Tjärnlund, Bottai, Werth, Pilkington, de Visser, Alfredsson, Amato, Barohn, Liang, Singh, Aggarwal, Feldman, Garcia-De La Torre, Gordon, Kohsaka, Lachenbruch, Lang, Li, Miller, Rider.

REFERENCES

1. Plotz PH, Rider GL, Targoff IN, Raben N, O'Hanlon TP, Miller FW. Myositis: immunologic contributions to understanding cause, pathogenesis, and therapy. Ann Intern Med 1995;122:715–24.
2. Dalakas MC. Inflammatory muscle diseases. N Engl J Med 2015;372:1734–47.
3. Rider LG, Giannini EH, Brunner HI, Ruperto N, James-Newton L, Reed AM, et al. International consensus on preliminary definitions of improvement in adult and juvenile myositis. Arthritis Rheum 2004;50:2281–90.
4. Oddis CV, Rider LG, Reed AM, Ruperto N, Brunner HI, Koneru B, et al. International consensus guidelines for trials of therapies in the idiopathic inflammatory myopathies. Arthritis Rheum 2005; 52:2607–15.
5. Medsger TA Jr, Dawson WN Jr, Masi AT. The epidemiology of polymyositis. Am J Med 1970;48:715–23.
6. DeVere R, Bradley WG. Polymyositis: its presentation, morbidity and mortality. Brain 1975;98:637–66.
7. Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). N Engl J Med 1975;292:344–7.
8. Bohan A, Peter JB. Polymyositis and dermatomyositis (second of two parts). N Engl J Med 1975;292:403–7.
9. Griggs RC, Askanas V, DiMauro S, Engel A, Karpati G, Mendell JR, et al. Inclusion body myositis and myopathies. Ann Neurol 1995;38:705–13.
10. Tanimoto K, Nakano K, Kano S, Mori S, Ueki H, Nishitani H, et al. Classification criteria for polymyositis and dermatomyositis. J Rheumatol 1995;22:668–74.
11. Targoff IN, Miller FW, Medsger TA Jr, Oddis CV. Classification criteria for the idiopathic inflammatory myopathies. Curr Opin Rheumatol 1997;9:527–35.
12. Mastaglia FL, Phillips BA. Idiopathic inflammatory myopathies: epidemiology, classification, and diagnostic criteria. Rheum Dis Clin North Am 2002;28:723–41.
13. Van der Meulen MF, Bronner IM, Hoogendijk JE, Burger H, van Venrooij WJ, Voskuyl AE, et al. Polymyositis: an overdiagnosed entity. Neurology 2003;61:316–21.
14. Dalakas MC, Hohlfeld R. Polymyositis and dermatomyositis. Lancet 2003;362:971–82.
15. Hoogendijk JE, Amato AA, Lecky BR, Choy EH, Lundberg IE, Rose MR, et al. 119th ENMC international workshop: trial design in adult idiopathic inflammatory myopathies, with the exception of inclusion body myositis, 10–12 October 2003, Naarden, The Netherlands. Neuromuscul Disord 2004;14:337–45.
16. Troyanov Y, Targoff IN, Tremblay JL, Goulet JR, Raymond Y, Senécal JL. Novel classification of idiopathic inflammatory myopathies based on overlap syndrome features and autoantibodies: analysis of 100 French Canadian patients. Medicine (Baltimore) 2005;84:231–49.
17. Miller FW, Rider LG, Plotz PH, Rutkove SB, Pestronk A, Wortmann RL, et al. Polymyositis: an overdiagnosed entity [letter]. Neurology 2004;63:402.
18. Bradley WG. Polymyositis: an overdiagnosed entity [letter]. Neurology 2004;63:402.
19. Hengstman GJ, van Engelen BG. Polymyositis: an overdiagnosed entity [letter]. Neurology 2004;63:402–3.
20. Engel AG, Arahata K. Mononuclear cells in myopathies: quantitation of functionally distinct subsets, recognition of antigen-specific cell-mediated cytotoxicity in some diseases, and implications for the pathogenesis of the different inflammatory myopathies. Hum Pathol 1986;17:704–21.
21. Betteridge Z, McHugh N. Myositis-specific autoantibodies: an important tool to support diagnosis of myositis. J Intern Med 2016;280:8–23.
22. Rider LG, Nistala K. The juvenile idiopathic inflammatory myopathies: pathogenesis, clinical and autoantibody phenotypes, and outcomes. J Intern Med 2016;280:24–38.
23. Love LA, Leff RL, Fraser DD, Targoff IN, Dalakas M, Plotz PH, et al. A new approach to the classification of idiopathic inflammatory myopathy: myositis-specific autoantibodies define useful homogeneous patient groups. Medicine (Baltimore) 1991;70: 360–74.
24. Classification and Response Criteria Subcommittee of the American College of Rheumatology Committee on Quality Measures. Development of classification and response criteria for rheumatic diseases [editorial]. Arthritis Rheum 2006;55:348–52.
25. Dougados M, Gossec L. Classification criteria for rheumatic diseases: why and how? Arthritis Rheum 2007;57:1112–5.
26. Van de AH, Delbecq AL. The effectiveness of nominal, delphi, and interacting group decision making processes. Acad Manage J 1974;17:605–21.
27. Fink A, Kosecoff J, Chassin M, Brook RH. Consensus methods: characteristics and guidelines for use. Am J Public Health 1984; 74:979–83.
28. Ruperto N, Meiorin S, Iusan SM, Ravelli A, Pistorio A, Martini A. Consensus procedures and their role in pediatric rheumatology. Curr Rheumatol Rep 2008;10:142–6.

29. Totikidis V. Applying the Nominal Group Technique (NGT) in community based action research for health promotion and disease prevention. Aust Community Psychol 2010;22:18–29.
30. ARA Glossary Committee. Dictionary of the rheumatic diseases. Vol. I. Signs and symptoms. New York: Contact Associates International; 1982.
31. ARA Glossary Committee. Dictionary of the rheumatic diseases. Vol. II. Diagnostic testing. New York: Contact Associates International; 1985.
32. Efron B, Tibshirani R. Improvements on cross-validation: the 632+ bootstrap method. J Am Stat Assoc 1997;92:548–60.
33. Hsiung SH, Chan EF, Elenitsas R, Kolasinski SL, Schumacher HR, Werth VP. Multicentric reticulohistiocytosis presenting with clinical features of dermatomyositis. J Am Acad Dermatol 2003; 48 Suppl 2:S11–4.
34. Fett N, Liu RH. Multicentric reticulohistiocytosis with dermatomyositis-like features: a more common disease presentation than previously thought. Dermatology 2011;222:102–8.
35. Aggarwal R, Ringold S, Khanna D, Neogi T, Johnson SR, Miller A, et al. Distinctions between diagnostic and classification criteria? Arthritis Care Res (Hoboken) 2015;67:891–7.
36. Casciola-Rosen L, Mammen AL. Myositis autoantibodies. Curr Opin Rheumatol 2012;24:602–8.
37. Lloyd TE, Mammen AL, Amato AA, Weiss MD, Needham M, Greenberg SA. Evaluation and construction of diagnostic criteria for inclusion body myositis. Neurology 2014;83:426–33.