Exploring Road of Classification Criteria for Idiopathic Inflammatory Myopathy

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Key words: Autoimmune Diseases; Criteria; Dermatomyositis; Polymyositis

Idiopathic inflammatory myopathies (IIMs) are heterogeneous disorders characterized by chronic muscle weakness and muscle fatigue and mononuclear cell infiltration into skeletal muscle.[1] The most common subgroups in adults are dermatomyositis (DM), polymyositis (PM), amyopathic DM (ADM), inclusion body myositis (IBM), and juvenile DM (JDM). Several diagnostic or classification criteria for IIM have been developed.[2‑5] Classification criteria are mostly used in research and clinical trials, not daily in practice. Great efforts have been dedicated in pursuing new criteria in the past decades.

Development of Classification Criteria in Idiopathic Inflammatory Myopathy

More than four decades ago, Bohan and Peter proposed a set of five criteria to facilitate the diagnosis of IIM patients.[2,3] DM and PM were differentiated by the presence of DM skin rashes for the first time. Definitions for “definite,” “possible,” and “probable” diagnosis for each subset were proposed, and exclusion criteria to eliminate IIM mimickers were provided. These criteria have been widely used in clinical practice due to its feasibility and simplicity.

The discovery of myositis-specific autoantibodies (MSAs) and myositis-associated autoantibodies (MAAs) has led to the proposal of a serologic approach to complement the Bohan and Peter classification system, as significantly associations of MSAs with clinical features were observed.[6] Certainly, the addition of autoantibody profiles, characteristic histopathologic features, and magnetic resonance imaging (MRI) could significantly strengthen the current criteria and better define these disorders.[7‑11]

A classification of IIM was proposed by Love et al.[6] in 1991 based on MSAs. The “anti-synthetase syndrome” was well described in this classification which refers to association of interstitial lung disease (ILD), myositis, fever, mechanic’s hand, arthritis, and antisynthetase autoantibody positivity. Tanimoto et al.[9] outlined a new set of nine criteria in a few years later to classify patients as either DM or PM based on a multicenter retrospective study with chart review and questionnaires. The criteria added one disease-specific criterion, anti-Jo-1 antibody, but the diagnosis of IIM can be made without this antibody. In 1997, Targoff et al.[12] published new modifications to Bohan and Peter criteria with the goal of improving sensitivity and utility of the original criteria which added MSAs (antisynthetase, anti-Mi-2, and anti-signal recognition particle [SRP]). The revised criteria could allow the diagnosis of definite PM without a biopsy if myositis-related autoantibodies are identified.

For decades, ADM has been recognized by clinicians. ADM was integrated in the revised Dalakas criteria in 2003. One year later, the European Neuromuscular Center (ENMC) criteria published with clinical and laboratory criteria for IIM classification, which included seven IIM subset: IBM, PM, DM, ADM, possible DM sine dermatitis, nonspecific myositis, and immune-mediated necrotizing myopathy (IMNM).[13] In 2005, Troyanov et al.[15] published a clinic-serological IIM classification which considered overlap features, such as ILD, arthritis, or Raynaud phenomenon, as key components of the classification scheme. The classification included four subsets: overlap

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How to cite this article: Li YH, Wang GC, Li ZG. Exploring Road of Classification Criteria for Idiopathic Inflammatory Myopathy. Chin Med J 2018;131:2773-5.
myositis, pure DM, pure PM, and cancer-associated myositis.

**THE LATEST EUROPEAN LEAGUE AGAINST RHEUMATISM/AMERICAN COLLEGE OF RHEUMATOLOGY CLASSIFICATION CRITERIA**

New criteria of IIM studied by International Myositis Classification Criteria Project were released in 2017 with improved sensitivity and specificity by 93% and 88% with muscle biopsy.[14] It is consistent with recent recognized subgroups, clinical ADM and IMNM.

These new criteria are based on data from 976 IIM patients and 624 non-IIM patients with mimicking conditions. All the cases were collected from 46 sites between 2008 and 2011. The criteria consist of 16 variables including clinical features, laboratory measurements, and histological result of muscle. Each item is assigned a weighted score. The total score corresponds to a probability of having IIM. Patients can be further subclassified into PM, IBM, DM, ADM, JDM, or other juvenile myositis according to a classification tree. A web calculator was published as an aid to score the new criteria (www.imm.ki.se/biostatistics/calculators/iim).

The new European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria provide a score with a corresponding probability of having IIM. Compared to most previous criteria, the new criteria are superior in sensitivity, specificity, and classification accuracy [Table 1]. In EULAR/ACR criteria, about 10% of cases were contributed from China.

**NON-INVASIVE CRITERIA: INEVITABLE IN IDIOPATHIC INFLAMMATORY MYOPATHY**

There are limitations of new criteria. First, these criteria do not include MSAs except anti-Jo-1 antibody commonly used in practice and the criteria cannot distinguish the difference between PM and IMNM which are still in the same subgroup. Therefore, the recently held 224th ENMC further clarified IMNM[13] and new items for IMNM were added. The new criteria emphasized the purpose of anti-SRP and anti-HMGCR autoantibodies. If both autoantibodies are negative, then clinical (proximal muscle weakness and high creatine kinase) and pathological requirements (necrotic fibers, myophagocytosis, regeneration, and pauci lymphocytic infiltrate) need to be satisfied.

MRI is important for diagnostic purposes of IIM, whereas MRI data were only collected available for 38% of cases in new criteria. Another limitation of EULAR/ACR criteria for IIM is that the score system was complicated for clinicians, so these criteria are proposed as classification criteria in research and in clinical trials, not proposed as diagnostic criteria.

In summary, many experts have proposed various classification criteria for IIM and have provided contributions to IIM disease. Bohan and Peter criteria continue to be widely used and provided deep understanding of IIM to rheumatologists. The new IIM classification criteria which published by IMACS is a valuable addition to IIM disease with high accuracy. However, a future update of the classification criteria should include more noninvasive method such as recent-identified MSAs, biomarkers, muscle ultrasound, and artificial intelligence.

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