



Published Classification Criteria for Idiopathic Inflammatory Myopathies

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The Problem

“The Master said,... If names are not correct, language is not in accordance with the truth of things. If language is not in accordance with the truth of things, affairs cannot be carried out to success.... Therefore a superior man considers it necessary that the names he uses be spoken appropriately.... What the superior man requires, is just that in his words there may be nothing incorrect.”

Confucius, Chinese sage and philosopher, 551-479 BC, from Book XIII

Chronology of Published Diagnostic/Classification Criteria for IIM

- Medsger et al. 1970, Am. J. Med 48:715 (IIM)
- DeVere & Bradley 1975, Brain 98:637 (IIM)
- Bohan & Peter 1975, NEJM 292:344 and 403 (PM/DM)
- Dalakas 1991, NEJM 325:1487 (PM/DM/IBM)
- Griggs et al. 1995, Ann Neurol 38:705 (IBM)
- Tanimoto et al. 1995, J Rheum 22:668 (PM/DM)
- Targoff et al. 1997, Curr Opin Rheum 9:527 (IIM)
- Mastaglia & Phillips 2002, RDCNA 28:723 (PM/DM/IBM)
- Van der Meulen et al. 2003, Neurol 61:316 (PM/DM/other)
- Dalakas & Hohlfeld 2003, Lancet 362:971 (PM/DM)
- Hoogendijk, Amato et al. 2003, Neuro Dis 14:337 (PM/DM)

Early Published Classification Criteria for PM/DM

- Medsger et al. 1970
 - Weakness
 - Inflammatory biopsy
 - Typical EMG changes
 - Enzyme elevations
 - Response to corticosteroids
- DeVere & Bradley 1975
 - Weakness
 - Muscle pain and tenderness
 - Inflammatory biopsy
 - Typical EMG changes
 - CK elevation

Bohan and Peter 1975 PM/DM Criteria

First rule out all other forms of myopathy!

- Symmetrical weakness, usually progressive, of the limb-girdle muscles
- Muscle biopsy evidence of myositis
 - Necrosis of type I and type II muscle fibers, Phagocytosis, Degeneration and regeneration of myofibers with variation in myofiber size, Endomysial, perimysial, perivascular or interstitial mononuclear cells
- Elevation of serum levels of muscle-associated enzymes
 - CK, Aldolase, LD, Transaminases (ALT/SGPT and AST/SGOT)
- Electromyographic triad of myopathy
 - Short, small, low-amplitude polyphasic motor unit potentials
 - Fibrillation potentials, even at rest
 - Bizarre high-frequency repetitive discharges
- Characteristic rashes of dermatomyositis

Definite PM=all first 4, probable PM=3 of first 4, possible PM=2 of 4;

Definite DM= rash + 3 other; probable DM=rash + 2 other; possible DM=rash + 1 other

Bohan and Peter PM/DM Criteria Limitations

- Case series and data developed from a single institution and based on clinical observations
- No clear instructions as to how to rule out all other forms of myopathy – IBM had not yet been identified
- Degree or number of abnormalities of each criterion not specified and are observer-dependent
- Most criteria non-specific
- Characteristic rashes of dermatomyositis not specified
- Sensitivity and specificity not studied for many confounding dermatologic or neuromuscular conditions
- However, in a cohort of PM/DM, SSc and SLE subjects, sensitivity = 93% and specificity = 93% (Oddis & Medsger 1995, Clin Rheum 9:497)

Dalakas 1991 PM/DM/IBM Criteria

Essentially repeated Bohan and Peter criteria but added specificity to some characteristics and made probable disease focused on unclear biopsy results

- Symmetrical weakness, usually progressive, of the limb-girdle muscles
- Muscle biopsy evidence of the specific type of myositis – PM, DM or IBM
- Elevation of enzymes
- Electromyographic triad of myopathy
- Rashes

Definite disease = all present

Probable disease = all but diagnostic biopsy

Tanimoto et al. 1995

Classification Criteria for PM and DM

Multicenter retrospective study by questionnaire in Japanese Dermatology, Neurology, Rheumatology academic centers assessing many features (see handout)

- Rashes – Heliotrope rash or Gottron's sign or linear extensor erythema
- Proximal weakness, UE or LE and trunk
- Elevation of CK or Aldolase
- Muscle pain on grasping or spontaneous muscle pain
- Electromyographic triad of myopathy
- Anti-Jo-1 autoantibody
- Non-destructive arthritis or arthralgias
- Systemic inflammatory signs (fever >37 at axilla, elevated CRP or ESR)
- Muscle biopsy evidence of myositis
 - Inflammatory infiltrate with degeneration or necrosis of muscle, active phagocytosis, central nuclei or active regeneration

Definite PM= any 4 of 9 without rash (sensitivity = 99% [180/182]; specificity of PM and DM against all other diseases = 95% [373/392])

Definite DM = rash + 4 others (sensitivity = 94% [127/135]; specificity against SLE and SSc skin lesions = 90% [214/237])

Tanimoto et al. Classification Criteria

Limitations

- Although rheumatologists, neurologists and dermatologists were included, their experience and training in myositis and consistency of evaluation and completion of questionnaires are unclear
- There were limited numbers and types of alternative disorders and IBM, CAM and JIIM were excluded
- Based on questionnaires and retrospective chart reviews
- PM diagnosed only by rheumatologists and neurologists; DM diagnosed only by dermatologists and rheum
- Assessment of anti-Jo-1 not clear – likely ELISA which has sensitivity and specificity problems
- Gottron's papules not assessed?

Targoff et al. 1997

Proposed Criteria for IIM

- First exclude all non-inflammatory myopathies by state-of-the art methods (will change over time)
- 6 primary classification criteria for IIM
 - 5 per Bohan and Peter – but with DM specifically defined by Heliotrope rash or Gottron's papules or Gottron's sign - plus
 - Any of the myositis-specific autoantibodies now commercially available performed by a validated assay: anti-synthetase, anti-Mi-2 or anti-SRP
- Definitions of IIM
 - Definite IIM = any 4 of the 6 criteria
 - Probable IIM = any 3 of the 6 criteria
 - Possible IIM = any 2 of the 6 criteria
- Subclassification criteria - DM defined by any one of the rashes above; IBM defined by also meeting Griggs et al. 1995 criteria; JIIM defined by age of onset <18, amyopathic DM by AAD criteria, etc.)
- Further study is needed to develop new criteria for the future including: other specific signs, symptoms, biopsy findings, MRI, genetics (HLA DR3 already shown to be useful in IBM)

Van der Meulen et al. 2003 Criteria

- Of 269 retrospective subjects, 103 excluded due to IBM or other myopathies, insufficient data, no biopsy - leaving 165 for study
- Definite PM (seen in 9/5%)
 - CK > 2X ULN
 - Mononuclear cells (MNC) surrounding (ideally invading) endomysial myofibers
- Definite DM (seen in 54/33%)
 - “Typical skin rash” or perifascicular atrophy
- Unspecified myositis (seen in 38/23%)
 - Perimysial or perivascular MNC without endomysial MNC or perifascicular atrophy or rash
- Possible myositis (seen in 29/18%)
 - CK > 2X ULN and necrotizing myopathy with few or no MNC
- Each category further subdivided into isolated myositis or CTM (with defined CTD) or CAM (cancer within 2 yrs of myositis Dx)
- Conclusion = PM is an over diagnosed entity and other categories of myositis should be established

Mastaglia & Phillips 2002, Hoogendijk, Amato et al. 2003, Dalakas & Hohlfeld 2003

- For these criteria sets see handouts

IIM Criteria Summary

- Many diagnostic/classification criteria have been proposed for different forms of IIM over the last 3 decades
- Most have been based on clinical impressions rather than data analyses and none have been fully tested for sensitivity or specificity using appropriately powered studies against all the appropriate disease confounders
- Recent splits in criteria by different specialties threaten to create difficulties in comparing studies and clinical trials in the future
- New large, multicentered and multispecialty studies and analyses are needed to meet this need