PROGRESS REPORT ON THE DEVELOPMENT OF NEW CLASSIFICATION CRITERIA FOR ADULT AND JUVENILE IDIOPATHIC INFLAMMATORY MYOPATHIES

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WHY DO WE NEED NEW CRITERIA?

There is no consensus on the classification of idiopathic inflammatory myopathies. Novel disease entities such as necrotising autoimmune myopathy and a/hypomyopathic dermatomyositis are identified, and

The Bohan and Peter criteria which are still often used are unspecific; they do not distinguish PM from IBM or from mimics, and

Drugs in the pipeline

AIMS

Develop criteria for use by basic and clinical researchers that distinguish idiopathic inflammatory myopathies (IIM) from other major mimicking conditions with high sensitivity and specificity; and

Develop criteria for use by basic and clinical researchers that separate the major subgroups of the IIM from each other with high sensitivity and specificity, and

Test reliability of new classification criteria

Combined effort to address both adult-onset and childhood-onset myositis

PROCESS

A retrospective study

A total of 75 clinical and laboratory variables were to be collected in a web-based questionnaire.

Crude pair-wise associations among all variables measured and between each variable and clinician's diagnosis assessed.

Sample size (aim)

- 1000 myositis patients (200 per major subgroup)
  - Actual: 973 myositis (245 PM, 239 DM, 176 IBM, and 246 JDM, 67 others; Amyopathic and Hypomyopathic DM, immune mediated necrotizing myopathy, IMNM)
- 1000 comparators (700 adult, 300 juvenile) with mimicking conditions
  - Actual: 629 mimickers (509 adults, 120 children)

Process cont'd

Analysis

1. Traditional: case defined by specified number of items from a set
2. Probability/Risk score: patient assigned a probability risk score by summing score-points associated with the variables

Validation

- Internal validation
- External validation

INCLUSION CRITERIA

Idiopathic Inflammatory Myopathy

i. The subject has been diagnosed for at least 6 months.
ii. The physician is certain of the diagnosis – only cases with known idiopathic inflammatory myopathy (IIM) or, as comparators, known non-IIM cases who do not have myositis but where myositis could be within the general differential diagnosis.
iii. The patients in whom most complete data are available.
iv. The most recent cases are chosen first – these would likely result in more consistent evaluations and therapy.

Comparator cases

- Dystrophies
- Drug/toxin associated myopathies
- Metabolic myopathies
- Mitochondrial myopathies
- Endocrine myopathies
- Rheumatic conditions
- Dermatologic conditions

THE INTERNATIONAL MYOSITIS CLASSIFICATION CRITERIA PROJECT VARIABLES

- Demographic data
  - Gender
  - Age
  - Ethnicity
- Clinical muscle variables
  - Pattern of weakness
- Skin manifestations
- Muscle biopsy
  - Histopathology
  - Immunohistochemistry
  - Electron microscopy
- Other clinical variables
  - ILD
  - Dysphagia
  - Response to treatment
- Laboratory data
  - Muscle enzymes
  - Autoantibodies
- Electromyogram (EMG)
- Magnetic resonance imaging (MRI)

GEOGRAPHIC DISTRIBUTION
47 CENTERS IN 21 COUNTRIES

NORTH AMERICA	**17**
Canada	2
Mexico	1
USA	14
SOUTH AMERICA	**1**
Brazil	1

EUROPE	**23**
Czech Republic	2
Denmark	1
France	1
Germany	1
Greece	1
Hungary	2
Italy	1
Netherlands	2
Norway	1
Poland	2
Spain	1
Sweden	3
Switzerland	1
UK	4

ASIA	**6**
China	1
Japan	4
South Korea	1

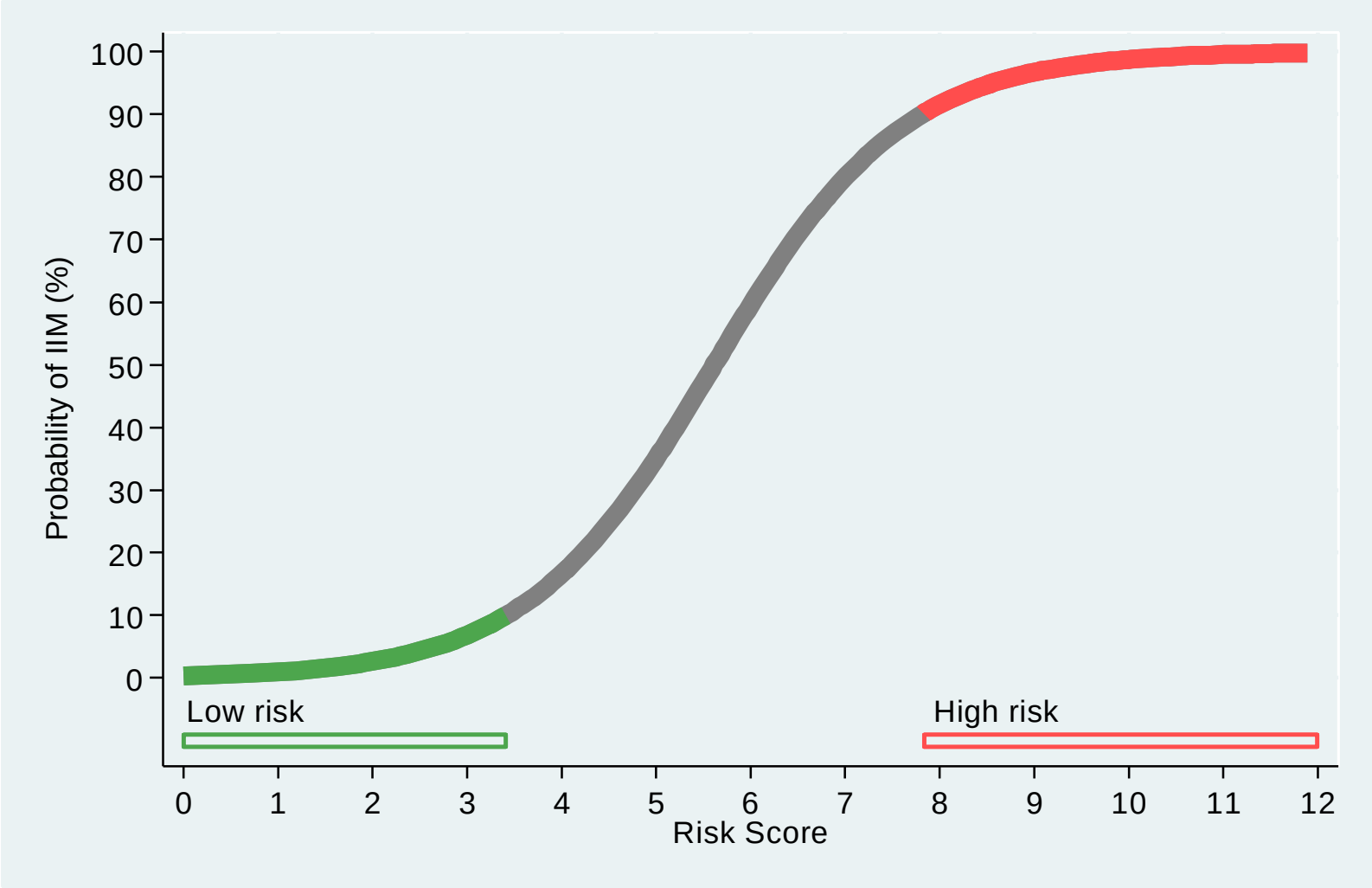
PROBABILITY/RISK SCORE

VARIABLE	SCORE POINTS
18 ? Age of onset of first symptom < 40	1.6
Age of onset of first symptom ?ƒ40	2.3
Clinical Muscle Variables	
Objective symmetric weakness, usually progressive, of the proximal upper extremities	0.7
Objective symmetric weakness, usually progressive, of the proximal lower extremities	0.6
Neck flexors are relatively weaker than neck extensors	1.6
In the legs proximal muscles are relatively weaker than distal muscles	1.5
Skin variables	
Heliotrope rash	3.3
Gottron´s papules	2.3
Gottron's sign	3.4
Other Clinical Variables	
Dysphagia or esophageal dysmotility	0.7

PROBABILITY/RISK SCORE

Cont'd VARIABLE	SCORE POINTS
Laboratory Variables	
Serum creatine kinase activity (CK) activity or, Serum lactate dehydrogenase (LDH) activity or, Serum aspartate aminotransferase (ASAT/AST/SGOT) activity or, Serum alanine aminotransferase (ALAT/ALT/SGPT) activity	1.2
Anti-Jo-1 (anti-His) antibody positive	4.2
Score-sum from above items*	0.9
Muscle Biopsy Variables	
Endomysial infiltration of mononuclear cells surrounding, but not invading, myofibers	1.4
Perimysial and/or perivascular infiltration of mononuclear cells	1.2
Perifascicular atrophy	1.6
Rimmed vacuoles	2.2
** When muscle biopsies are available, multiply the score-sum of all other variables by 0.9 and then add the scores of the positive biopsies.*	

PROBABILITY/RISK SCORE



PERFORMANCE

PERFORMANCE OF NEW AND EXISTING CLASSIFICATION / DIAGNOSTIC CRITERIA FOR IIM								
Performance (%)	Probability/Risk Score [a]			Bohan & Peter[b]	Tanimoto *et al*.	Targoff *et al*.[b]	Dalakas & Hohlfeld[b]	Hoogendijk *et al*.[b]
	Without muscle biopsy data	With muscle biopsy data						
Sensitivity	87	88		98	96	93	6	51
Specificity	88	89		55	31	88	99	96
Correctly classified	87	88		86	79	91	45	70

[a] Cut point for probability: 55%

[b] Definite and probable polymyositis and dermatomyositis

PERFORMANCE

Current subgroups (%)	Probability/Risk Score		Bohan& Peter	Tanimoto *et al*.	Targoff *et al*.	Dalakas & Hohlfeld	Hoogen dijk *et al*.
	Without muscle biopsy data	With muscle biopsy data					
Amyopathic DM	86	80	25	14	0	0	0
DM	95	96	100	96	99	8	83
Hypomyopathic DM	83	100	80	40	67	0	20
IMNM	100	100	100	100	100	0	11
IBM	78	95	97	97	91	1	1
JDM	97	95	100	96	97	5	86
PM	73	74	95	99	84	11	8
Non IIM	12	9	45	69	12	1	4

UPCOMING

2013:

Validation of new criteria (ongoing)

- Internal validation using bootstrap method
- Other cohorts (Euromyositis register, Juvenile DM Register UK and Ireland)

Consensus on new classification criteria

Post consensus:

Dissemination and implementation of new classification criteria, publications

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CARRA

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