I nuovi criteri ACR/EULAR per la classificazione dell’artrite reumatoide

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Topics

• 1987 ACR classification criteria for RA
• Classification versus diagnostic criteria
• Limits of 1987 RA criteria
• 2010 ACR/EULAR classification criteria for RA
• Advantages of 2010 criteria
• Limitations of 2010 criteria
# The 1987 ACR Criteria for the Classification of RA

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Morning stiffness</td>
<td>Morning stiffness in and around the joints, lasting at least 1 h</td>
</tr>
<tr>
<td>2. Arthritis in 3 or more joint areas (right or left PIP, MCP, wrist, elbow, knee, ankle, MTP)</td>
<td>Soft tissue swelling or fluid (not bony overgrowth) observed by a physician, present for at least 6 weeks</td>
</tr>
<tr>
<td>3. Arthritis of hand joints</td>
<td>Swelling of wrist, MCP or PIP for at least 6 weeks</td>
</tr>
<tr>
<td>4. Symmetric arthritis</td>
<td>Simultaneous involvement of the same joint areas (defined in 2) on both sides of the body for at least 6 weeks</td>
</tr>
<tr>
<td>5. Rheumatoid nodules</td>
<td>Subcutaneous nodules over bony prominences, extensor surfaces or in juxta-articular regions, observed by a physician</td>
</tr>
<tr>
<td>6. Rheumatoid factor</td>
<td>Detected by a method positive in less than 5% of normal controls</td>
</tr>
<tr>
<td>7. Radiographic changes</td>
<td>Typical of RA on posteroanterior hand and wrist radiographs (erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints)</td>
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</tbody>
</table>

At least 4 criteria must be fulfilled for classification for RA.
Diagnostic and/or Classification Criteria

Diagnostic Criteria
Not established
No disease marker

Classification Criteria

Sensitivity

Specificity
The Treatment Paradigm for RA is Shifting Towards Early Intervention and Prevention

- The need to initiate treatment early in order to prevent irreversible damage and loss of function has led to an increasing emphasis on early diagnosis and intervention.

Strategie terapeutiche
Le novità “evidence based”

• Il danno articolare è un evento precoce
• Ritardare anche di poco l’inserimento di un farmaco di fondo peggiora l’esito
• Un trattamento precoce aggressivo rallenta l’evoluzione

Fase iniziale = “a window of opportunity”
Some points to consider

• The rate of spontaneous remission in recent-onset UA is 40-50%
• Only one third of pts with UA will develop RA
• MTX treatment in patients with early UA hampers progression to RA and progression of joint damage
• Ideally, only the patients with UA in whom RA develops would be treated with DMARDs,
• Avoid to treat patients with UA who remits spontaneously

Major goal of RA criteria

• We need criteria:
  - that are able to identify, among pts with newly presenting UA, a subset with high risk of chronicity and erosive damage
  - that can be used as a basis for starting DMARD therapy
Limits of 1987 ACR criteria for RA

• The 1987 criteria were based on patients in whom the average disease duration was 7 years.
• These criteria were derived by trying to discriminate patients with established RA from those with other rheumatological conditions.
• They lack of sensitivity in early disease.

Cohen and Emery, Arthritis Rheum 2010
Limits of 1987 ACR criteria for RA

- The studies regarding the importance of Ab to citrullinated proteins in RA occurred subsequent to these criteria
- ACPAs are present before the onset of RA symptoms and are predictive of RA development
- ACPA assays are a valuable diagnostic test early in the course of disease

Aggarwal et al, Arthritis Rheum 2009
2010 Rheumatoid Arthritis Classification Criteria

An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative


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 external data set. All ACR/EULAR-approved criteria sets are expected to undergo intermittent updates.

The American College of Rheumatology is an independent, professional, medical and scientific society which does not guarantee, warrant, or endorse any commercial product or service.
Aims of 2010 ACR/EULAR RA classification criteria

- To provide a standardized approach for discriminating, from population of individuals presenting with UA, the subgroup with the highest probability of persistent or erosive RA, who may be enrolled into clinical trials and other studies through the use of uniform criteria

Aletaha et al, Arthritis Rheum 2010
Aims of 2010 ACR/EULAR RA classification criteria

• Not to develop diagnostic criteria

• Not to provide a referral tool for primary care physicians

• To facilitate the study of persons at earlier stages of the disease

• To identify patients who would benefit from early effective intervention

Aletaha et al, Arthritis Rheum 2010
## The 2010 ACR/EULAR classification criteria for RA

<table>
<thead>
<tr>
<th>Target population (Who should be tested?): Patients who</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) have at least 1 joint with definite clinical synovitis (swelling)</td>
<td></td>
</tr>
<tr>
<td>2) with the synovitis not better explained by another disease</td>
<td></td>
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</tbody>
</table>

### Classification criteria for RA (score-based algorithm: add score of categories A-D; a score ≥ 6/10 is needed for classification of a patient as having definite RA)

<table>
<thead>
<tr>
<th>A. Joint involvement</th>
<th>Score</th>
</tr>
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<tbody>
<tr>
<td>1 large joint</td>
<td>0</td>
</tr>
<tr>
<td>2-10 large joints</td>
<td>1</td>
</tr>
<tr>
<td>1-3 small joints (with or without involvement of large joints)</td>
<td>2</td>
</tr>
<tr>
<td>4-10 small joints (with or without involvement of large joints)</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 10 joints (at least 1 small joint)</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. Serology (at least 1 test result is needed for classification)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative RF and negative ACPA</td>
<td>0</td>
</tr>
<tr>
<td>Low-positive RF or low-positive ACPA</td>
<td>2</td>
</tr>
<tr>
<td>High-positive RF or high positive ACPA</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C. Acute-phase reactants (at least 1 test result is needed for classification)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal CRP and normal ESR</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal CRP or abnormal ESR</td>
<td>1</td>
</tr>
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</table>

<table>
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<tr>
<th>D. Duration of symptoms</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 6 weeks</td>
<td>0</td>
</tr>
<tr>
<td>≥ 6 weeks</td>
<td>1</td>
</tr>
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</table>

Classification as “definite RA” is based on the achievement of a total score of 6
Some points to consider

• The criteria are aimed at classification of newly presenting patients
• Patients with erosive disease typical of RA with a history compatible with prior fulfilment of the 2010 criteria should be classified as having RA
• Patients with longstanding disease, including those whose disease is inactive who, based on retrospectively available data, have previously fulfilled the 2010 criteria should be classified as having RA
• Differential diagnosis includes SLE, PsA, and gout
Some points to consider

- Although patients with a score < 6/10 are not classifiable as having RA, the criteria might be fulfilled cumulatively over time.
- Joints involvement refers to any swollen or tender joint on examination, which may be confirmed by imaging evidence of synovitis.
- Negative refers to IU values that are less than or equal to the ULN for the laboratory and assay; low-positive refers to IU values that are higher than the ULN but ≤ 3 times the ULN; high-positive refers to IU values that are > 3 times the ULN.
- Where RF information is only available as positive or negative, a positive result should be scored as low-positive for RF.
Methods

• Phase 1: utilizing a data-driven approach based on 3 cohorts of patients with early arthritis, the working group identified factors that were associated with the subsequent decision by physicians to initiate MTX therapy, and their relative weights
Methods

• Phase 2: it was consensus-driven, with a science-based approach informed by data from phase 1.
• Phase 3: it was the derivation from the previous 2 phases with the definition of the final classification criteria set
• The final criteria set was validated with 3 cohorts not used in phase 1
• The criteria are a mix of expert opinion and a science-driven approach
Differences from 1987 ACR criteria

• Presence of synovitis in at least 1 joint is required

• Symmetric arthritis is not required

• The presence of structural joint damage is not required

• The presence of rheumatoid nodules is not required
Advantages of the new criteria

• They will impact patient selection for clinical trials encouraging studies of the disease in patients previously labeled as having UA:
  - with 1-2 swollen joints and anti-citrullinated protein antibody positivity, who score sufficiently to be labeled as having RA
Aim
- To evaluate differences in classification between these 2 criteria in an early arthritis cohort

- To assess the sensitivity and specificity of the 2010 criteria for RA
Method

- A total of 2,258 pts with early arthritis included in the Leiden Early Arthritis Clinic cohort were studied.
- Fulfillement of the 1987 and 2010 criteria for RA was determined at baseline.
- The diagnosis of each patient at 1 year was assessed.
- The sensitivity and specificity of the 2010 criteria were determined using the following outcome measures:
  - initiation of MTX therapy during the 1st year of followup.
  - initiation of any DMARD therapy during the 1st year of followup.
  - having persistent arthritis during 5 years of followup.
Results
- At their first presentation, 1,099 patients fulfilled the 2010 criteria, and 726 the 1987 criteria for RA
- 297 pts fulfilled the 1987 criteria during the first year but not a baseline
- Among these 297 patients, 202 (68%) did fulfill the 2010 criteria at baseline
- 18% of patients fulfilling 2010 criteria at baseline were classified differently after 1 year of followup
Results
- The sensitivity and specificity of the 2010 criteria were:
  - 0.84 and 0.60 with MTX therapy as the outcome
  - 0.74 and 0.74 with DMARD therapy as the outcome
  - 0.71 and 0.65 with persistent arthritis as the outcome
Diagnostic Accuracy of ACR/EULAR 2010 Criteria for Rheumatoid Arthritis in a 2-Year Cohort

Sophie Varache, Divi Cornee, Johanne Morvan, Valérie Devauchelle-Pensec, Jean-Marie Berthelot, Catherine Le Henaff-Bourhis, Sylvie Hoang, Jean-Baptiste Thorel, Antoine Martin, Gérard Chalès, Emmanuel Nowak, Sandrine Jousse-Joulin, Pierre Youinou and Alain Saraux

DOI: 10.3899/jrheum.101227
http://www.jrheum.org/content/early/2011/05/12/jrheum.101227
**Results.**

- At baseline, 111 of the 270 patients had better alternative diagnoses and 16 had erosions typical for RA; of the 143 remaining patients, 52 had more than 6 ACR/EULAR 2010 points (indicating definite RA) and 91 had fewer than 6 points.
- After 2 years, 11/16 patients with erosions and 40/52 with more than 6 points had RA.
- 100 of the 270 patients met the reference standard for RA.
- Sensitivity were 51/100 (51%), specificity 153/170 (90%), PPV 51/68 (75.4%), and NPV 153/202 (75.7%),
- Diagnostic accuracies of the ACR/EULAR score and ACR 1987 criteria were not statistically different.
Final diagnosis of rheumatoid arthritis (RA) in the overall population according to the ACR/EULAR criteria.
ROC curve of the criteria sets in the subgroup meeting the 3 conditions for ACR/EULAR scoring (synovitis, no better alternative diagnosis, and no typical erosions; panel A; n = 143) and in the overall population (panel B; n = 270).
Conclusion.

• Much of the improvement of the ACR/EULAR criteria was ascribable to the use of exclusion criteria in the algorithm.
Conclusion

- Compared with the 1987 criteria, the 2010 criteria classify more pts with RA and an earlier phase of the disease

- The discriminative ability of the 2010 criteria is acceptable
Limitations of the 2010 criteria

• 2010 criteria may increase heterogeneity by including different phenotypes making basic science studies more difficult
• These criteria were not developed as a diagnostic tool
• These criteria were not created as a referral tool for primary care physicians
• The discriminative ability of the criteria is reasonable, but not excellent
Grazie per l'attenzione