Is Anti CCP a more specific test for RA than RF?
WELCOME TO Topic Discussion On

Is Anti CCP Ab a more specific test for Rheumatoid Arthritis than RF?

Presented by:

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Rheumatoid Arthritis Diagnosis

Depends on

I) Clinical manifestation &

II) Lab investigation.
Rheumatologists set some criteria for the diagnosis of RA

1) ARA Criteria-1957

2) ACR Criteria-1987

Ann Rheum Dis 2008;67:1557-61
Proposed Criteria under investigation

1) ACR + Anti CCP
2) CCP - 7
3) CCP - 6
### Comparison of different diagnostic criteria.

<table>
<thead>
<tr>
<th><em>Arthritis symptoms ≥ 6 WKs.</em></th>
<th>1987 ACR criteria</th>
<th>1987 ACR criteria+ antiCCP</th>
<th>CCP 7 criteria</th>
<th>CCP 6 criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Morning stiffness &gt; 1h*</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>2. Arthritis ≥ 3 joints*</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>3. Hand arthritis*</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>4. Symmetric arthritis*</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>5. Rheumatoid nodules</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6. RF positive</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>7. Radiographic changes</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>8. AntiCCP positive</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>NO. of criteria required</td>
<td>≥4 of 7</td>
<td>≥4 of 8</td>
<td>≥3 of 7</td>
<td>≥3 of 6</td>
</tr>
</tbody>
</table>

*Ann Rheum Dis 2008;67:1557-61*
## Results of Investigation of Different Criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1987 ACR criteria</td>
<td>51</td>
<td>91</td>
</tr>
<tr>
<td>1987 ACR criteria+ anti CCP</td>
<td>55</td>
<td>91</td>
</tr>
<tr>
<td>CCP 7 criteria</td>
<td>77</td>
<td>79</td>
</tr>
<tr>
<td>CCP 6 criteria</td>
<td>74</td>
<td>81</td>
</tr>
</tbody>
</table>
Rheumatoid factors are antibodies

Directed against Fc fragment of Ig G

These are usually IgM antibodies

But may be IgG or IgA.
Rheumatoid Factor

A Chance Event
An IgG Antibody is Made to the Fc Portion of an IgG

B-cell

Rheumatoid Factor Produced
It is non specific & may be present in

- Healthy elderly persons
- Other autoimmune &
- Infectious disease.
# RF as a diagnostic marker

<table>
<thead>
<tr>
<th>Assays</th>
<th>Specificity</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgM RF</td>
<td>82%</td>
<td>66%</td>
</tr>
<tr>
<td>IgG RF</td>
<td>91%</td>
<td>43.7%</td>
</tr>
<tr>
<td>IgA RF</td>
<td>88%</td>
<td>50.9%</td>
</tr>
</tbody>
</table>

Ann Rheum Dis 2004;63:1079-84
Anticyclic citrullinated peptides antibodies (anti CCP Ab)

Potentially important markers for diagnosis & prognosis of RA.
1998 - Schellekens, Van Jaarsveld & Coworkers first described this antibody as Anti CCP antibody.
The amino acid citrulline
Contd.

Principle of anti CCP ELISA

- Synthetic CCP
- Human antibody Against CCP
- Peroxidase-labelled Anti-human antibody
- Colourless chromogen
- Stain

@ euroimmun.de- www.euroimmun.de
Contd.

Anti-CCP ELISA
First generation of ELISA for anti CCP Ab

Using several flaggrine epitope

Had high specificity (98%) for RA & Sensitivity of 60-70%
Contd.

CCP-2

• Second generation of anti CCP antibodies

By using true conformational epitopes.

Increases the sensitivity to 80% while retaining specificity 98%
Contd.

Anti CCP Ab as early diagnostic marker of RA

Using stored sample, Anti CCP Ab could be detected 1.5-9 year before the onset of RA.

Progression from undifferentiated polyarthritis to RA

93% in Anti CCP Ab positive individuals having arthritis.

Prognostic value as a marker of erosive disease

Anti CCP Ab positive early RA patient develops a more erosive disease than negative patients.
The use of Anti CCP Ab helps in the decision whether a patient should be treated aggressively at an early stage of disease or not.

### Comparison between Anti CCP Ab & RF

<table>
<thead>
<tr>
<th>Traits</th>
<th>Anti CCP Ab</th>
<th>RF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specificity</td>
<td>98%</td>
<td>82% (IgM)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>80%</td>
<td>66% (IgM)</td>
</tr>
<tr>
<td>Early detection</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Prediction before appear symptoms</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Prediction for erosive disease</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>As a marker of joint damage</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Availability</td>
<td>Limited centre</td>
<td>Widely available</td>
</tr>
<tr>
<td>Cost effectivity</td>
<td>Costly</td>
<td>Less costly</td>
</tr>
</tbody>
</table>
Conclusion

So

**Anti CCP Ab**

a more specific test for Rheumatoid Arthritis than **RF**
