Recommendation 4: Antibody Testing in Patients with UPIA

Recommendation 4

Learning Objectives

At the end of this section participants should be able to:

- Describe the value of autoantibody tests in predicting specific diagnoses in patients with UPIA
- Describe the value of autoantibody tests in predicting prognosis in patients with UPIA
- State the importance of RF and ACPA in the evaluation of patients with UPIA

Recommendation 4

Testing of RF and/or ACPA should be performed in the evaluation of patients with UIPA, as these factors are predictive of RA diagnosis and prognosis; negative tests do not exclude progression to RA [1a, A].

If a connective tissue disease/systemic inflammatory disorder is suspected, additional autoantibody tests should be considered [5,D].

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Testing of RF and/or ACPA should be performed in the evaluation of patients with UIPA, as these factors are predictive of RA diagnosis and prognosis; negative tests do not exclude progression to RA [1a, A]. If a connective tissue disease / systemic inflammatory disorder is suspected, additional autoantibody tests should be considered [5, D].

This recommendation had a strong agreement of 9.1/10.

96% of rheumatologists felt that this recommendation was already implemented in their practice.

Undifferentiated Arthritis
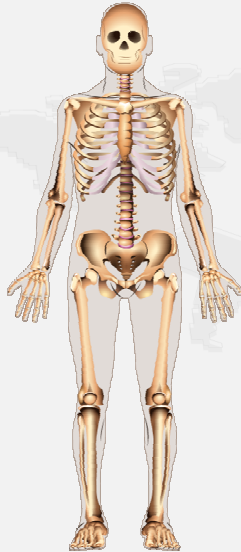
Undifferentiated Arthritis

- Early stage of classifiable disease

- Part of an overlap of disease

- Partial form of a defined disease

- Disease of unknown origin

UA envelops a heterogeneous group of recent onset arthritides that are not classifiable within established criteria sets such as those of the American College of Rheumatology (ACR) and The European League Against Rheumatism (EULAR).

UA may represent an early stage of a classified form of arthritis that will eventually be definable; an overlap of more than one disease; a partial form of a defined disease; or a disease of unknown origin. UA overall has a better prognosis than RA as it encompasses a spectrum of self-limited disorders. As compared to RA, a patient with UA usually presents with fewer affected joints, less radiographic erosions, better functional ability, and a greater likelihood of being seronegative. Patients with UA are also less likely than patients with RA to require treatment that involves the use of corticosteroids (such as Prednisone) or DMARDs and a substantial proportion of UA patients remit spontaneously.

Hitchon CA, Peschken CA, Shaikh S, El-Gabalawy HS. Early undifferentiated arthritis. *Rheum Dis Clin N Am*. 2005;31:605-626.
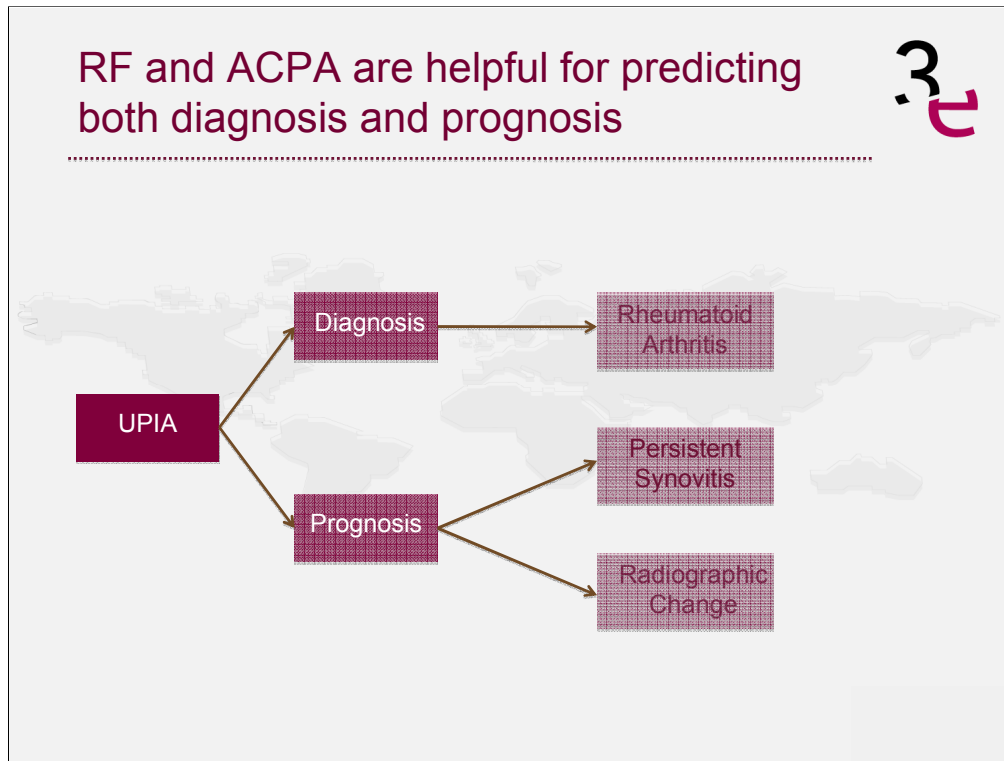
Rheumatoid Factor & ACPA
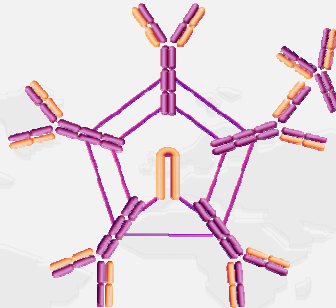
- **Rheumatoid factor (RF): IgM antibody directed to the Fc portion of self IgG antibodies**
- **ACPA: Anti-citrullinated peptide antibodies: Antibodies directed to citrullinated proteins Citrullination is common with inflammation**

•Rheumatoid factor (RF): IgM antibody directed to the Fc portion of self IgG antibodies

•ACPA: Anti-citrullinated peptide antibodies: Antibodies directed to citrullinated proteins

•Citrullination is common with inflammation

Rheumatoid factor and ACPA are autoantibodies which are associated with rheumatoid arthritis.

RF and ACPA are helpful for predicting both diagnosis and prognosis

The association of ACPA and RF with a diagnosis of RA at follow-up was compelling in the retrieved literature. The presence of ACPA or RF also increased the probability of developing persistent synovitis or having a worse radiographic outcome.
The absence of ACPA or RF was diagnostically less helpful, and thus, if negative, would not exclude a diagnosis of rheumatoid arthritis

Other Antibodies and Soluble Biomarkers

- **For anti-keratin antibodies (AKA) and anti-perinuclear factor (APF), evidence suggests diagnostic usefulness, AKA also has some prognostic value**

- **For all other markers, including auto-antibodies and bone & cartilage biomarkers, the evidence on diagnostic or prognostic value is scarce, negative, or controversial**

Other antibodies and soluble biomarkers

•For anti-keratin antibodies (AKA) and anti-perinuclear factor (APF), evidence suggests diagnostic usefulness, AKA also has some prognostic value

•For all other markers, including a variety of other autoantibodies as well as bone and cartilage biomarkers, the evidence on diagnostic or prognostic value is scarce, negative, or controversial

Other antibodies and soluble biomarkers have been studied, but there was insufficient evidence to make a general recommendation. Availability of these tests is also poor.

Other Auto-antibodies

- **Experts also advised clinicians to consider performing additional auto-antibody tests if non-RA systemic inflammatory disorders are suspected**

Other Autoantibodies

•Based on clinical experience, experts also advised clinicians to consider additional autoantibody tests if non-RA systemic inflammatory disorders are suspected

Additional autoantibodies, including ANA and ENA tests may be helpful in the right context. Some autoantibodies are very specific and in the right clinical context can be very useful in establishing a diagnosis.

Summary

- **RF and ACPA are important tests in the evaluation of patients with UPIA**

- **In patients with UPIA, a positive RF and/or ACPA indicates a higher risk of progression to RA, and the development of a persistent and/or erosive arthritis**

- **Other auto-antibodies may be of value, especially if a connective tissue disorder or systemic inflammatory disorder is suspected**

Summary

•RF and ACPA are important tests in the evaluation of patients with UPIA

•In patients with UPIA, a positive RF and/or ACPA signifies a higher risk of progression to RA, and the development of a persistent and/or erosive arthritis

•The evidence is scarce, but other autoantibodies may have value, especially if a connective tissue disorder or systemic inflammatory disorder is suspected

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