A Primer on Rheumatologic Laboratory Tests

What They Mean and When to Order Them

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KEYWORDS

• ANA • ANCA • CCP • CRP • ESR • RF

KEY POINTS

- Laboratory tests in rheumatology should be interpreted depending on the clinical scenario because they are rarely diagnostic of any particular disease.
- A positive antinuclear antibody can be found in normal individuals and in patients with other inflammatory and autoimmune diseases and is not diagnostic of systemic lupus erythematosus.
- Rheumatoid factor (RF) and anticyclic citrullinated peptide (anti-CCP) antibodies support the diagnosis of rheumatoid arthritis, and anti-CCP is more specific than RF.
- A positive antineutrophilic cytoplasmic antibody test with antiproteinase 3 or antimyeloperoxidase specificity supports the clinical diagnoses of systemic necrotizing vasculitis but is not diagnostic. A biopsy is necessary to confirm the diagnosis.

INTRODUCTION

The diagnosis of a rheumatologic disease is challenging and requires careful integration of a patient's symptoms, physical examination findings, and results of diagnostic tests. A thorough history and physical examination are the best screening tests in the initial evaluation of a rheumatologic disease, and the results of laboratory tests should be used only to further refine the diagnosis. Many tests are now available that may aid in rapid diagnosis, but false positive results may lead to inappropriate therapy and unnecessary health care expenses. Laboratories perform different assays, and this can be a source of discrepancy and is often the reason that some laboratory tests are repeated when people are seen by rheumatologists. Hence, results should be interpreted judiciously based on their test characteristics in the appropriate clinical context.[1]

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CONSIDERATIONS WHEN INTERPRETING LABORATORY TESTS

Clinicians should have some familiarity with the terms used for interpretation of a test's characteristics (Table 1).[1]

The important issue in deciding whether to use a diagnostic test in a particular patient is whether the posttest probability will be significantly different from the pretest probability, given a positive or negative test result.[1] The pretest probability and the posttest probability are the probabilities of the presence of a particular disease before and after ordering a diagnostic test, respectively. The pretest probability is the rough estimate that a clinician makes based on clinical presentation and the prevalence of the disease in question. Table 2 lists the overall prevalence of selected rheumatologic diseases in the United States.

The sensitivity and specificity of a test are not sufficient to calculate the probability of disease for a given patient. The likelihood ratio (LR) is meant to provide an additional measure that can be of greater value in daily practice. LRs allow the clinician to calculate the posttest probability based upon the pretest probability and the test result. Tests are recommended as being very useful, useful, or not useful based on their associated LRs (Table 3).[1]

For example, a 29-year-old African American woman presents with joint swelling, oral ulcers, alopecia, and a facial rash. The clinician thinks her chances of having systemic lupus erythematosus (SLE) are greater than that of the general population and estimates that the patient's pretest probability of SLE is 10%. The clinician wants to order a test (such as an antinuclear antibody [ANA] or related autoantibody test) to confirm this suspicion. If the test has a high positive LR (eg, 10) and the test result is positive, then the posttest probability will be greatly increased. If the LR of the

Table 1
Calculation for sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios

Test Result	Disease Present	Disease Absent
Positive	a	b
Negative	c	d

False positive	Positive test result in a patient without the disease
False negative	Negative test result in a patient with the disease
Sensitivity	$\frac{\text{Number of persons with a positive test with the disease (a)}}{\text{Total number of persons who have the disease (a+c)}}$
Specificity	$\frac{\text{Number of persons with a negative test without the disease (d)}}{\text{Number of persons without the disease (b+d)}}$
Positive Predictive value Probability that subjects with a positive screening test truly have the disease (depends on prevalence)	$\frac{\text{Number of persons with a positive test with the disease (a)}}{\text{Number of persons with a positive test (a+b)}}$
Negative predictive value Probability that subjects with a negative screening test truly do not have the disease (depends on prevalence)	$\frac{\text{Number of persons with a negative test without the disease (d)}}{\text{Number of persons with a negative test (c+d)}}$
Positive LR+ (Sensitivity)/(1 – Specificity)	$\frac{\text{Probability of an individual } \textit{with} \text{ the disease having a positive test}}{\text{Probability of an individual } \textit{without} \text{ the disease having a positive test}}$
Negative LR– (1 – Sensitivity)/Specificity	$\frac{\text{Probability of an individual } \textit{with} \text{ the disease having a negative test}}{\text{Probability of an individual } \textit{without} \text{ the disease having a negative test}}$