Spotlight on Health

Quest Diagnostics™

Rheumatoid Arthritis

Elderly patients who complain of joint pain and stiffness usually have osteoarthritis (OA), but other forms of arthritis should also be considered. Rheumatoid arthritis (RA), for example, is an autoimmune disorder rather than a degenerative disorder that affects patients at all ages. Early diagnosis and treatment of RA can prevent or minimize irreversible joint damage.[1] So it's especially important to diagnose or rule out RA when a person presents with joint pain. In this newsletter, we'll talk about a way to optimize diagnosis of early RA (symptoms <6 months duration).[2]

Diagnostic Approach

The American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) has created a classification scheme designed to identify early RA. Diagnosis begins with a history and physical. It's important to note the number and size of joints involved and how long the patient has had symptoms. Inflammatory marker (C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) test results, as well as rheumatoid factor (RF) and cyclic citrullinated peptide (CCP) antibody test results, should be obtained. This information is used in a scoring system designed to identify early-stage patients who are at high risk of persistent and/or erosive disease.[3] Details of the scoring system and classification criteria can be found in the Figure and reference 3.

Optimizing Early RA Diagnosis

As discussed above, use of the ACR/EULAR classification criteria can help identify early RA. The serologic markers used (RF and CCP), however, are more sensitive in established RA than in early RA (Table). Combined use of RF and CCP does improve sensitivity, but it is still relatively low for early disease. Between 28% and 44% of early RA patients are seronegative, ie, they test negative for both RF and CCP.[4,5]

Table. Sensitivity and Specificity of RF, CCP, and 14-3-3 eta for RA[4]

Markers	Early RA Sensitivity (%)	Established RA Sensitivity (%)	Specificity[a]
RF	57	84	85
CCP	59	79	99
14-3-3 eta	64	77	93
RF and CCP[b]	72	88	84
14-3-3 eta, RF, and CCP[b]	78	90	78

RA, rheumatoid arthritis; RF, rheumatoid factor; CCP, cyclic citrullinated peptide antibody.
[a] Comparison with healthy controls.
[b] Results considered positive for RA if any of the biomarkers are positive.

Rheumatoid Arthritis Clinical Presentation

- Rapid onset (weeks to months)
- Symptoms may come and go in "flares"
- Pain, swelling (soft and tender), and stiffness in joints, especially in hands and feet
- Multiple joints affected, often the same joints on both sides of the body (symmetry)
- Morning stiffness lasts >1 hour
- Fatigue, general feeling of illness
- Limited range of motion in affected joints
- Synovitis of ≥1 joint
- Joint erosion and/or cysts visualized by imaging (in later stages)
- Other parts of the body affected: skin, blood vessels, heart, lungs, eyes, and mouth

A novel biomarker, called 14-3-3η (eta), offers a way to further increase sensitivity for early disease. 14-3-3η is released from joints that are inflamed by RA. The 14-3-3η protein is slightly more sensitive than the other markers in early RA. It is more specific than RF but less specific than CCP (Table).[4] When 14-3-3η is combined with RF and CCP, sensitivity for early RA diagnosis rises to nearly 80%. This improved sensitivity is due to the 14-3-3η test identifying 21% of seronegative patients with early RA.[6]

How the Laboratory Can Help

Quest Diagnostics offers a selection of tests for ruling in, or ruling out, RA. These include tests for the general inflammatory markers (ESR, CRP) and the serologic markers (RF, CCP, and 14-3-3η). The serologic tests can be ordered separately or in a panel. Quest also offers tests that help differentiate RA from other conditions such as primary Sjögren syndrome, systemic sclerosis, gout, OA, and certain infections. Viral infections that may present with joint pain include hepatitis B and C, parvovirus B19, and rubella. Mosquito- and tick-borne infections such as chikungunya and Lyme disease may also cause joint pain.

Additional Information

Prevalence estimates for arthritis in the US population are[7-9]:

- 30.8 million people with osteoarthritis
- 8.3 million people with gout
- 1.5 million people with rheumatoid arthritis
- 740,000 to 2.0 million people with psoriatic arthritis

You can find more information at these Web sites:

- The Quest Diagnostics Test Center
  - Rheumatoid Arthritis Diagnostic Panel IdentRA® with 14-3-3 eta test summary
  - Osteoarthritis and Rheumatoid Arthritis clinical focus
  - Autoimmune Rheumatic and Related Diseases clinical focus
- ACR/EULAR classification criteria for RA: ard.bmj.com/content/69/9/1580.full
- American Academy of Family Physicians guidelines for RA diagnosis and management: www.aafp.org/afp/2011/1201/p1245.html

References

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