AIR Investigators Report on Ability of 14-4-3ηAssayto Identify Inflammatory Arthritis in Patients with Osteoarthritis

By Stanley J. Naides, M.D.
Medical Director, Immunology, Quest Diagnostics Nichols Institute, San Juan Capistrano, CA

An Arthritis Internet Registry (AIR) study on osteoarthritis (OA) was presented at the 2015 European League against Rheumatism (EULAR) meeting held in Rome, Italy, June 10-13.[1] In collaboration with Quest Diagnostics, National Data Bank for Rheumatic Diseases investigators studied the utility of a new biomarker for rheumatoid arthritis (RA) and erosive psoriatic arthritis (ePsA) to identify inflammatory arthritis in patients followed for osteoarthritis.[2] The biomarker, 14-3-3η (eta), is found in joint-lining tissue, synovium, and brain tissue. Synovium releases 14-3-3η into synovial fluid and serum in RA patients and, to a lesser extent, ePsA patients. 14-3-3η itself promotes joint inflammation.[3] Serum measurement of 14-3-3η aids RA diagnosis (sensitivity 64% in early RA and 77% in established RA) and prognosis, and may have utility for assessing disease activity.[4,5] Differentiating RA or ePsA from OA, or identifying inflammatory arthritis in the presence of co-existing OA, can be difficult. Examination and traditional biomarkers such as C-reactive protein (CRP), rheumatoid factor (RF), and cyclic citrullinated peptide antibody (CCP) may be insufficient, especially for physicians without specialized training and experience.

The purpose of this AIR study was to estimate the specificity of 14-3-3η among a cohort of patients with physician confirmed osteoarthritis. AIR participants were surveyed by questionnaire, and physician and/or medical records were queried. Serum samples from 166 participants with a physician-confirmed diagnosis of OA were tested for CRP and RF bynephelometry; CCP by a commercial enzyme-linked immunosorbent assay (ELISA); and 14-3-3η by a proprietary laboratory-developed ELISA. The thresholds for defining elevated levels of each biomarker were as follows: CRP, ≥0.8 mg/dL; CCP, ≥20 units; RF, ≥14 IU/mL; and 14-3-3η, ≥0.2 ng/mL.

Of the 166 participants with physician-diagnosed OA, 11 (6.6%) were positive for 14-3-3η. However, 1 of the 11 with elevated 14-3-3η (1.9 ng/mL) was subsequently reclassified as having RA because of elevated levels of RF (123 IU/mL) and CCP (>250 units). Another participant had normal CRP, RF, and CCP levels, but elevated 14-3-3η (3.1 ng/mL); this patient was subsequently diagnosed with PsA based on swelling in 2 fingers, joint pain, and changes in fingernails, all in the absence of prior psoriasis. A third participant with physician-diagnosed OA had been previously treated for RA (methotrexate and entanercept); this patient had elevated CRP (4.4 mg/dL), RF (>1200 IU/mL), (CCP >250 units), and 14-3-3η (>20 ng/mL). Excluding the 3 participants with

subsequent diagnoses of RA or PsA, only 8 (4.9%) of the remaining 163 OA participants were 14-3-3η positive. Thus, the specificity of 14-3-3η as a marker of inflammatory arthritis in OA participants was 95.1%.

The study concluded that serum 14-3-3η was positive in 6.6% of individuals with an initial physician diagnosis of OA, and 4.9% after exclusion of participants with subsequent diagnoses of RA or PsA. Quest Diagnostics investigators and their collaborators previously demonstrated a similarly low frequency of 14-3-3η in normal donors; of the few positive for 14-3-3η, several had RF suggesting preclinical inflammatory disease. In the present study, the low frequency of 14-3-3η in a cohort of individuals with OA supports the high specificity of 14-3-3η observed for RA. Further, 14-3-3η may be used to help identify RA or PsA patients amongst those being followed for OA. 14-3-3η may be particularly useful in the primary care setting to screen OA patients for misclassification of RA or PsA as OA, or for concurrent inflammatory arthritis in the setting of OA.

References:

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