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14-3-3eta: Key Findings from Recent Publications

1. Serum 14-3-3eta is a novel marker that complements current serological measurements to enhance detection of patients with rheumatoid arthritis (RA)[1]
   - Improves diagnostic capacity for early RA by 6 points, from 72% to 78%
   - Is elevated in RA and erosive psoriatic arthritis, but not in other inflammatory diseases
   - High specificity of 14-3-3eta at 93%
   - Differentiates RA vs. osteoarthritis (OA) since it is positive only in RA patients or RA/OA patients
   - Informs response to therapy because it is a modifiable marker. A decrease marks response to the disease-modifying anti-rheumatic or biologic drug used to treat RA.[2,3]

2. 14-3-3eta in "Seronegative" RA[4]
   - 14-3-3eta has utility beyond rheumatoid factor (RF) and cyclic citrullinated peptide (CCP) because it confirms joint-specific inflammation in the absence of the traditional markers
   - 28% to 44% of patients with early RA test negative for RF and CCP[5]
   - 14-3-3eta identifies 21% of RF/CCP seronegative patients in early RA and 67% of RF/CCP seronegative patients in established RA

3. Serum levels of 14-3-3eta protein supplement C-reactive protein (CRP) and RA-associated antibodies to predict clinical and radiographic outcomes in a prospective cohort of patients with recent-onset inflammatory polyarthritis[6]
   - Elevation of 14-3-3eta >0.19 ng/mL should be considered positive. Levels >0.50 ng/mL predict even poorer clinical and radiographic outcomes, a high risk of clinically refractory RA disease, and significant joint damage over the next 5 years.
   - This helps primary care providers prioritize patients for rapid referral to rheumatologists and facilitate early intervention with biological therapies
   - High levels of 14-3-3eta and CRP at baseline and with patients under treatment independently represent poor prognosis that likely results in significant joint deterioration

4. Serum 14-3-3eta level is associated with severity and clinical outcomes of RA, and its pretreatment level is predictive of Disease Activity Score 28 (DAS28) remission with tocilizumab[7]
   - 14-3-3eta is modifiable. Decreases in 14-3-eta in response to therapy are associated with better outcomes, while increases imply worse prognosis.
   - Baseline 14-3-3eta measurement is an independent predictor of remission (as defined by DAS28-erythrocyte sedimentation rate) in patients treated with the biologic, tocilizumab

5. A prospective cohort study of 14-3-3eta in anti-citrullinated protein antibody (ACPA) and/or RF-positive patients with arthralgia[8]
   - 14-3-3eta is detected up to 5 years prior to onset of clinical arthritis and is associated with arthritis development in arthralgia subjects pre-selected by RF and ACPA criteria

References

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