14. CRP and 14-3-3η are each associated with joint damage progression, their titres do not correlate and are better predictors of progression together than alone.

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Background: As a marker of inflammation, C-Reactive Protein (CRP) is routinely used in clinical practice. Higher or sustained levels of CRP are associated with a worse prognosis. 14-3-3η is a joint derived mechanistic biomarker that up-regulates cytokines and enzymes that perpetuate disease. Similar to CRP, higher or persistent levels of 14-3-3η are associated with a worse prognosis, and a corresponding decrease in circulating levels is associated with better clinical outcomes. Inflammation and joint damage are now understood to be processes that uncouple along the course of disease. Since CRP is an acute phase reactant and 14-3-3η, a joint damage mechanism marker, the combined information they provide may enhance clinical management strategies.

Objectives: The aim of this study was to examine both the independent and combined effects of CRP and 14-3-3η on radiographic progression.
Methods: Baseline (BL) serum 14-3-3η titres were assessed in 331 recent onset polyarthritis patients from the Sherbrooke EUPA Cohort with 5 years of radiographic follow-up data. Patients were DMARD naïve at BL, median age was 60 years, and 62% were female. CRP and 14-3-3η positivity were defined as > 8 mg/L and ≥ 0.19ng/ml, respectively. Spearman correlation was performed to assess the relationship between 14-3-3η and CRP titres. Radiographic changes (change in total Sharp/van der Heijde (ΔSHS) score over 30 months were assessed in relation to CRP and 14-3-3η coexpression using ANOVA analysis. Chi-square was used to assess the relationship between CRP positivity with radiographic changes at 30 months based on ΔSHS ≥1, 3, and 5 unit cut-offs.

Results: Of 331 patients, 191 (58%) and 153 (46%) were CRP and 14-3-3η positive at BL, respectively. Spearman correlation revealed that titres of CRP and 14-3-3η did not correlate, r= -0.00025 p=0.996. Chi-square analysis returned both CRP and 14-3-3η as significantly associated with radiographic changes. Cumulative probability plots illustrate that patients who were positive for both CRP and 14-3-3η had the significantly greatest increase in radiographic progression (p<0.0001) with over 50% of patients having ΔSHS>5 over the 30 month period.

Conclusions: CRP and 14-3-3η are both associated with joint damage progression at 3 years and titres do not correlate, consistent with their distinct roles in RA disease processes. Interaction analysis further reveals that the combination of these two markers is a better predictor of future radiographic damage than either marker alone. Concomitant serial testing of both these modifiable markers may assist with tight control RA treatment strategies.