

# **Paper IV**



# S100-Proteins in Rheumatoid Arthritis: Calprotectin and S100A12 are Associated with Disease Activity, Extra-Articular Manifestations and Concomitant Cardiovascular Disease

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## **ABSTRACT**

**Background.** Leukocyte proteins calprotectin (S100A8/S100A9) and S100A12 have been studied for their involvement in inflammatory processes and their presence in synovium, synovial fluid and blood from patients with rheumatoid arthritis (RA).

**Objectives.** The aims of the study were to investigate the relationship of serum levels of calprotectin and S100A12 to measures of disease activity, as to the prognostic factors rheumatoid factor (RF), anti-CCP, extra-articular manifestations (ExRA) and concomitant cardiovascular (CV) disease.

**Methods.** 129 patients with RA were clinically assessed with common measures of disease activity and presence of ExRA and CV disease. In addition to routine laboratory tests including ESR and CRP, serum samples were analyzed by ELISA for calprotectin and S100A12. Univariate correlations between variables were performed, and a logistic regression model was used to test associations with CV disease and ExRA.

**Results.** Among the 129 patients 43 (33.3%) had ExRA and 17 (13.2%) had CV disease. The serum concentrations of both calprotectin and S100A12 correlated with all performed measures of RA disease activity ( $p < 0.01$ ). The median level of S100A12 was higher in patients positive for rheumatoid factor ( $p < 0.001$ ), anti-CCP ( $p < 0.001$ ) and in patients with ExRA ( $p = 0.001$ ) than in those without these features. In the logistic regression analysis, S100A12 was independently associated with concomitant CV disease (OR 1.055, CI 1.011-1.101).

**Conclusion.** Serum levels of calprotectin behave as a biomarker for the disease activity of RA, comparable to CRP and ESR, while S100A12 is associated with RF, anti-CCP, ExRA and concomitant CV disease. S100A12 may thus be of prognostic value in RA patients.