Circulating survivin, a novel and independent predictor of joint destruction in early RA.

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Objectives: To assess the predictive role of survivin, a key member of the apoptosis inhibitor family, for the radiological outcome of early rheumatoid arthritis (RA).

Patients and methods: Serum survivin was measured at inclusion by a sandwich ELISA in 698 consecutive RA patients with a disease duration of median 6 months. Values of circulating survivin above 300 pg/ml, corresponding to 3SD of a healthy control group, were defined as high (1).

X-rays of hands and feet were obtained at baseline, and after 1, 2, and 5 years. van der Heijde modified Sharp scores were calculated for total Sharp score (TS) and erosion scores (ES). Radiological progression of RA was defined as a change in TS over 5 years by >5.8 (smallest detectable change). Antibodies to citrullinated peptides (aCCP) and rheumatoid factor (RF) were assessed as previously described (2).

Results: At baseline, high levels of survivin were measured in 60% (391/651) of patients with early RA. The distribution of survivin levels was skewed, median (IQR) was 0.950 (0-4.560). There was no gender difference between the groups but low survivin was associated with high age and short disease duration (p=0.029 and 0.026, respectively).

Patients with high levels of survivin had higher TS and ES compared to patients with low levels of survivin (p=0.042 and 0.020) at inclusion. These differences became more evident after 1, 2 and 5 years of follow-up (p=0.0005 for all measurements). Indeed, after 5 years 73.7% of the patients in the group expressing high survivin levels at the time of inclusion displayed one or more erosion versus 48.6% in the low survivin group (OR 3.0 (95%CI 2.0-4.6)). Radiological progression at 5 years of follow-up was significantly more frequent in patients with high levels of survivin compared with those displaying low survivin levels (66.2 versus 33.8%, OR 3.1 (95%CI 2.0-4.8)).

At baseline, the levels of survivin correlated significantly with the levels of aCCP (r= 0.474, p=0.0005) and RF (r=0.606, p=0.0005). However, a backward multiple logistic regression analysis model showed that high level of extracellular survivin was an independent predictor of radiological progression at 5 years. Into this model age and disease duration, survivin, aCCP, RF, DAS28, CRP and TS were entered in step one. In the last step, survivin, aCCP and baseline TS remained as significant independent predictors with OR (95%CI) of 1.72 (1.01-2.93), 3.35 (1.99-5.64) and 1.02 (1.07-1.12), respectively.

Conclusion: In a prospective follow-up study of patients with early RA it was shown that high serum levels of survivin are associated with progressive joint destruction. Importantly, the prognostic value of survivin for the outcome in early RA appears to be independent of other established prognostic parameters including aCCP and rheumatoid factor.

References: 1. Maria Bokarewa , Sofia Lindblad, Dimitry Bokarew, Andrej Tarkowski. Arthritis Res Ther. 2005;7(2):R349-58.

2. Kristina Forslind, Monica Ahlmén, Kerstin Eberhardt, Ingiäld Hafström and Björn Svensson for the BARFOT study group. Ann Rheum Dis 2004;63:1090-5.