Circulating survivin is a negative predictor of remission in early RA

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Purpose: In a BARFOT cohort of patients with early RA we have recently shown that circulating survivin is an independent predictor for radiological progression of joint destruction. This communication will address the question whether the measurement of circulating survivin also predicts clinical outcome of RA after 5 years of follow-up.
Patients and methods :Serum survivin was measured at inclusion by a sandwich ELISA in 651 of 698 consecutive patients with early (duration ≤1 year) RA participating in the BARFOT study. Values of circulating survivin above 300 pg/ml, corresponding to 3SD of a healthy control group, were defined as "survivin positive". Remission was defined (a) as DAS28 <2.6 (EULAR criteria) and (b) as no swollen joints, no tender joints and normal ESR (Mäkinen criteria). *Point* remission was assessed after two and five years of follow-up and patients in remission at both these time points were considered to be in *sustained* remission.
Results: At baseline, median (IQR) survivin level was 0.950 (0-4.560) and 391 of 651 patients (60%) were survivin positive. Survivin positive patients received treatment with DMARDs and prednisolone more frequently than survivin negative patients.
Survivin positive patients had lower rates of *point* and *sustained* remission as compared to survivin negative patients. Applying the EULAR criteria after 5 years of follow-up, *point* remission was achieved by 34% of survivin positive patients vs 47% of survivin negative patients (p=0.002) and *sustained* remission by 22% vs 34%, respectively (p=0.001). By the more stringent Mäkinen criteria, *point* remission was achieved by 20% of survivin positive patients vs 32% of survivin negative (p=0.001) and *sustained* remission by 8% of survivin positive patients vs 19% of survivin negative (p=0001).
The mean HAQ score was similar in the survivin positive and negative groups, both at baseline (1.0 vs 1.0) and after 5 years (0.7 vs 0.6).
Multiple stepwise logistic regression analyses (including age, sex, disease duration, baseline DAS28, HAQ, CRP, survivin, aCCP, RF and one year HAQ into the models) showed that in the last step, survivin negativity consistently remained as an independent predictor of *point* and *sustained* remission of RA according to both sets of criteria. Thus, survivin positivity was associated with a reduced likelihood of remission, as e.g. EULAR point remission after 5 years with an OR (95%CI) of 0.52 (0.35-0.77), p=0.001.
Conclusion: Our data indicate that the absence of circulating survivin is an independent predictor of remission in early RA. Therefore, the presence of survivin might be regarded as a warning sign for persistent disease activity.

This study was performed on behalf of the BARFOT study group.