Serum biochemical markers of synovial tissue turnover, but not cartilage markers, predict radiological progression in very early rheumatoid arthritis

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BACKGROUND

In early rheumatoid arthritis (RA), radiographic assessments are insensitive to identify patients at high risk of progression, because the extension of joint damage, especially cartilage degradation, is rather limited.

Biochemical markers reflecting dynamic processes of tissue remodelling may be more sensitive to predict progression in early RA.

To investigate whether soluble markers of matrix-metalloprotease (MMP) driven type I (C1M) and type II (C2M) collagen degradation as:

1. Indicators of synovial and cartilage tissues remodelling respectively
2. Predict progression of joint damage in a prospective longitudinal cohort of patients with early RA.

METHODS

Patients from the prospective ESPOIR cohort included **813 patients** with definitive or probable clinical diagnosis of **early RA** (ACR-EULAR 2010 criteria) or a diagnosis of undifferentiated arthritis (**UA**) with potential for progression to RA.

All patients presented with swelling of two or more joints, 6 weeks to 6 months' symptom duration and no previous treatment with DMARD or glucocorticoids.

Hand and feet radiographs were obtained at baseline and after 1- and 5-year follow-up and scored for bone erosion, joint space narrowing (JSN) and total damage by the modified van der Heijde Sharp (vHS) score. **Progression was defined as an increase of 1 or 5 unit(s) in vHS between baseline and 1 or 5 years, respectively.**

Serum C1M and C2M were measured at baseline using validated ELISAs. The cross-sectional associations of C1M and C2M with age, BMI, DAS 28 and CRP were analysed using regression analyses. The association between baseline levels of C1M and C2M and radiological progression over 1 and 5 years was assessed by logistic regression.

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RESULTS

This study investigated markers of joint damage progression in Early RA patients.

- C1M levels were higher in patients with more severe disease activity and inflammation.
- Higher C1M at baseline predicted increased bone damage at 1 year, even after accounting for other factors.
- The other marker, C2M, did not show this association with disease progression.

Overall, C1M may be a useful marker for predicting bone damage in early RA.

Table 1.
Patient overview

Variable	Mean (SD) or %
Age (years)	48.1 (12.5)
Sex	77 % females
BMI (kg/m2)	25.0 (4.7)
No. RA patients	81.4 %
No. anti-CCP pos.	39 %
DAS28	5.1 (1.3)
CRP (mg/L)	22.2 (33.6)
Total vHS	3.211 (5.150)
Erosion vHS	0.629 (2.257)
JSN vHS	2.608 (3.981)

Table 2
Correlation (r, p values) of soluble markers (log transformed) with baseline variables .

Baseline variable	C1M	C2M
DAS28	**0.45, <0.0001**	**0.09,0.012**
LogCRP	**0.87, <0.0001**	**0.11, 0.0001**
JSN vHS	**0.087, 0.017**	0.009, ns

Table 3
1-year and 5-year odds-ratio (OR) of radiological progression for each SD increase of baseline C1M (adjusted for age, sex, BMI and diagnosis of RA.

Progression	1 year OR (95%-CI)	5 year OR (95%-CI)
Total vHS	**1.29 (1.10-1.51)**	**1.35 (1.12-1.64)**
Erosion vHS	**1.46 (1.19-1.80)**	1.18 (0.91-1.53)
JSN vHS	**1.23 (1.05-1.44)**	**1.26 (1.05-1.51)**

CONCLUSION

Increased baseline serum C1M is consistently associated with a higher risk of radiographic progression in patients with early RA. Synovial tissue remodelling may be a prominent determinant of progression in the early phase of the disease whereas cartilage turnover is likely to play a minor role at this stage.