The impact of rheumatoid factor and ACPA on bone erosion in rheumatoid arthritis

In their letter, Van Steenbergen and colleagues present data on the radiographic progression in rheumatoid arthritis (RA) patients stratified for anti-citrullinated protein antibody (ACPA) and rheumatoid factors (RFs) in two different patient cohorts.[1] They show that the presence of ACPA is associated with a more pronounced progression of structural damage when scoring conventional radiographs by the standardised Sharp–van der Heijde method.[1] These findings (i) underline previous radiographic findings that ACPAs are associated with radiographic progression in RA,[2] (ii) stay in line with the known pathophysiologic function of ACPA in osteoclast differentiation[3] and (iii) also support our high-resolution CT data showing the relevance of ACPA in bone erosions.[4]

The authors, however, found no difference in radiographic progression whether RF was present or not. At first sight, this finding seems to contradict our recently published high-resolution CT data, where we could dissect the role of ACPA and RF on bone erosion showed that RF also affects bone loss in RA patients in addition to ACPA.[4] However, limitations of conventional radiographs are likely being a simple explanation for the fact that Van Steenbergen and colleagues were not able to detect differences between RF-positive and RF-negative individuals. Based on the 2D nature and its limited resolution, a substantial number of erosions escape their detection by conventional radiography when compared with high-resolution CT.[5] The latter technique with a resolution of slightly more than 100 μm can even detect very small lesions with a volume of less than 1 mm^3, independent at which anatomical site they are localised. Hence, we believe that the detection threshold with respect to lesion size and localisation for conventional radiography is simply too high to pick up the more subtle differences in erosions; one can accurately pick up by high-resolution CT. This situation creates an 'insufficient' signal-to noise ratio to detect a certain process, which cannot simply be compensated by increasing the sample size or including more joints without changing the method itself. Hence, the intrinsic limitations of the method will be still present even when increasing the number of measurements.

Although we think that the aforementioned point sufficiently explains these differences between our approach and the one by Van Steenbergen and colleagues, another important factor may additionally affect the results presented in this letter: RF, in contrast to ACPA, is much more linked to disease activity. Hence, effective treatment of RA, which for sure has been initiated in the patients included in these two cohorts, may have cleared the RF-immune complexes in these patients over time and level out the differences between the two groups of ACPA-positive RA patients.

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