Title

Which joints and what pathological findings need to be evaluated on ultrasound in CCP+ at-risk individuals? The fifth MTP joints for bone erosion is a good starting point. Response to Correspondence by Becciolini et al

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We thank Becciolini et al. for their interest in our recent paper, in which we demonstrated that a focused ultrasound (US) examination of the classical sites for rheumatoid arthritis (RA) damage, in particular the fifth metatarsophalangeal (MTP) joints, may improve risk stratification for progression to RA in anti-cyclic citrullinated peptide antibody positive (CCP+) at-risk individuals (1).

Becciolini and colleagues suggest that scanning the pisotriquetal joint (PTJ) could improve the US sensitivity for the assessment of inflammation in patients with early inflammatory arthritis (IA) (2). The logic of this suggestion is based on the results of magnetic resonance imaging (MRI) studies showing that synovitis and bone erosions can be frequently found in the carpal bones, including the PTJ, in patients with early RA (3,4). The authors have also provided pictorial examples to show how US pathological findings (i.e., synovitis and bone erosions) can be detected at this level in one patient with RA.

In recent years, US and MRI have shown the ability to predict progression to IA, and its timing, in at-risk individuals without clinical synovitis, raising important implications for the management of these individuals, including preventive approaches (5). The US studies carried out in at-risk cohorts have used comprehensive protocols evaluating multiple pathological findings (i.e., power Doppler signal, grey scale synovitis and/or bone erosions) in most or all relevant joints. Although feasible in a research setting, this can be time-consuming and therefore challenging in daily clinical practice. Which joints, and indeed how many joints, need to be evaluated for optimum predictive accuracy in at-risk individuals is still an unanswered question.

In our study, we evaluated only the joints which have been reported as the most specific for the detection of US bone erosions in RA: the second and fifth metacarpophalangeal joints and the fifth MTP joint (6). Our study has the potential to provide to rheumatologists, who are now routinely being referred at-risk individuals in clinical practice, a valuable tool which can be readily used in the clinical setting for the management and risk stratification of these individuals. We acknowledge however that targeting US to only these sites of RA damage might potentially exclude other anatomical sites (i.e., distal ulna or PTJ) from being evaluated which, as a result, might lead to underestimating the overall prevalence of bone erosions in CCP+ at-risk individuals.

Both the pisiform and triquetrum have been long known to be sites for early radiographic bone erosions in RA (7). During an US assessment, the triquetrum would normally be scanned as part of the existing European League Against Rheumatism (EULAR) scanning views of the ulnar-carpal aspect of the wrist with the triquetrum forming the 'carpal part'. The pisiform however has been a less favoured area to evaluate, unless there was a specific clinical indication to do so (e.g. a site of significant pain). This practice is partly historical as US image resolution in the past was not good enough to clearly demonstrate this small region. In addition, older machines with larger transducers provided limited adequate transducer access. Anatomically, the positioning of the pisiform on the triquetrum, also precludes the comprehensive

visualisation of the joint, especially in perpendicular planes, which is likely to have an impact on reliability. We also note that the PTJ, like other aspects of the wrist, is a frequent location for osteoarthritis (OA) and therefore prone to both degenerative related bone irregularity/erosion and synovitis raising the question of lesion specificity in these areas (8). However, we agree with Becciolini et al, that US may visualise synovitis in the surrounding recesses of the PTJ but whether this offers any additional information to more conventional areas, needs to be further investigated. In conclusion, this area warrants further investigation but more data is required before it is suggested as a standard site to evaluate.

Contributors

All authors were involved in conception, drafting or revising the article. All authors approved the final version to be submitted for publication.

Competing interests

Kulveer Mankia reports personal fees from Abbvie, UCB and Eli Lilly, outside the submitted work. Richard J Wakefield has received honoraria from Abbvie, Novartis and GE for ultrasound related educational activities. Paul Emery reports consultant fees from BMS, AbbVie, MSD, Pfizer, Novartis, and Roche, outside the submitted work. He also reports research grants from UCB, AbbVie, BMS, Pfizer, MSD and Roche, outside the submitted work. Paul Emery reports consultant fees from BMS, AbbVie, MSD, Gilead, Galapagos, Lilly Novartis, Pfizer, Roche, and Samsung outside the submitted work. He also reports research grants from AbbVie, BMS, Lilly, Novartis and Roche, outside the submitted work.

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