Reply to:
High prevalence of ultrasound-defined enthesitis in patients with metabolic syndrome

Sirs,

We thank Falsetti *et al*. for their interest in our paper (1) in which we explored the prevalence of the ultrasound (US) findings indicative of enthesitis, according to the Outcome Measures in Rheumatology (OMERACT) definitions (2), in a group of 82 healthy subjects.

In our paper, we found a relatively high prevalence of the US findings indicative of "active" inflammation (34.1% of the subjects, in 8.4% of the scanned entheses) at the entheses of the lower limb in a group of healthy subjects.

Our results raise the need for a more specific definition of "active" enthesitis. This should include a combination of grey-scale (GS) abnormalities and power Doppler (PD) signal (*i.e*. PD signal ≥1 + entheseal thickening and/or hypoechogenicity), as well as considering as pathological only PD grades higher than 1.

The paper by Falsetti *et al*. (3) shows an even higher prevalence of US findings indicative of enthesitis, according to the OMERACT criteria, in a group of patients with metabolic syndrome. Healthy subjects with a known history of metabolic syndrome were excluded from our study as the entheses, as well as the tendons, are anatomic areas which are frequently affected in these conditions (4, 5).

Similar to our study, the authors found a very low prevalence of PD signal at the enthesis (1% of the entheses examined), suggesting that PD signal might represent a reliable US biomarker of "active" inflammation.

Interestingly, the authors found a high prevalence of US findings indicative of "structural damage", such as bone erosions, calcifications and enthesophytes.

In our paper, we found a frequent association between the US findings of "active" inflammation, especially entheseal thickening and hypoechoic areas, and "structural damage", suggesting that subjects showing hypoechogenicity and, mostly, entheseal thickening, should be investigated with regard to previous episodes of enthesitis and/or the presence of pathologic conditions which may affect the enthesis (*i.e*. metabolic disorders). As shown by our paper and by Falsetti *et al*., other aspects, such as age or the body mass index, should be taken into account in the US assessment of the enthesis.

Entheseal involvement is a well-known cardinal feature of spondyloarthritis (SpA) (6), but it has been shown also in patients with connective tissue diseases, such as systemic lupus erythematosus (7, 8), as well as in patients with metabolic, degenerative and post-traumatic disorders (9). Among the different imaging techniques, US has the potential to become the gold standard for diagnosis and monitoring of entheseal pathologies due to its very high sensitivity, excellent safety profile and low running costs.

In conclusion, our paper and that of Falsetti *et al*. showed a high prevalence of US findings indicative of "active" enthesitis, according to the OMERACT definition, in healthy subjects and in patients with metabolic syndrome respectively, highlighting the need of a more specific definition of US enthesitis.

We agreed with Falsetti *et al*. that the US findings of "active" enthesitis should be differently weighted, as entheseal thickening and hypoechoic areas could be frequently detected in the entheses of asymptomatic healthy subjects, as well as in other non-inflammatory conditions. Moreover, PD signal appears the most specific US finding of "active" inflammation and its value cannot be dependent on the mandatory presence of GS findings, especially when PD grade at entheseal level is higher than 1.

In our study, we proposed a cut-off of "active" enthesitis (PD signal ≥1 + entheseal thickening and/or hypoechogenicity or PD grades greater than 1) which has to be validated in patients with SpA, including psoriatic arthritis and ankylosing spondylitis.

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Competing interests: this study was conducted while A. Di Matteo was an "Articulum Fellow"; E. Filippucci has received speakers fees from AbbVie, Bristol-Myers Squibb, Celgene, Roche, UCB Pharma and Novartis; W. Grassi has received speakers fees from AbbVie, Celgene, Grünenthal, Pfizer and UCB Pharma; E. Cipoletta has declared no competing interests.

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