Dr. Solmaz, *et al* reply

To the Editor:

We sincerely thank Dr. Masi, *et al* for their comments in response to our manuscript, "Entheseal Changes in Response to Age, Body Mass Index and Physical Activity: An Ultrasound (US) study in Healthy People"[1,2]. Our study had demonstrated that US changes within the enthesis are associated with older age, higher BMI, physical activity, and male sex. As seen in Figure 1 of the original manuscript, the slope of the US scores are different for patients younger and older than 50 years old; therefore, Masi, *et al* suggested looking at these subgroups separately in detail[2].

In Table 1, we have provided the multiple regression analysis for US scores of patients who are < and ≥ 50 years old. While we acknowledge that the sample sizes for these subgroups are rather small (48 and 27, respectively), with correspondingly low power to detect statistical significance, we do believe that they lend support to Masi, *et al*'s hypothesis[2] that the effect of biomechanical factors contributing to enthesitis may change with age. In particular, all 3 models found the effects of BMI to be higher in the older group than in the younger (Table 1). Looking in further detail, in the younger population, the entheseal changes were mostly seen as signs of damage, that was linked to high physical activity and male sex, with borderline significance for the latter. In the elderly, both inflammatory changes were observed within the entheses as well as features of damage being linked to some of the investigated factors. More specifically, age and BMI were found to increase the inflammatory changes on US in the elderly, and damage was again increased with BMI, although to a lesser degree.

Our group has previously shown that patients with osteoarthritis (OA) may have similar features of enthesitis as patients with spondyloarthritis (SpA), which may explain the remarkable increase in the US scores after the age of 50 years[3]. Only 8 patients in our sample had clinically detectable OA.

Upon repeating our analysis excluding these participants, we observed the same pattern of effects with the same factors achieving statistical significance. Degeneration is likely to increase after the age of 50, which may not always lead to clinical symptoms of OA. Standard screening with radiographs in the elderly may therefore lead to a higher prevalence of OA than clinical tools. In our study, radiographs were not performed to diagnose OA and therefore it is possible that there may have been some subclinical OA in the participants.

We appreciate the guidance that Masi, *et al*[2] had provided regarding the potential use of multivariate adaptive regression spline (MARS) modeling to explore complex interactions in this setting, but this approach will require a larger sample size. We plan to collect more data and hope to present a more robust and nuanced analysis in a future manuscript.

In conclusion, our results indicate that age, BMI, physical activity, and sex affect the inflammation and damage scores on entheseal US, but the relationship is likely complex and changes with advanced age. Further work is clearly required to gain a full understanding of the biology of healthy entheses with a larger sample size and how it responds to biomechanical stress, and how this relates to the pathogenesis of SpA.

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Table 1. Multivariate regression results of factors affecting ultrasound scores, according to subgroups of younger (< 50 yrs) and older (≥ 50 yrs) age.

| | < 50 Years, n = 48 | | | | | |
| | Inflammation Score | | Damage Score | | Total Score | |
	B (95% CI)	P	B (95% CI)	P	B (95% CI)	P
Intercept	−1.65 (−6.7 to 3.64)	0.51	−5.3 (−11.1 to 0.4)	0.06	−7.0 (−16.0 to 1.9)	0.12
Age	0.17 (−0.8 to 0.11)	0.73	0.79 (−0.3 to 0.19)	0.17	0.09 (−0.08 to 0.2)	0.28
Sex (men vs women)	1.07 (−0.4 to 2.6)	0.16	1.6 (−0.1 to 3.3)	0.06	2.7 (−0.1 to 5.4)	0.051
Smoking (ever vs never)	0.99 (−0.6 to 2.6)	0.23	0.9 (−0.9 to 2.8)	0.33	1.9 (−0.1 to 4.8)	0.19
BMI	0.12 (−0.4 to 0.29)	0.14	0.15 (−0.3 to 0.34)	0.10	0.27 (−0.1 to 0.5)	0.06
Physical activity (high vs low/ moderate)	1.29 (−02 to 2.8)	0.99	**1.9 (0.2–3.6)**	**0.02**	**3.2 (0.5–5.9)**	**0.02**

| | ≥ 50 Years, n = 27 | | | | | |
| | Inflammation Score | | Damage Score | | Total Score | |
Variables	B (95% CI)	P	B (95% CI)	P	B (95% CI)	P
Intercept	**−38.9 (−59 to −17)**	**0.001**	**−29.0 (−50 to −7)**	**0.01**	**−68 (−102 to −33)**	**0.001**
Age	**0.27 (0.13–0.53)**	**0.040**	0.29 (0.02–0.5)	0.34	**0.56 (0.13–0.99)**	**0.01**
Sex (men vs women)	3.08 (−1.2 to 7.4)	0.15	1.8 (−2.5 to 6.3)	0.39	4.9 (−2.2 to 12.1)	0.16
Smoking (ever vs never)	−1.9 (−6.0 to 2.2)	0.34	−1.5 (−5.7 to 2.6)	0.45	−3.4 (−10 to 3.3)	0.30
BMI	**1.06 (0.4–1.6)**	**0.001**	**0.66 (0.09–1.2)**	**0.02**	**1.7 (0.8–2.6)**	**0.001**
Physical activity (high vs low/ moderate)	4.0 (−0.4 to 8.6)	0.075	3.7 (−0.9 to 8.4)	0.11	**7.8 (0.3–15.3)**	**0.04**

Significant differences are in bold.

REFERENCES

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