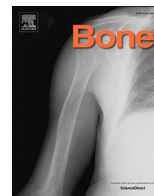




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Correspondence

Response to the correspondence letter

Dear Editor,

In the presented study, the authors performed a Mendelian randomization analysis to increase the statistical power to examine the suspected association between bone mineral density (BMD) and severe course of a COVID-19 infection.

This relationship has already been postulated by us in march 2021 and confirmed by several other studies. However, due to a small number of patients and heterogeneously distributed confounding patient-related factors, a causal link between low BMD and adverse outcome of COVID-19 infections could not be established thus far [1–3].

In the presented study, the authors match genetic characteristics of low BMD patients taken from the Genetic Factors for Osteoporosis (GEFOS) Consortium of different age groups with 8779 very severe respiratory confirmed COVID-19 cases from the COVID-19 Host Genetics Initiative [4,5]. Thus, the authors were able to show that only in the age group of patients over 60 years, a higher BMD is a significant protective factor for the severe course of COVID-19 disease independent of further confounders. In this way, they demonstrate that BMD is a predictor of severe COVID-19 particularly in the elderly population, potentially predicting the need for treatment in an intensive care unit.

In our opinion, the authors' approach and study design represent a highly effective and valid mathematical procedure for demonstrating this association. The results are consistent with our reported findings and explain why low BMD is no independent risk factor within a multivariate regression analysis in the age range of the patient cohort we

included.

We thank the authors for this detailed analysis of this relationship and congratulate them upon this substantial scientific insight.

Abbreviations

BMD	Bone mineral density
GEFOS	Genetic Factors for Osteoporosis Consortium

References

- [1] J. Kottlors, N.G. Hokamp, P. Fervers, J. Bremm, F. Fichter, T. Persigehl, O. Safarov, D. Maintz, S. Tritt, N. Abdullayev, Early extrapulmonary prognostic features in chest computed tomography in COVID-19 pneumonia: bone mineral density is a relevant predictor for the clinical outcome—a multicenter feasibility study, *Bone* 144 (2021).
- [2] S. Battisti, N. Napoli, C. Pedone, M. Lombardi, G. Leanza, F. Tramontana, M. Faraj, V. Agnoletti, M. Verna, L. Viola, E. Giampalma, R. Strollo, Vertebral fractures and mortality risk in hospitalised patients during the COVID-19 pandemic emergency, *Endocrine* (2021).
- [3] M. Tahtabasi, N. Kilicaslan, Y. Akin, E. Karaman, M. Gezer, Y.K. Icen, F. Sahiner, The prognostic value of vertebral bone density on chest CT in hospitalized COVID-19 patients, *J. Clin. Densitom.* (2021).
- [4] C. Medina-Gomez, et al., Life-course genome-wide association study meta-analysis of total body BMD and assessment of age-specific effects, *Am. J. Hum. Genet.* 102 (1) (2018) 88–102.
- [5] C.-H.G. Initiative, The COVID-19 host genetics initiative, a global initiative to elucidate the role of host genetic factors in susceptibility and severity of the SARS-CoV-2 virus pandemic, *Eur. J. Hum. Genet.* 28 (6) (2020) 715–718.