Bone 127 (2019) 675

Contents lists available at ScienceDirect

Bone

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Correspondence

Response to: Letter to editor in response to article published by Leanza et al.

We thank Dr. Shah for the important comment, questioning whether the increased fracture risk that we reported with longer diabetes duration in type 1 diabetes (T1D) may be confounded by "age at onset." Dr. Shah suggests that analysis of age at onset may provide a better understanding of fracture risk in T1D compared with disease duration. Subjects with longer disease duration are indeed more likely to have younger age at diabetes onset, which might negatively impact on bone quality [1]. Accordingly, as reported in our study age at onset tended to be higher in subjects without previous history of fragility fractures (median [interquartile range] age: 21 [11 − 31] years) compared to those with positive history of one (19 [13 − 31] years) or ≥ two fractures (15 [11–18] years) ($p = 0.061$) [2]. On the other hand, diabetes duration reflects both age at onset and a longer exposure to diabetes-related detrimental factors, such as hyperglycaemia or complications, and was associated with fracture risk in unadjusted models. We note that in the context of an age-adjusted model, age at onset and diabetes duration are essentially providing the same information, and it is not reasonable to adjust one for the other. As Dr. Shah acknowledges in his recent report on age at onset and bone properties [3], it is not possible to clearly distinguish the effects of age, age at onset and diabetes duration. We chose to report a final multivariate model with diabetes duration as we believe this best reflects the long-term deleterious effects of diabetes on the skeleton [2]. Of course, if we substituted age at onset for diabetes duration in our multivariate model, younger age at onset was associated with increased risk of multiple fractures, similar to our findings for diabetes duration. Thus, we agree in part with Dr. Shah that our finding that longer disease duration is associated with higher fracture risk may be explained by the effects of earlier age at onset on developing bone. However, our finding may also be explained by longer exposure to diabetes, or to a combination of these factors. The development of studies that can test whether age of onset contributes to fracture risk, beyond its effect on duration of diabetes, would be an important focus in future research.

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Giulia Leanza[a], Ernesto Maddaloni[a], Ann Schwartz[b], Nicola Napoli[a,c,*]

[a] *Department of Medicine, Unit of Endocrinology and Diabetes, Campus Bio-Medico University of Rome, Italy*

[b] *Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, USA*

[c] *Division of Bone and Mineral Diseases, Washington University in St Louis, USA*

E-mail address: n.napoli@unicampus.it (N. Napoli).

DOI of original article: https://doi.org/10.1016/j.bone.2019.06.026

* Corresponding author.

https://doi.org/10.1016/j.bone.2019.06.028