To the Editor:

First and foremost, we appreciate the great interest of Dutta and colleagues in our work. We provide a few comments and clarifications.

First, Dutta and colleagues question several aspects of our study design. As clarification, we would like to point out that our study was part of the German Cushing registry. The aim of the registry is to collect data to improve the diagnostic approach and therapy of patients with Cushing’s syndrome but also to shed light on pathophysiologic mechanisms in Cushing’s syndrome. Overall, it is an observational, non-interventional, best practice study approach. Diagnostic tests and treatment decisions are performed according to the current clinical standards in Germany. For example, in case of bone mineral density measurement, German guidelines for the treatment of osteoporosis recommend repeat measurements usually not earlier than 2 years after the initial scan. For the same reasons, we only conducted follow-up radiographs when there was a clinical suspicion for fractures. We do agree that we might have missed fractures, but this was already stated in the article as a limitation at the end of the discussion.

Second, Dutta and colleagues suggest including hypogonadism and hormone deficiencies after pituitary surgery or menopause in the regression analysis. This is a very good point, which we of course also considered and analyzed. We did not find a difference between patients with or without menopause or cycle disorders at time of diagnosis and 2 years post-surgery. We acknowledge that the significant change could be a measurement error. Considering the current literature regarding the reported increases of BMD after surgical cure of Cushing’s syndrome, both the time course and the BMD changes in our patients are expected, whereas a type 1 error appears less likely. The GE Lunar Prodigy Advance is used in our clinic.

Third, Dutta and colleagues ask whether there was a difference in osteocalcin levels between patients with or without diabetes. In our study, 33 patients had type 2 diabetes (7 without Cushing’s syndrome and 26 with Cushing’s syndrome). Comparison of osteocalcin levels showed that there was not a significant difference between patients with or without type 2 diabetes (neither in patients with or without Cushing’s syndrome: $p = .8$ and $p = .7$).

We did not consider the absence of association between osteocalcin levels and type 2 diabetes relevant, which is why we decided not to include it in the final version of the article.

Finally, Dutta and colleagues comment that the least significant change of the bone mineral density (BMD) measurements was not exceeded 2 years in remission. Nevertheless, there was a statistically significant difference between T-score at time of diagnosis and 2 years post-surgery. We acknowledge that the significant change could be a measurement error. Considering the current literature regarding the reported increases of BMD after surgical cure of Cushing’s syndrome, both the time course and the BMD changes in our patients are expected, whereas a type 1 error appears less likely. The GE Lunar Prodigy Advance is used in our clinic.

Thank you again for the interest in our work. We hope that we were able to clarify all of your questions and look forward to answering further comments and questions if any remain.

Disclosures

The authors state that they have no conflicts of interest.

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