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LETTER TO THE EDITOR

Reply to "Predictors of surgical outcome and early criteria of remission in acromegaly—some controversial issues"

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Recently, Wang and Xing wrote a letter [1] with some comments about our recently published study [2]. We read the authors' concerns about it and we would like to clarify these points.

First, the authors questioned that we defined surgical remission with the GH and IGF-I levels 3 months after surgery. They cited their own unpublished data to question this time period of evaluation and also the last Endocrine Society guideline [3]. We agree that in some cases, normalization of IGF-I can take more than 12 weeks, but in these cases there is generally a great decrease of IGF-I levels after 12 weeks and, also, GH levels are below 1.0 µg/L. From the 38 patients not cured by surgery, only three patients presented GH levels below 1.0 µg/L 3 months after surgery. In these three patients, medical therapy with octreotide was started and despite 1 year of treatment with the maximum dose, they still presented elevated IGF-I levels, therefore, we can assure that they were not cured by surgery. The other 35 patients also presented elevated random and post-glucose GH levels and it is highly improbable that GH levels take more than 12 weeks to normalize. In addition, considerable data in the literature show that although IGF-I levels can take more than 12 weeks to normalize, it is not common. For that reason, in the same guideline cited by the authors, it is stated that "IGF-1 levels measured at 12 weeks after surgery are a valid reflection of surgical remission" [3]. Therefore, we do believe that our period of evaluation of surgical cure is appropriate.

The second point raised by the authors is the use of IGF-I levels as predictors of surgical cure. They state and are correct that IGF-I assays may have a lot of interference, like liver and renal function and nutritional status [1]. However, it is unlikely that any of these factors have changed from the preoperative period to the first 2 days after surgery. Also, the immediate postoperative IGF-I levels were previously evaluated in two studies and in both it was also demonstrated that it was a predictor of surgical cure. Thus, our data reinforce the previous studies showing that, indeed, precocious postoperative IGF-I levels can be useful.

The third point addressed by the authors is the possible influence of previous medical treatment in our evaluation of surgical cure. It is correct that somatostatin receptor ligands (SRL) can have a long half-life and this could be a concern, but in our study medical treatment was stopped at least 1 month before surgery and, thus, the 3 months post-surgery evaluation was done at least after 4 months of SRL withdrawal. Therefore, it is unlikely that medication had any role in the normalization of GH and IGF-I levels in the four patients (5.8% of the patients included in the study) that used SRL before surgery and were considered in remission after surgical treatment. Furthermore, to help clarify this point, these four patients have now a follow-up of 22, 36, 42, and 44 months after surgery and all still have normal GH and IGF-I levels, allowing to assure that they were not erroneously considered in remission after surgery due to a residual action of the SRL treatment. In addition, we also performed in our study [2] the analysis excluding the patients submitted to medical treatment before surgery (data presented in Table 4 of the original article) and the results confirmed that both early GH and IGF-I are predictors of surgical cure.

In conclusion, we do acknowledge the concerns regarding our study, but hope we have clarified them, and we do agree that this is a very interesting area that needs more research and data in the literature.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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