Transsphenoidal surgery for pituitary adenoma: indications and outcomes

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Transsphenoidal surgery for pituitary adenoma: indications and outcomes

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To the Editor: We read with great interest the article by Marić et al (1) on the outcomes of pure endoscopic transsphenoidal surgery (PEETS). Since PEETS is a relatively new surgical technique, data on its effectiveness and safety are very valuable, which makes this article an important contribution to the field. However, we have some concerns about the protocol of the study regarding the biochemical criteria for remission of acromegaly, assessment of pituitary function, and the indications for surgical treatment of prolactinoma.

In order to estimate the acromegaly remission, the authors performed the measurement of insulin-like growth factor-1 (IGF-1) on the seventh postoperative day. In our opinion, this might be too early because IGF-1 may remain elevated for months after a successful surgery. According to the Consensus on Criteria for Cure of Acromegaly (2,3), successfulness of surgical treatment of acromegaly is defined by the adequate suppression of the growth hormone after the glucose load and normalization of IGF-1 three to six months after surgery. The level of IGF-1 in the immediate postoperative period might therefore be misleading in the estimation of acromegaly remission.

With regard to the assessment of pituitary function, the usual criterion for the postoperative improvement of hypogonadism in women of reproductive age is the resumption of the menstrual cycle, rather than the normalization of the estrogen level on the seventh postoperative day, as used in the study. Moreover, in the assessment of the adrenal function, the authors measured urinary free cortisol in some patients who were taking hydrocortisone replacement therapy at the same time. We agree with the authors that the insulin tolerance test (ITT), which is the gold standard in the assessment of the hypothalamo-pituitary-adrenal (HPA) axis, is a rather demanding procedure. Therefore in practice, the simpler, short synacthen test is usually applied as an alternative to ITT. To the best of our knowledge, the measurement of urinary free cortisol in patients under hydrocortisone therapy does not have proven specificity and sensitivity for the detection of HPA axis abnormalities.

Furthermore, the number of patients in the study who underwent pituitary surgery for prolactinoma was surprisingly high. Surgical management of prolactinoma has its controversies: potential surgical and endocrinological complications, as well as the recurrence of hyperprolactinemia. On the other hand, dopamine agonists are remarkably effective in normalization of serum prolactin level, restoration of gonadal function, and reduction of tumor size in patients with prolactinoma (4). We would like to emphasize that, according to the Endocrine Society Clinical Practice Guidelines (5) and our own experience, only a minority of patients with prolactinoma requires surgical treatment. In our cohort, for example, only one out of 62 patients treated for prolactinoma in the last three years required surgery. It is known that up to 40% of patients who have undergone an initial surgical remission might have a recurrence of the disease (6). Therefore, the authors' conclusion that surgery leads to remission of microprolactinoma in 100% of cases should be taken with some caution as they did not present the data from the follow-up period.

In conclusion, because of insufficient research on PEETS, studies like this are highly valuable. Nevertheless, we appeal to the authors to use contemporary diagnostic tests and cutoff values in the evaluation of pituitary disorders in order to have the results comparable to those of other authors in the field.

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In Reply: We are pleased that our article (1) has provoked interest and encouraged discussion among endocrinologists and pituitary surgeons since it presents data from a rather complex clinical field.

First, we are aware of the "Consensus on Criteria for Cure of Acromegaly," which define disease remission as suppression of the growth hormone after the glucose load beneath 1 ng/mL and normalization of insulin-like growth factor-1 (IGF-1) 3 to 6 months after surgery (2). However, based on our experience and several other studies (3-5), early postoperative IGF-1 and growth hormone in oral glucose tolerance test is a good predictor of long-term remission. Also, to the best of our knowledge, no studies have shown that early postoperative IGF-1 gave false-positive results. We measured IGF-1 in all patients with acromegaly seven days, three months, and nine months after surgery and performed oral glucose tolerance test in patients with IGF-1 within the upper third of the reference range interval. Measuring IGF-1 in patients with acromegaly seven days after surgery is crucial for early detection of active disease and planning other treatment modalities since residual aggressive somatotropinomas can progress tremendously within three to six months.

Regarding the diagnosis of secondary adrenal insufficiency, neither insulin tolerance test (ITT) nor synacthen test is mandatory to exclude adrenal insufficiency. Performing ITT within six weeks after the surgery has its risks and is not recommended (6). Therefore, we administered hydrocortisone replacement therapy to all our patients postoperatively. In patients receiving hydrocortisone replacement, urinary-free cortisol above 200 nmol/L is a clear sign of over-replacement and compensated pituitary function, while that above 500 nmol/L indicates normal pituitary function (7). Hence, hydrocortisone was gradually decreased in all patients with over-replacement and discontinued if morning cortisol exceeded 500 nmol/L. In others, ITT was performed prior to replacement discontinuation. Patients with urinary-free cortisol from 100 nmol/L to 200 nmol/L on hydrocortisone replacement were considered to have adrenal insufficiency.

Dopamine agonist therapy is the first line treatment for prolactinomas, as highlighted in the introduction to our article. We must point out that surgical patients with microprolactinoma greatly differ from all patients with prolactinoma treated in our Center, and the majority of the patients with microprolactinoma receive dopamine agonist therapy. However, medication therapy is associated with a decrease in life quality, side-effects, and high costs (8). On the other hand, pituitary surgery has substantially improved over the years and the most recent studies report recurrence rates of 5%-10% after surgical treatment of microprolactinomas (cited in our article). Our neurosurgeons have great experience in pituitary surgery (more than 50 operations per year) and therefore we offer our patients endoscopic pituitary surgery as an alternative to dopamine agonist therapy. This approach is in accordance with the practice in most of the leading pituitary centers in the world (9).

In conclusion, treatment of patients with pituitary adenomas is challenging and requires individualized approach

in order to achieve good results and low treatment costs. Therefore, the diagnosis and treatment algorithm often differs from clinical guidelines proposed by clinicians and scientists from the world's wealthiest countries.

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