Response to Letter to the Editor: "Surgery as a Viable Alternative First-Line Treatment for Prolactinoma Patients. A Systematic Review and Meta-Analysis"

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We thank Tang and Wu for their letter highlighting the current controversy in the management of prolactinoma and the upcoming role of endoscopic transsphenoidal surgery. We fully agree with them that weighing the benefits and risks of endoscopic surgery or treatment with dopamine agonists needs to be interpreted in the context of the individual patient. In particular, when multiple treatment options are available, the choice for treatment should be discussed with the patient through shared decision-making. Individual characteristics of the patient, accessibility of treatment, treatment costs, and available information on patient-relevant outcomes should all be considered. Ideally, outcome data are presented for different subgroups of patients, facilitating more tailored treatment decisions. These outcomes should not only focus on control and remission rates, but also on side effects and complications, health-related quality of life (HRQoL), symptoms, and treatment costs.

Our systemic review and meta-analysis was conducted to summarize current literature regarding these outcomes for both treatment modalities in order to make the best possible comparison (1). While surgery has been gaining more attention as a first-line treatment in recent years, a main pitfall in the interpretation of literature is the fact that the included cohorts are not comparable between both treatment modalities. This holds especially for the published surgical cohorts, as the guidelines advise to reserve surgery for selected patients with intolerance to dopamine agonists or a resistant prolactinoma (2). Results have also not been presented according to subgroups of patients with prolactinoma

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Abbreviations: CI, confidence interval; HRQoL, health-related quality of life.

with better and poor odds for surgical remission according to tumor size and extension (3).

Therefore, our group is currently comparing both treatment modalities on these outcomes in a nationwide randomized controlled trial for selected patients with micro and noninvasive prolactinoma and in a prospective cohort study for all patients with prolactinoma (ClinicalTrials.gov Identifier: NCT04107480).

From a surgical perspective, prolactinomas can be roughly divided into 3 clinically relevant subgroups: 1) nearly visible, very small, and difficult to delineate prolactinoma (eg, hyperprolactinemia and uncertain prolactinoma); 2) clearly visible, noninvasive prolactinoma (micro and smaller macroadenoma; and 3) invasive (macro) prolactinoma and giant prolactinoma. Groups 1 and 3 are clearly less than ideal candidates for surgery, and in these patients, there will be a preference for dopamine agonists, with the exception of specific cases (eg, intolerance, resistance, cerebrospinal fluid leak).

Group 2 is the group of particular interest for considering endoscopic surgery instead of treatment with dopamine agonists to achieve remission. With the lack of a comparative study, current evidence shows no preference for either surgery or dopamine agonist treatment. While treatment with dopamine agonists is the standard of care, treatment decisions for this group of patients are primarily based on response, side effects, evaluation of resectability by surgeons, and patients' personal preferences.

While the available literature does not completely allow us to present the available data separately for these 3 clinically different subgroups, we focused our review on obtaining the best available data for patients with clearly visible noninvasive prolactinoma. In patients with magnetic resonance imaging-diagnosed microprolactinoma, the control rate during treatment with dopamine agonists was 91% (95% confidence interval [CI], 85-96), however up to 30% of patients suffered from side effects. Remission rate after dopamine agonist withdrawal was just 36% (95% CI, 21-52), compared with 83% (95% CI, 76-90) after surgery. The most reported surgical complication was transient diabetes insipidus in 16% of patients. Limited evidence was found on HRQoL and costs.

Contrary to what Tang and Wu report, we also separately assessed giant prolactinoma. We reported that 41% (95% CI, 28%-54%) of these patients achieve normalized prolactin levels during medical treatment, which is lower than the 69% reported in the study performed by Wu and colleagues (4). However, we encourage readers to carefully interpret the results on giant tumors, as the number of patients in all analyses is small and no formal meta-analysis was performed by Wu and colleagues.

We agree with them that the Egger test could have provided extra information on possible publication bias, which could result in an overrepresentation of published studies reporting high effectiveness of treatment. However, the results of the individual studies indicate a large heterogeneity in the effectiveness of treatment for both treatment modalities, supporting that articles with less positive results were also published.

While we await the results of our randomized controlled trial and cohort study, including both clinician- and patient-reported outcome data, we believe that the results of our meta-analysis provide relevant data for more tailored treatment decision-making. Results show that in selected patients with clearly visible noninvasive smaller prolactinoma, surgery could be considered as first-line treatment (1, 3). Centers interested in participating in the ongoing registry are encouraged to contact us.

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Additional Information

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