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Reply to 'Tumour fibrosis in dopamine agonist-exposed prolactinomas is a diminishing concern'

We thank De Sousa and co-authors for their comments on our recently published Pituitary Society Consensus Statement on diagnosis and management of prolactin-secreting pituitary adenomas. In our Consensus Statement (Petersenn, S. et al. Diagnosis and management of prolactin-secreting pituitary adenomas: a Pituitary Society international Consensus Statement. *Nat. Rev. Endocrinol.* **19**, 722–740 (2023)[1]), we recommended discussion of first-line surgery alongside first-line medical treatment with dopamine agonists by expert endocrinologists and neurosurgeons in a selected subgroup of patients. In their correspondence (De Sousa, S. et al. Tumour fibrosis in dopamine agonist-exposed prolactinomas is a diminishing concern. *Nat. Rev. Endocrinol.* https://doi.org/10.1038/s41574-024-00976-y (2024)[2]), De Sousa and co-authors question the routine offer of surgery before attempting cabergoline, given the risk of potentially permanent operative complications in contrast to the reversibility of dopamine-induced toxicity. Certainly, risk–benefit reasoning should account for factors that might influence treatment outcomes (such as mass morphology, baseline serum levels of prolactin and sex) and also consider treatment-associated adverse effects or complications and patient preference. However, we would like to point to a few additional important considerations.

First, the number of neurosurgical complications is low in centres with experienced pituitary surgeons (≤2%) and mortality is negligible[3]. As we mention in our guidelines[1], patients should seek care at a centre with dedicated pituitary surgeons as well as neuroendocrinologists, to discuss the most favourable personalized treatment choices. Second, medical treatment is indicated at least until menopause for most female patients, as approximately four-fifths of patients with prolactinomas do not maintain remission after cabergoline withdrawal[4]. Patients should therefore be informed about surgery as a possible alternative and potentially curative therapeutic approach. Third, adverse effects of cabergoline are usually mild and improve with time but can be ongoing and disabling in individual patients. A meta-analysis published in 2020 found relevant dopamine agonist-induced nausea, headache, fatigue and sleep disorders in at least 10% of patients, and lower quality of life scores are consistently reported compared with healthy control individuals[5]. When patients consider surgery as a last-resort option, they might cycle through multiple dopamine agonists with many years of treatment intolerance before considering surgical resection[6]. High dose, long-term cabergoline treatment could rarely be associated with cardiac valvular dysfunction[7]. A need for regular monitoring[1] might increase patient anxiety over this potential adverse effect, as well as increase costs for repeat echocardiograms during follow-up. Finally, work from De Sousa[8] and others[9] highlighting the potential for neuropsychiatric adverse effects, including compulsive buying, gambling, aggression, changes in mood and hypersexuality, is important. Although rare, these effects might further increase patient anxiety about use of cabergoline.

We agree that the relevance of cabergoline-induced fibrosis in subsequent surgery is currently unknown, although we note that bromocriptine is still regularly used to treat prolactinoma in some countries[10]. Nevertheless, the low risk of surgical complications must still be weighed against long-term adverse effects of medical treatment and the need for continuous ongoing follow-up, both of which could represent a notable burden for some patients. Therefore, patients should be educated about efficacy and adverse effects of both medical and surgical treatment to enable an individualized choice.

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Competing interests

The authors declare no competing interests.