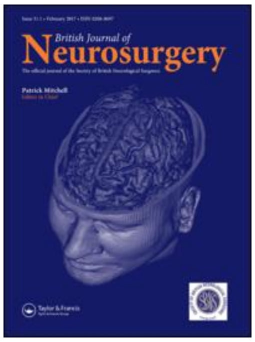

British Journal of Neurosurgery

ISSN: 0268-8697 (Print) 1360-046X (Online) Journal homepage: http://www.tandfonline.com/loi/ibjn20

Clinical outcomes of endoscopic versus microscopic trans-sphenoidal surgery for large pituitary adenoma

Hamideh Akbari, Mojtaba Malek, Mohammad Ghorbani, Seyed Mahmoud Ramak Hashemi, Mohammad Ebrahim Khamseh, Ali Zare Mehrjardi, Zahra Emami & Ameneh Ebrahim Valojerdi

BRITISH JOURNAL OF NEUROSURGERY, 2018
https://doi.org/10.1080/02688697.2018.1429569

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Clinical outcomes of endoscopic versus microscopic trans-sphenoidal surgery for large pituitary adenoma

Hamideh Akbari[a], Mojtaba Malek[b], Mohammad Ghorbani[c], Seyed Mahmoud Ramak Hashemi[c], Mohammad Ebrahim Khamseh[a], Ali Zare Mehrjardi[d], Zahra Emami[a] and Ameneh Ebrahim Valojerdi[a]

[a]Endocrine Research Center, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences, Tehran, Iran; [b]Research Center for Prevention of Cardiovascular Disease, Institute of Endocrinology and Metabolism, Iran University of Medical Sciences, Tehran, Iran; [c]Department of Neurosurgery and Neuro-Intervention, Firouzgar Hospital, Iran University of Medical Sciences, Tehran, Iran; [d]Department of Pathology, Firouzgar Hospital, Iran University of Medical Sciences, Tehran, Iran

ABSTRACT

Objective: To compare clinical outcomes of large pituitary adenomas (≥3 cm in maximum diameter), operated on by Endoscopic Transsphenoidal Surgery (ETS), versus Microscopic Transsphenoidal Surgery (MTS).
Methods: Medical records and MRI Scans of patients with a diagnosis of pituitary adenoma for whom transphenoidal surgery was done were reviewed. Complete pre and post-operative data were available for 121 patients. Thirty five patients had large pituitary adenoma and were enrolled in this study. ETS was done in 16 patients, and 19 underwent MTS. All patients were followed for at least six months. Clinical and imaging characteristics were reported in details. Post-operative clinical outcomes were defined as clinical outcomes persisted 6 months after surgery.
Results: The average tumor size was 36.3 ± 4.4 mm in ETS group, and 34.0 ± 4.6 mm in MTS group, ($p = .46$). Six months after surgery, tumor size was 4.6 ± 6.6 mm in ETS and 17.7 ± 12.2 mm in MTS group, ($p = .002$). Gross total resection (GTR) was observed in the 81.2% of the patient in the ETS group. In the MTS group, GTR was observed in 15.8%.
Post-operative clinical outcomes including new onset hypopituitarism, visual impairment, and permanent diabetes insipidus (DI) were comparable between the two groups.
Conclusion: ETS is superior to MTS in treatment of large pituitary adenomas with comparable post-operative complications.

ARTICLE HISTORY
Received 12 March 2017
Revised 11 November 2017
Accepted 15 January 2018

KEYWORDS
Trans-sphenoidal surgery; large pituitary adenoma

Introduction

Treatment modalities for pituitary adenoma (PA) include surgery, radiotherapy, and medical treatment.[1] Except for prolactinoma where medical therapy is the treatment of choice, transsphenaid surgery is the treatment of choice.[2]

Microscopic transsphenoidal surgery (MTS) has been considered as the standard.[3] However, endoscopic endonasal transsphenoidal surgery (ETS) has become an alternative in recent years.[4]

The efficacy of ETS for management of pituitary adenomas has been reported.[3,5,6] However, reports on gross total resection (GTR) and complications are inconsistent.

Large pituitary adenomas are those with maximum diameter of 30 mm or more. They may extend into cavernous sinus or suprasellar regions.[7,8] These features provide major neurosurgical challenges.[9,10] GTR for smaller pituitary adenomas **is** reported to be comparable for ETS and MTS.[11] However, the results for large pituitary tumors are variable.[11] GTR for invasive/macro adenoma is reported to be up to 78% and 31% for ETS, and MTS respectively.[10,12–14] Furthermore, the reported incidence of postoperative complications including new onset hypopituitarism and permanent diabetes insipidus (DI) is diverse among different studies.[3,15,16]

The aim of this study was to compare the clinical outcomes of ETS and MTS for large pituitary adenomas, emphasizing GTR and postoperative complications.

Methods

We retrospectively reviewed medical files of patients operated on for pituitary adenomas either by ETS or MTS from 2012 to 2014. Endoscopic surgery was performed by a single neurosurgeon who performed at least eight operations over the3 years. All microscopic surgeries were done by two neurosurgeons who performed at least ten operations per month over the 5 years up to 2014.

the microscopic approach was performed via the transseptal route in the supine position with slight head and neck elevation and under direct fluoroscopic guidance, using C-arm fluoroscopy. X-ray localization was used for all the patients. Lumbar drains were fixed pre-operatively and after removal of the tumor, 3 to 5 ml of saline were injected to displace remnant tumour into the operation field. Valsalva maneuvers were applied simultaneously, waiting 10-15 minutes for tumor remnant to appear.

CONTACT Mohammad Ebrahim Khamseh khamseh.m@iums.ac.ir Endocrine Research Center, Institute of Endocrinology and Metabolism, Firoozeh St, Vali-asr Sq, Tehran, Iran

the endoscopic approach was performed in the supine position with neck hyperextension with the two nostril technique. Submucosal resection was done and nasoseptal flaps raised for possible closure of large defects. After sphenoidotomy, a posterior septectomy was done. Using a high speed drill, a wide opening in the rostrum was created for the endoscope. 30°, and 70° angled endoscope was used for optimal visualization. This technique eliminates the need for valsalva maneuver and lumbar drain insertion. Neuronavigation system (parsis, Parsis Teb, Tehran, Iran) was applied via right nostril. Bare endoscopes were used for visualization only. Instruments were inserted parallel to the endoscopes rather than via separate working channels in the endoscope instrument.

Patients who were followed for at least six months after surgery were included in this study. The preoperative MRI scans were reviewed by a neuroradiologist. Pituitary adenomas were confirmed post operatively by immunohistochemical (IHC) staining. Patients with other sellar or parasellar lesions were excluded. Visual fields were evaluated before and 6 months after surgery for all patients.

To determine tumor resection rate, post-operative MRI Scans were reviewed six months after surgery. Post contrast T1WI scans were used to calculate residual tumor size.

Recorded imaging characteristics included tumor size, shape (round, dumbbell, multilobular), extension into the cavernous sinus (CSI) only, CSI plus suprasellar, suprasellar only, and evidence of apoplexy. Cavernous sinus invasion was evaluated according to the Knosp criteria and was confirmed intraoperatively.

Early post-operative complications were recorded 3 months after surgery. New onset pituitary dysfunction was defined as biochemical pituitary dysfunction or initiation of new hormone replacement. Permanent post-operative clinical outcome was defined as clinical outcome that persisted 6 months after surgical intervention.

Gross total resection (GTR) was defined as optic apparatus (nerves/chiasm/tract) decompression and less than 20% residual tumor volume after surgery. In patients with acromegaly remission was defined as GH level <1 µg/dl after OGTT, and restoration of IGF-I levels to normal for the age and sex.[17] Remission of prolactinoma was defined as normal serum prolactin without medical treatment for at least 6 months after surgery.[1,2]

Results

Of 121 patients who had complete pre-operative and post-operative data, 35(29%) with large pituitary adenoma were eligible to enroll in this study.

The type of surgery was ETS in 16 (45.7%), and MTS in 19 (54.3%).

Nonfunctional pituitary adenomas were the most frequent, followed by medication-resistant prolactinoma, and GH-secreting pituitary adenoma. The median diameter of adenomas was 35 mm (36.3 ± 4.4 mm) in ETS group and 32 mm (34.00 ± 4.6) mm in MTS group. ($p = .46$). Clinical characteristics of the participants are shown in Table 1.

Immunohistochemical staining was performed for all surgical specimens. In NFPA, 37% had no immunoreaction to all 6 hormones (null cell adenoma). On the other hand, in 63% of the remaining clinically NFPAs, LH were the commonest subtype comprised 59% of the subjects. One tumor was positive for LH + FSH, and 1 for LH + ACTH. No significant statistical difference between clinical presentations in immunoreactive and non-immunoreactive NFPAs was observed.

In five patients with GH producing adenoma, 3 were positive for GH and 2 for GH and LH.

In prolactinomas, 5 were positive for prolactin and 1 for GH plus prolactin.

After applying monoclonal antibody MIB-1 to all surgical specimens, Ki-67 antigen more than 3% were detected in 14.3%. This subgroup had tumor extension to suprasellar region and Cavernous sinus simultaneously.

Review of the MRI scans showed various tumor shapes, pattern of extension, and contrast enhancement. Large pituitary adenomas were rounded in 11 cases (31.42%), dumbbell shaped in 10 (28.58%), and multilobular in 14 (40%).

Regarding tumor extension, 8 tumors (22.85%) occupied cavernous sinus only, 14 (40%) extended only to the suprasellar region, and 13 (37.14%) had cavernous sinus plus suprasellar extension. Homogeneous enhancement after contrast administration was detected in 11 patients (31.42%), while 24 (68.58%) showed heterogeneous enhancement (Table 2).

Early post-operative complications including CSF leak, meningitis, and new onset hypopituitarism were similar in both groups (Table 3).

Six months after surgery, the average tumor size was significantly smaller in ETS group: 4.6 ± 6.6 mm vs. 17.7 ± 12.2 ($p = .002$).

The proportion of patients with lack of GTR was higher in the MTS group compared to ETS group: 16 (84.2%) vs. 3

Table 1. Baseline characteristics of the study participants.

	Endoscopic-TSS ($n = 16$)	Microscopic-TSS ($n = 19$)	p value
Mean age (years) ±SD	39.43 ± 15.21	43.06 ± 11.29	.45
Male, n (%)	9 (56%)	10 (53%)	.83
Tumor size (mm) ±SD	36.3 ± 4.4	34.0 ± 4.6	.46
Hypopituitarism, n (%)	7 (43.7%)	4 (21.0%)	.27
Visual field impairment, n (%)	10 (62.6%)	9 (47.4%)	.37
Diabetes insipidus, n (%)	2 (12.5%)	0	.2

Table 2. Imaging characteristics of the pituitary adenomas.

	Endoscopic TSS ($n = 16$)	Microscopic TSS ($n = 19$)	p value
Size			
30–40 mm	13	15	.99
>40 mm	3	4	
Shape			
Rounded	4	7	.49
Dumbbell	5	5	.75
Multilobular	7	7	.68
Extension			
CSI Only	3	5	.70
CSI and suprasellar	5	8	.51
Suprasellar Only	8	6	.27
Contrast Enhancement			
Homogeneous	6	5	.48
Heterogeneous	10	14	

CSI: cavernous sinus invasion.

Table 3. Early post-operative complications*.

	Endoscopic TSS ($n = 16$)	Microscopic TSS ($n = 19$)	p value
CSF leak, n (%)	3 (18.8%)	2 (10.5%)	.66
Meningitis, n (%)	2 (12.5%)	1 (5.2%)	.60
Death, n (%)	2 (12.5%)	2 (10.5%)	.999
New onset hypopituitarism, n (%)	5 (31.25%)	7 (36.8%)	.99

*Complications occurred up to three months after surgery.

Table 4. Permanent post-operative clinical outcomes*.

	Endoscopic TSS ($n = 16$)	Microscopic TSS ($n = 19$)	p value
Hypopituitarism, n (%)	12 (75%)	11 (57.8%)	.28
Visual field impairment, n (%)	5 (31.2%)	5 (26.3%)	.75
DI (permanent), n (%)	5 (31.2%)	4 (21%)	.999
Average tumor size (mm ± SD)	4.57 ± 6.58	17.69 ± 12.25	.002
Lack of GTR, n (%)**	3 (18.7%)	16 (84.2%)	.007

*Clinical outcomes persisted 6 months after surgery.
**More than 20% residual tumor after surgery.

Table 5. Gross total resection* stratified by type of surgery.

	Endoscopic TSS ($n = 13$)	Microscopic TSS ($n = 3$)	p value
Size			
≥30 Mm	13	3	<.001
Shape			
Rounded	3	2	.21
Dumbbell	3	1	.61
Multilobular	7	0	.15
Extention			
Csi Only	3	0	.99
Csi and Suprasellar	2	0	.99
Suprasellar Only	8	3	.51
Contrast enhancement			
Homogeneous	6	1	.99
Heterogeneous	7	2	

*More than 80% resection rate.

(18.7%) $p = .007$. In the ETS group, two patients had residual tumor in the cavernous sinus plus suprasellar regions, and one patient had remnant in suprasellar area. On the other hand, in the MTS group, residual tumor was detected in the suprasellar plus cavernous sinus, and suprasellar only in 9 and 7 patients respectively.

Permanent post-operative clinical outcomes including hypopituitarism, visual field impairment and diabetes insipidus (DI) were not different between the two groups (Table 4).

We also evaluated the frequency of GTR according to the pre- operative characteristics in all patients. Among various characteristics, only tumor extension showed statistically significant effect on the outcome of surgery. Tumors with suprasellar extension only showed the highest GTR (78.5%), while GTR in patients with CSI plus suprasellar extension was 15.3%.

Tumors with cavernous sinus invasion or those with cavernous sinus plus suprasellar extension were associated with lack of GTR: 62.5%, and 84.6% respectively. Only 4 patients in ETS and 3 patients in MTS group had sphenoid sinus invasion as well. This had no effect on GTR in final analysis. Those with suprasellar extension only, had the best outcome: 78.5% showed GTR, ($p = .002$).

When we compared GTR between the two types of surgery, among all variables measured, tumor size showed statistically significant effect on this outcome (Table 5).

Discussion

In this study, we found that ETS was associated with higher GTR compared to MTS in patients with large pituitary adenomas: 81.3% vs. 15.8%.

Literature comparing endoscopic and microscopic TSS for large pituitary adenomas is still limited. There is no clear distinction between pituitary macroadenomas and large pituitary adenomas other than by size. The lower limit for classification of a large pituitary adenoma ranges from 30 to 40 mm in maximal diameter.[8–10] Many of these tumors invade the cavernous sinus and complete resection is often a technical challenge.[9,18,19] Although transsphenoidal surgery is known as the optimum technique for resecting pituitary tumors within the sella turcica, the surgical approach for adenomas with suprasellar extensions or cavernous sinus invasion remains controversial.[10,20] Clinical presentation, tumor anatomy and biology rather than tumor size have been reported as the main determinates of the surgical approach.[9] By obtaining maximal tumor resection, surgery could help to relief mass effect on visual pathways and neurovascular structures.[21–23]

The benefits and limitations of the various surgical approaches including ETS, MTS and open surgery on giant pituitary adenomas have been explored. One of the strengths of the microscopic technique is stereoscopic depth perception in contrast with the monoscopic and wide view of the endoscope.[24] In addition, MTS provides the opportunity for the implementation of more than one instrument simultaneously. However, the width of the visible field is limited and complete resection of the tumor may be problematic.

The safety and efficacy EST has been repoerted.[3,5,6] The technique could improve visualization of the surgical field and significantly extends the field of view.[9] Other advantages of ETS include preservation of sinonasal function, and reduced complications.[5]

We used wide-angled 30° and 70° endoscopes to allow surgical views of lateral and superior structures to identify tumor parts that could not be explored with the straight view of the microscope. The main limitation of ETS is its failure when severe bleeding occrued.[24] further limitations include less room for the surgeon to manipulate surrounding structures, and longer duration of operation time.[12,25]

Higher rates of GTR (47.2%)[26,27] and improved visual outcome (91.1%) are reported in patient operated with ETS in comparison to transcranial and MTS.[10,26,27] In another study, low rate of GTR was reported, regardless of type of surgical approach. However, the rate of GTR was highest for the endoscopic endonasal approach.[10,27] The difference could be explained by better visualization provided by the endoscopic approach.[14] Moreover, improvement of surgical oucomes is correlated with the numbers of patients operated on.

Tumor size, configuration, and extension should be considered for evaluating the maximum tumor resection using endonasal transphenoidal approach.

In our study, tumors with cavernous sinus invasion or those with cavernous sinus plus suprasellar extension were associated with significant residual tumor after surgery. Tumors with suprasellar extension only, had the best outcome: 78.5% showed no residual tumor after surgery. The major limitation with the endoscopic approach is cavernous sinus invasion,[20,21,28] while for the microscopic transsphenoidal surgery, suprasellar extension is the main barrier.[22]

Other barriers to ETS include tumor size[29], multilobular configuration and extension to the middle fossa.[10,23] In our study, the maximum tumor diameter was 41mm and there was no significant difference between the two groups considering the shape of adenomas.

Visual outcomes are a major advantage of the ETS approach in comparison with other surgical techniques.[30] Landeiro *et al.* analysed their initial experience in the management of 35 patients with giant nonfunctioning pituitary adenomas operated on by endonasal endoscopic transphenoidal resection. They found improvement of visual acuity and visual field in (80%) and (73.9%) of the patients respectively.[31] Chabot *et al.* hypothesized that the endoscope approach protects the optic apparatus and its blood supply and provides a better visual field.[30]

The rates of visual improvement for ETS are reported from 73% to 91.1%.[23,29,32] This figure is 45.7% for open transcrandial, and 34.8% for microscopic transphenoidal approches.[26]

In our study, visual field improvement was comparable in both groups: 50% of the patients showed improvement of the visual fields six months after surgery. Moreover, there were no differences in permanent post-operative complications including new onset hypopituitarism, and permanent diabetes insipidus (DI) between the two groups. These findings are limited by the number of the patients in each group and the duration of follow-up.

Previous studies comparing clinical outcomes of large pituitary tumors explored the issue in different populations and clinical settings. This study examines the outcomes using data from a single clinical care setting. However, we had some limitation: the retrospective design of the study, surgical procedures were performed by different neurosurgeons and limited sample size **limits** subgroup analysis.

Conclusion

ETS is superior to MTS in the treatment of large pituitary adenomas with comparable post-operative complications. However, the success rate decreases for large adenomas with cavernous sinus invasion.

Disclosure statement

The authors report no declarations of interest.

References

1. Primeau V, Raftopoulos C, Maiter D. Outcomes of transsphenoidal surgery in prolactinomas: improvement of hormonal control in dopamine agonist-resistant patients. *Eur J Endocrinol* 2012;166:779–86.
2. Melmed S, Casanueva FF, Hoffman AR, *et al.* Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2011;96:273–88.
3. Singh H, Essayed WI, Cohen-Gadol A, *et al.* Resection of pituitary tumors: endoscopic versus microscopic. *J Neurooncol* 2016;130:309–17.
4. Guo-Dong H, Tao J, Ji-Hu Y, *et al.* Endoscopic Versus Microscopic Transsphenoidal Surgery for Pituitary Tumors. *J Craniofac Surg* 2016;27:e648–55.
5. Goudakos JK, Markou KD, Georgalas C. Endoscopic versus microscopic trans-sphenoidal pituitary surgery: a systematic review and meta-analysis. *Clin Otolaryngol* 2011;36:212–20.
6. Tabaee A, Anand VK, Barrón Y, *et al.* Endoscopic pituitary surgery: a systematic review and meta-analysis. *J Neurosurg* 2009;111:545–54.
7. Garibi J, Pomposo I, Villar G, Gaztambide S. Giant pituitary adenomas: clinical characteristics and surgical results. *Br J Neurosurg* 2002;16:133–9.
8. Goel A, Nadkarni T, Muzumdar D, *et al.* Giant pituitary tumors: a study based on surgical treatment of 118 cases. *Surg Neurol* 2004;61:436–45.
9. Cusimano MD, Kan P, Nassiri F, *et al.* Outcomes of surgically treated giant pituitary tumours. *Can J Neurol Sci* 2012;39:446–57.
10. Constantino ER, Leal R, Ferreira CC, *et al.* Surgical outcomes of the endoscopic endonasal transsphenoidal approach for large and giant pituitary adenomas: institutional experience with special attention to approach-related complications. *Arq Neuro-Psiquiatr* 2016;74:388–95.
11. Zaidi HA, Awad AW, Bohl MA, *et al.* Comparison of outcomes between a less experienced surgeon using a fully endoscopic technique and a very experienced surgeon using a microscopic transsphenoidal technique for pituitary adenoma. *J Neurosurg* 2016;124:596–604.
12. Gao Y, Zheng H, Xu S, *et al.* Endoscopic versus microscopic approach in pituitary surgery. *J Craniofac Surg* 2016;27:e157–9.
13. Alahmadi H, Dehdashti AR, Gentili F. Endoscopic endonasal surgery in recurrent and residual pituitary adenomas after microscopic resection. *World Neurosurg* 2012;77:540–7.
14. Dhandapani S, Singh H, Negm HM, *et al.* Cavernous sinus invasion in pituitary adenomas: systematic review and pooled data meta-analysis of radiologic criteria and comparison of endoscopic and microscopic surgery. *World Neurosurg* 2016;96:36–46.
15. Gao Y, Zhong C, Wang Y, *et al.* Endoscopic versus microscopic transsphenoidal pituitary adenoma surgery: a meta-analysis. *World J Surg Onc* 2014;12:94.
16. Halvorsen H, Ramm-Pettersen J, Josefsen R, *et al.* Surgical complications after transsphenoidal microscopic and endoscopic surgery for pituitary adenoma: a consecutive series of 506 procedures. *Acta Neurochir* 2014;156:441–9.
17. Shirakawa M, Yoshimura S, Yamada K, *et al.* Effectiveness of endoscopic endonasal transsphenoidal surgery using a neuronavigation: clinical results of 178 pituitary adenomas. *J Neurol Neurosci* 2016;7:6.
18. Agrawal A, Cincu R, Goel A. Current concepts and controversies in the management of non-functioning giant pituitary macroadenomas. *Clin Neurol Neurosurg* 2007;109:645–50.
19. Cappabianca P, Cavallo LM, Esposito F, *et al.* Extended endoscopic endonasal approach to the midline skull base: the evolving role of transsphenoidal surgery. *Adv Tech Stand Neurosurg* 2008;33:151–99.
20. McLaughlin N, Eisenberg AA, Cohan P, *et al.* Value of endoscopy for maximizing tumor removal in endonasal transsphenoidal pituitary adenoma surgery. *J Neurosurg* 2013;118:613–20.
21. Gondim JA, Almeida JP, Albuquerque LA, *et al.* Giant pituitary adenomas: surgical outcomes of 50 cases operated on by the endonasal endoscopicapproach. *World Neurosurg* 2014;82:e281–90.
22. Cappabianca P, Cavallo LM, de Divitiis O, *et al.* Endoscopic endonasal extended approaches for the management of large pituitary adenomas. *Neurosurg Clin N Am* 2015;26:323–31.
23. Koutourousiou M, Gardner PA, Fernandez-Miranda JC, *et al.* Endoscopic endonasal surgery for giant pituitary adenomas: advantages and limitations. *J Neurosurg* 2013;118:621–31.
24. Guvenc G, Kizmazoglu C, Pinar E, *et al.* Outcomes and complications of endoscopic versus microscopic transsphenoidal surgery in pituitary adenoma. *J Craniofac Surg* 2016;27:1015–20.
25. Razak AA, Horridge M, Connolly DJ, *et al.* Comparison of endoscopic and microscopic trans-sphenoidal pituitary surgery: early results in a single centre. *Br J Neurosurg* 2013;27:40–3.
26. Komotar RJ, Starke RM, Raper DM, *et al.* Endoscopic endonasal compared with microscopic transsphenoidal and open transcranial resection of giant pituitary adenomas. *Pituitary* 2012;15:150–9.
27. Komotar RJ, Starke RM, Raper DM, *et al.* Endoscopic skull base surgery: a comprehensive comparison with open transcranial approaches. *Br J Neurosurg* 2012;26:637–48.
28. Nakao N, Itakura T. Surgical outcome of the endoscopic endonasal approach for non-functioning giant pituitary adenoma. *J Clin Neurosci* 2011;18:71–5.
29. Hofstetter CP, Nanaszko MJ, Mubita LL, *et al.* Volumetric classification of pituitary macroadenomas predicts outcome and morbidity following endoscopic endonasal transsphenoidal surgery. *Pituitary* 2012;15:450–63.
30. Chabot JD, Chakraborty S, Imbarrato G, Dehdashti AR. Evaluation of outcomes after endoscopic endonasal surgery for large and giant pituitary macroadenoma: a retrospective review of 39 consecutive patients. *World Neurosurg* 2015;84:978–88.
31. Landeiro JA, Fonseca EO, Monnerat AL, *et al.* Nonfunctioning giant pituitary adenomas: Invasiveness and recurrence. *Surg Neurol Int* 2015;6:179.
32. Juraschka K, Khan OH, Godoy BL, *et al.* Endoscopic endonasal transsphenoidal approach to large and giant pituitary adenomas: institutional experience and predictors of extent of resection. *J Neurosurg* 2014;121:75–83.