Endoscopic Endonasal Transsphenoidal Approach for Apoplectic Pituitary Tumor: Surgical Outcomes and Complications in 45 Patients

Rucai Zhan^{1,2} Xueen Li¹ Xingang Li¹

¹Department of Neurosurgery, Qilu Hospital of Shandong University, Brain Science Research Institute, Shandong University, Jinan, China

²Department of Neurosurgery, Jinan Third People's Hospital, Jinan, Shandong, China

Address for correspondence Xingang Li, MD, PhD, Department of Neurosurgery, Qilu Hospital of Shandong University, 107 Wenhua Xilu Rd, Jinan, Shandong, China 250012 (e-mail: lixg@sdu.edu.cn).

J Neurol Surg B 2016;77:54–60.

Abstract

Objective To assess the safety and effectiveness of the endoscopic endonasal transsphenoidal approach (EETA) for apoplectic pituitary adenoma.

Design A retrospective study.

Setting Qilu Hospital of Shandong University; Brain Science Research Institute, Shandong University.

Participants Patients admitted to Qilu Hospital of Shandong University who were diagnosed with an apoplectic pituitary tumor and underwent EETA for resection of the tumor.

Main Outcome Measures In total 45 patients were included in a retrospective chart review. Data regarding patient age, sex, presentation, lesion size, surgical procedure, extent of resection, clinical outcome, and surgical complications were obtained from the chart review.

Results In total, 38 (92.7%) of 41 patients with loss of vision obtained visual remission postoperatively. In addition, 16 patients reported a secreting adenoma, and postsurgical hormonal levels were normal or decreased in 14 patients. All other symptoms, such as headache and alteration of mental status, recovered rapidly after surgery. Two patients (4.4%) incurred cerebrospinal fluid leakage. Six patients (13.3%) experienced transient diabetes insipidus (DI) postoperatively, but none of these patients developed permanent DI. Five patients (11.1%) developed hypopituitarism and were treated with replacement of hormonal medicine. No cases of meningitis, carotid artery injury, or death related to surgery were reported.

Conclusion EETA offers a safe and effective surgical option for apoplectic pituitary tumors and is associated with low morbidity and mortality.

Keywords

- ▶ endoscope
- ▶ endonasal transsphenoidal approach
- ▶ outcome
- ▶ pituitary adenoma
- ▶ pituitary apoplexy

Introduction

Pituitary adenomas accounted for 15% of benign intracranial tumors.¹ However, apoplectic pituitary adenoma is a rare tumor, accounting for only 0.6 to 10.5% of pituitary tumors.²

Pituitary apoplexy is an uncommon clinical condition often associated with potential fatality, given rapid enlargement of a preexisting pituitary adenoma resulting from hemorrhage or infarction.³ The apoplexy rate of our series was 9%, which is comparable with reported rates. Presenting symptoms of this

received

March 21, 2015

accepted after revision

June 25, 2015

published online

August 20, 2015

© 2016 Georg Thieme Verlag KG
Stuttgart · New York

DOI <http://dx.doi.org/10.1055/s-0035-1560046>.
ISSN 2193-6331.

lesion include decreased vision, onset of severe headache, vomiting, and altered consciousness.^{4–7} Cerebral infarction,^{8,9} cranial nerve palsy,¹⁰ and meningitis are infrequent symptoms.⁹ Most cases of apoplexy occur in patients with a known or unknown history of pituitary adenoma. These tumors rarely occur in a nonadenomatous pituitary lesion (e.g., abscess).¹¹ The pathophysiologic mechanism of pituitary apoplexy is unclear; however, associated precipitating factors including hypertension, pregnancy, trauma, surgery, dynamic endocrine testing, stress, and medications are stressed in numerous reports.^{12–20} Regarding the treatment of apoplectic pituitary adenoma, emergent neurosurgical intervention is used to prevent catastrophic complications.²¹ However, most case reports on the surgical management of this lesion focus on a microscopic transsphenoidal approach. Few reports have focused on endoscopic endonasal transsphenoidal approach (EETA) for pituitary apoplexy in a high-volume series. In the present study, we report 45 patients at our institution with pituitary tumor apoplexy managed via EETA over a 4-year period.

Materials and Methods

Experimental Design

A retrospective chart analysis of 500 consecutive patients admitted to Qilu Hospital of Shandong University who underwent EETA for resection between June 2010 and July 2014 identified 45 patients with pituitary tumor apoplexy. Charts were reviewed for patient age, sex, presentation, lesion size, surgical procedure, extent of resection, clinical outcome, and surgical complications. Patients who underwent a microscopic transsphenoidal approach aided with an endoscope were excluded. The protocol for this study was reviewed and approved by the Ethics Committee of Qilu Hospital of Shandong University (No. KYLL-2013–010).

Preoperative Examination

Routinely endocrine evaluation, such as hormonal level (e.g., prolactin [PRL], growth hormone [GH], adrenocorticotropic

hormone [ACTH], thyroid-stimulating hormone, follicle-stimulating hormone), serum cortisol, and urinary free cortisol, as well as standard blood examinations including glycaemia, blood cell count, serum Na⁺, and urinary Na⁺ were performed on all patients upon admission to the hospital. At the same time, magnetic resonance imaging (MRI) (►Fig. 1) and computed tomography were used to evaluate size, location, and coherence of the tumor, which aided in decisions regarding surgical approach.

Endoscopic Technique

The procedure was performed via a 0-degree rigid endoscope (4 mm in diameter, 18 cm in length). The endoscope was introduced into the right nostril. In most case, the middle turbinate was easily located and pushed laterally. Then the endoscope was angled upward ~ 1.5 cm above the choana to reach the sphenoid ostium, an important anatomical landmark. After the sphenoid sinus was opened and the sphenoid separation was dissected, the floor of the sella turcica was explored and opened (►Fig. 2A) with a high-speed microdrill and Kerrison rongeur. In most cases the dural of the sellar floor was under high tension (►Fig. 2A) and occasionally colored bluish violet. The dural was typically opened cruciately, and the tumor was removed with curettage and suction (►Fig. 2B). Dark red bloody fluid was commonly noted during the operation. A 30-degree endoscope was applied to inspect the sellar region for residual tumor and cerebrospinal fluid (CSF) leak (►Fig. 2). If a CSF leak was suspected or confirmed, a multilayers repair technique with a vascularized pedicled nasoseptal flap (PNSF) was performed. After the surgical cavity was filled with Gelfoam, an autologous fat or fascia lata graft was placed within the dural defect as an inlay graft, and a synthetic dural graft was applied as an overlay graft. The vascularized PNSF was rotated and covered on overlay graft; then fibrin glue was applied over the PNSF. The procedure concluded by filling the sphenoid sinus with Gelfoam and packing the nasal cavity with pledgets.

Fig. 1 Preoperative magnetic resonance imaging (MRI). A 45-year-old man presented with a severe headache and sudden visual loss 3 days before surgery. T1-weighted MRI examination in the (A) coronal and (B) sagittal revealed a mild hyperintense sellar mass with evidence of hemorrhage (arrowheads) extending toward the suprasellar area and cavernous sinus.

Fig. 2 Intraoperative endoscopic views. The patient was subject to the endoscopic endonasal transsphenoidal approach procedure 2 days after admission. Endoscopic views demonstrate that the sellar floor was opened and the dura of sellar floor exhibited high tension. (A–C) The tumor was removed. (D) The sellae diaphragm dropped into view without residual tumor (arrowheads).

Postoperative Management

Fluid intake and urine output were monitored daily. Fluid and electrolyte balance were controlled systemically. A third-generation cephalosporin was intravenously infused for 3 to 7 days. Patients were instructed to rest with their head elevated ~ 15 degrees and to avoid any activity that might raise intracranial pressure such as straining or nose blowing. Hormone replacement therapy was administered to patients who had insufficient postsurgical hormonal

levels. Nasal packing was generally removed endoscopically for the first 1 to 3 days; MRI was obtained within 1 to 3 days and at 3 months following surgery to evaluate the extent of tumor resection²² (→Fig. 3). Lumbar drainage was applied to one patient who developed CSF leakage postoperatively. Replacement therapy for deficient hormones was administered to patients with postoperative diabetes insipidus (DI). The means of medicine replacement varied from subcutaneous injection of hypophysin to daily

Fig. 3 Postoperative magnetic resonance imaging (MRI). At the 1-year follow-up, (A) coronal and (B) sagittal T1-weighted MRI imaging indicate that the tumor had disappeared completely (arrowheads).

administration of Minirin based on the symptoms being controlled.

Results

In total, 26 males and 19 females were included into this cohort, ranging in age from 14 to 67 years (mean: 36.5 years). Follow-up ranged from 7 to 54 months (mean: 26 months). The most frequent clinical presentation was visual loss (41 of 45 [91.1%]) followed by serious headache (39 of 45 [86.7%]). In total, 42 patients were subject to emergent endoscopic surgery within 24 hours after symptom onset. Of these patients, 37 patients underwent surgery 12 to 16 hours after hospitalization. The remaining three patients (6.7%) did not exhibit typical symptoms of pituitary apoplexy and were subject to surgery 48 hours after admission; these patients experienced tumorous hemorrhage intraoperatively. In total, 28 (62.2%) of the 45 patients were diagnosed with a macroadenoma. On preoperative endocrinologic examination, 29 patients exhibited nonsecreting adenoma, and 16 patients had secreting tumors and presented symptoms of pituitary dysfunction, such as increased levels of GH, PRL, and ACTH (► **Table 1**).

In total, 39 patients (86.7%) achieved total resection, 6 experienced subtotal resection, and no patients experienced partial or insufficient resection. In total, 38 (92.7%) of 41 patients with loss of vision obtained visual remission postoperatively. Of 16 patients with secreting adenoma, postsurgical hormonal levels were normal or decreased in 14 patients. All additional symptoms, such as headache and alteration of mental status, recovered rapidly after surgery (► **Table 2**).

Two patients (4.4%) incurred CSF leakage that was managed successfully with CSF drainage. Six patients (13.3%) experienced transient DI postoperatively, and none of those patients developed permanent DI. Five patients (11.1%) de-

Table 1 Summary of clinical characteristics in 45 patients

	Number	Rate, %
Sex		
Male	26	57.8
Female	19	42.2
Presentations		
Headache	39	86.7
Nausea and vomiting	27	60
Visual loss	41	91.1
Alteration of mental status	12	26.7
Loss of consciousness	4	8.9
Seizure	2	4.5
Endocrinologic disorder	16	35.6
Radiography study		
Microadenoma	17	37.8
Macroadenoma	28	62.2

Table 2 Surgical outcomes and complications

	Number	Rate, %
Extent of resection		
Total resection	39	86.7
Subtotal resection	6	13.3
Initial symptom		
Headache		
Normalized	39/39	100
Nausea and vomiting		
Normalized	27/27	100
Visual deterioration		
Normalized	27/41	65.9
Improved	11/41	26.8
No changed	3/41	7.3
Alteration of mental status		
Normalized	12/12	100
Loss of consciousness		
Normalized	4/4	100
Seizure		
Normalized	2/2	100
Endocrinologic recovery		
Normalized	5/16	31.2
Improved	9/16	56.3
No changed	2/16	12.5
Surgical complication		
CSF leakage	2	4.4
Hypopituitarism	5	11.1
Transient DI	6	13.3
Persistent DI	0	0
Meningitis	0	0
Carotid artery injury	0	0
Death	0	0

Abbreviations: CSF, cerebrospinal fluid; DI, diabetes insipidus.

veloped hypopituitarism and were treated by replacement hormonal therapy. No cases of meningitis, carotid artery injury, and death related to surgery were noted (► **Table 2**).

Discussion

Since Apuzzo et al²³ reported the endoscopic transsphenoidal approach to the pituitary region in 1977, EETA has been adopted for the management of pituitary lesions. EETA is an option to treat pituitary adenoma apoplexy, which carries significant morbidity and mortality if untreated, especially for patients with altered consciousness, hypopituitarism, and visual loss. However, surgical intervention for subclinical pituitary adenoma apoplexy is controversial.^{2,24–26} Jho et al²⁷ recently classified patients with pituitary apoplexy

from adenoma into five grades based on clinical features to guide treatment options. In this study, we presented our experience of managing apoplectic pituitary adenoma via EETA in 45 patients with comparable results.

Surgical Outcomes

The most frequent complaint was sudden decrease of vision (91.1%) with total loss of vision noted in one patient, followed by headache (86.7%). Both decreased vision and headache were associated with rapidly expansion of pituitary adenoma due to hemorrhage or infarction; and headache may also have resulted from meningeal irritation.²⁸ Altered mental status was rare and more likely to indicate emergent surgical intervention. Three patients (6.7%) without symptoms of apoplexy were found to have apoplexy at the time of surgery that may indicate asymptomatic ischemia or hemorrhage of pituitary tumor.² Nonsecreting adenomas accounted for 76.2% of the apoplectic pituitary adenomas, which supported the prior conclusion from the Zhang et al study.²¹

Systematic treatment of apoplectic pituitary adenoma involves both surgical management and medicine therapy. For the patients with acute visual loss and altered consciousness, surgical intervention may be a first therapeutic option to prevent mortality, as indicated by many authors.^{29,30} In our experience, all apoplexy patients have a preexisting pituitary adenoma that requires resection via surgical means, and even surgical decompression of the optic chiasm and nerve is crucial for PRL adenoma with sudden deterioration of vision. In this study, all patients underwent an EETA for resection of an apoplectic pituitary tumor.

The total resection rate was 86.7%, comparable with the results of Zhang et al.²¹ In our experience, necrosis or hemorrhage of adenoma may facilitate resection with lower risks of damage to surrounding neurovasculature.^{2,24} After surgery, patients with serious headaches and altered consciousness recovered rapidly. The rate of visual remission was 92.7% in our series, which was consistent with those previously reported.³¹ The timely decompression of the optic chiasm is an effective treatment option for apoplexy as suggested by many authors.^{32–34} Surgical decompression of the pituitary gland not only optimized neuroophthalmologic recovery but also improved endocrine results.³⁵ Our data on endocrinological recovery also support this conclusion given that 14 (87.5%) of 16 patients with secreting adenoma obtained hormonal remission postoperatively.

Surgical Complications

CSF leakage still is one of the most common complications of EETA despite repair techniques for the skull base.^{36–38} Factors affecting postsurgical CSF leakage include surgical technique, tumor features, and surgical experience. Of those factors, the skull base reconstruction technique is potentially the most important. The unparalleled panoramic endoscopic view in EETA enables the detection of tiny fistulas that can be repaired with skull base reconstruction. We typically used a multilayer technique to reconstruct the skull base and made slight modifications by placing a small amount of muscle pulp in between the inner layer and the outer layer to enhance

graft adherence; this is called the sandwich technique. The PNSF was rotated and placed on the overlay graft if a CSF leak was suspected or confirmed intraoperatively. In the present study, two patients (4.4%) experienced postsurgical CSF leakage and were managed successfully with lumbar drainage, which is comparable with previously reported rates of CSF leakage from EETA to the sellar region.^{39–42}

DI, which can be transient or permanent, is a frequent complication related to endoscopic pituitary surgery and presents as dilute large-volume urine and elevated serum osmolality. Transient DI was noted in 13.3% of patients, which is greater than most reported results.^{43–45} It is possible that the surgical approach damaged the previously compromised blood supply to magnocellular neurons of the hypothalamus from apoplexy that resulted in a reversible disturbance of arginine vasopressin transport to the posterior pituitary. The presence of permanent DI was zero, which is lower than reported rates^{46–48} and supports a reversible lesion. All patients presenting with DI were treated with therapy to replace posterior hormones of the pituitary as well as supporting therapies, such as control of fluid and electrolyte balance.

Hypopituitarism, as characterized by variably decreased levels of pituitary hormones, was also observed in this series of patients, and hormonal replacement therapy was required. Postoperative endocrinologic evaluation of pituitary gland function indicated that five patients (11.1%) developed hypopituitarism in the present cohort, which is consistent with reported rates as high as 19.8%.^{1,37,39,49–51} Pituitary dysfunction may be explained by compression of the pituitary gland from the apoplectic adenoma, vascular compromise from apoplexy, and surgical manipulation.^{52,53} All patients presented who exhibited hypopituitarism were treated with replacement therapy with excellent results in the follow-up period (with a mean of 26 months).

Conclusion

Apoplectic pituitary tumor is a rare condition that may require timely surgical intervention to prevent progression and morbidity. EETA provides a safe and effective surgical option for acute and subclinical pituitary tumor apoplexy with low morbidity and mortality.

Funding Source

Funding was provided by the National Natural Science Foundation of China (NNSFC) (No. 81172404) and the Special Foundation for Taishan Scholars (No. Ts20110814).

References

1. Torales J, Halperin I, Hanzu F, et al. Endoscopic endonasal surgery for pituitary tumors. Results in a series of 121 patients operated at the same center and by the same neurosurgeon. *Endocrinol Nutr* 2014;61(8):410–416
2. Turgut M, Ozsunar Y, Başak S, Güney E, Kir E, Meteoglu I. Pituitary apoplexy: an overview of 186 cases published during the last century. *Acta Neurochir (Wien)* 2010;152(5):749–761

- 3 Chang CV, Felicio AC, Toscanini AC, Teixeira MJ, Cunha-Neto MB. Pituitary tumor apoplexy. *Arq Neuropsiquiatr* 2009;67(2A):328–333
- 4 Randeve HS, Schoebel J, Byrne J, Esiri M, Adams CB, Wass JA. Classical pituitary apoplexy: clinical features, management and outcome. *Clin Endocrinol (Oxf)* 1999;51(2):181–188
- 5 Sibai L, Ball SG, Connolly V, et al. Pituitary apoplexy: a review of clinical presentation, management and outcome in 45 cases. *Pituitary* 2004;7(3):157–163
- 6 Elsässer Imboden PN, De Tribolet N, Lobrinus A, et al. Apoplexy in pituitary macroadenoma: eight patients presenting in 12 months. *Medicine (Baltimore)* 2005;84(3):188–196
- 7 Dubuisson AS, Beckers A, Stevenaert A. Classical pituitary tumour apoplexy: clinical features, management and outcomes in a series of 24 patients. *Clin Neurol Neurosurg* 2007;109(1):63–70
- 8 Chokyu I, Tsuyuguchi N, Goto T, Chokyu K, Chokyu M, Ohata K. Pituitary apoplexy causing internal carotid artery occlusion—case report. *Neurol Med Chir (Tokyo)* 2011;51(1):48–51
- 9 Jeon BC, Park YS, Oh HS, Kim YS, Chun BK. Pituitary apoplexy complicated by chemical meningitis and cerebral infarction. *J Korean Med Sci* 2007;22(6):1085–1089
- 10 Zoli M, Mazzatenta D, Pasquini E, Ambrosetto P, Frank G. Cavernous sinus apoplexy presenting isolated sixth cranial nerve palsy: case report. *Pituitary* 2012;15(Suppl 1):S37–S40
- 11 Kingdon CC, Sidhu PS, Cohen J. Pituitary apoplexy secondary to an underlying abscess. *J Infect* 1996;33(1):53–55
- 12 Okuda O, Umezawa H, Miyaoka M. Pituitary apoplexy caused by endocrine stimulation tests: a case report. *Surg Neurol* 1994;42(1):19–22
- 13 Abbott J, Kirkby GR. Acute visual loss and pituitary apoplexy after surgery. *BMJ* 2004;329(7459):218–219
- 14 Kearney T, Dang C. Diabetic and endocrine emergencies. *Postgrad Med J* 2007;83(976):79–86
- 15 Fyrmpas G, Constantinidis J, Foroglou N, Selviaridis P. Pituitary apoplexy following endoscopic sinus surgery. *J Laryngol Otol* 2010;124(6):677–679
- 16 Liu JK, Nwagwu C, Pikus HJ, Couldwell WT. Laparoscopic anterior lumbar interbody fusion precipitating pituitary apoplexy. *Acta Neurochir (Wien)* 2001;143(3):303–306; discussion 306–307
- 17 Proust F, Hannequin D, Bellow F, et al. Stress-induced pituitary apoplexy in 2 phases [in French]. *Neurochirurgie* 1995;41(5):372–376
- 18 Sun T, Liu L, Sunnassee A, Zhuo L, Zhu S. Sudden death in custody due to pituitary apoplexy during long restriction in a sitting position: a case report and review of the literature. *J Forensic Leg Med* 2013;20(7):812–815
- 19 Sinnadurai M, Cherukuri RK, Moses RG, Nasser E. Delayed pituitary apoplexy in patient with advanced prostate cancer treated with gonadotrophin-releasing hormone agonists. *J Clin Neurosci* 2010;17(9):1201–1203
- 20 de Heide LJM, van Tol KM, Doorenbos B. Pituitary apoplexy presenting during pregnancy. *Neth J Med* 2004;62(10):393–396
- 21 Zhang X, Zhang W, Fu LA, et al. Hemorrhagic pituitary macroadenoma: characteristics, endoscopic endonasal transsphenoidal surgery, and outcomes. *Ann Surg Oncol* 2011;18(1):246–252
- 22 Frank G, Pasquini E. Endoscopic endonasal cavernous sinus surgery, with special reference to pituitary adenomas. *Front Horm Res* 2006;34:64–82
- 23 Apuzzo ML, Heifetz MD, Weiss MH, Kurze T. Neurosurgical endoscopy using the side-viewing telescope. *J Neurosurg* 1977;46(3):398–400
- 24 Onesti ST, Wisniewski T, Post KD. Clinical versus subclinical pituitary apoplexy: presentation, surgical management, and outcome in 21 patients. *Neurosurgery* 1990;26(6):980–986
- 25 Maccagnan P, Macedo CL, Kayath MJ, Nogueira RG, Abucham J. Conservative management of pituitary apoplexy: a prospective study. *J Clin Endocrinol Metab* 1995;80(7):2190–2197
- 26 Semple PL, Webb MK, de Villiers JC, Laws ER Jr. Pituitary apoplexy. *Neurosurgery* 2005;56(1):65–72; discussion 72–73
- 27 Jho DH, Biller BM, Agarwalla PK, Swearingen B. Pituitary apoplexy: large surgical series with grading system. *World Neurosurg* 2014;82(5):781–790
- 28 Bills DC, Meyer FB, Laws ER Jr, et al. A retrospective analysis of pituitary apoplexy. *Neurosurgery* 1993;33(4):602–608; discussion 608–609
- 29 Lubina A, Olchovsky D, Berezin M, Ram Z, Hadani M, Shimon I. Management of pituitary apoplexy: clinical experience with 40 patients. *Acta Neurochir (Wien)* 2005;147(2):151–157; discussion 157
- 30 Elsässer Imboden PN, De Tribolet N, Lobrinus A, et al. Apoplexy in pituitary macroadenoma: eight patients presenting in 12 months. *Medicine (Baltimore)* 2005;84(3):188–196
- 31 Zhang X, Fei Z, Zhang W, et al. Emergency transsphenoidal surgery for hemorrhagic pituitary adenomas. *Surg Oncol* 2007;16(2):115–120
- 32 Gsponer J, De Tribolet N, Déruez JP, et al. Diagnosis, treatment, and outcome of pituitary tumors and other abnormal intrasellar masses. Retrospective analysis of 353 patients. *Medicine (Baltimore)* 1999;78(4):236–269
- 33 Agrawal D, Mahapatra AK. Visual outcome of blind eyes in pituitary apoplexy after transsphenoidal surgery: a series of 14 eyes. *Surg Neurol* 2005;63(1):42–46; discussion 46
- 34 Arafah BM, Ybarra J, Tarr RW, et al. Pituitary tumor apoplexy: pathophysiology, clinical manifestations, and management. *J Intensive Care Med* 1997;12(3):123–134
- 35 Huang ME, Wartella JE, Kreutzer JS. Functional outcomes and quality of life in patients with brain tumors: a preliminary report. *Arch Phys Med Rehabil* 2001;82(11):1540–1546
- 36 Eloy JA, Shukla PA, Choudhry OJ, Singh R, Liu JK. Assessment of frontal lobe sagging after endoscopic endonasal transcribriform resection of anterior skull base tumors: is rigid structural reconstruction of the cranial base defect necessary? *Laryngoscope* 2012;122(12):2652–2657
- 37 Greenfield JP, Anand VK, Kacker A, et al. Endoscopic endonasal transthemoidal transcribriform transfovea ethmoidalis approach to the anterior cranial fossa and skull base. *Neurosurgery* 2010;66(5):883–892; discussion 892
- 38 Hadad G, Bassagasteguy L, Carrau RL, et al. A novel reconstructive technique after endoscopic expanded endonasal approaches: vascular pedicle nasoseptal flap. *Laryngoscope* 2006;116(10):1882–1886
- 39 Berker M, Aghayev K, Yücel T, Hazer DB, Onerci M. Management of cerebrospinal fluid leak during endoscopic pituitary surgery. *Auris Nasus Larynx* 2013;40(4):373–378
- 40 Berker M, Hazer DB, Yücel T, et al. Complications of endoscopic surgery of the pituitary adenomas: analysis of 570 patients and review of the literature. *Pituitary* 2012;15(3):288–300
- 41 Bokhari AR, Davies MA, Diamond T. Endoscopic transsphenoidal pituitary surgery: a single surgeon experience and the learning curve. *Br J Neurosurg* 2013;27(1):44–49
- 42 Cavallo LM, Dal Fabbro M, Jalalod'din H, et al. Endoscopic endonasal transsphenoidal surgery. Before scrubbing in: tips and tricks. *Surg Neurol* 2007;67(4):342–347
- 43 Senior BA, Ebert CS, Bednarski KK, et al. Minimally invasive pituitary surgery. *Laryngoscope* 2008;118(10):1842–1855
- 44 Shah S, Har-El G. Diabetes insipidus after pituitary surgery: incidence after traditional versus endoscopic transsphenoidal approaches. *Am J Rhinol* 2001;15(6):377–379
- 45 Sigounas DG, Sharpless JL, Cheng DM, Johnson TG, Senior BA, Ewend MG. Predictors and incidence of central diabetes insipidus after endoscopic pituitary surgery. *Neurosurgery* 2008;62(1):71–78; discussion 78–79
- 46 Koutourousiou M, Gardner PA, Fernandez-Miranda JC, Paluzzi A, Wang EW, Snyderman CH. Endoscopic endonasal surgery for giant

- pituitary adenomas: advantages and limitations. *J Neurosurg* 2013;118(3):621–631
- 47 Yano S, Kawano T, Kudo M, et al. Endoscopic endonasal transsphenoidal approach through the bilateral nostrils for pituitary adenomas. *Neurol Med Chir (Tokyo)* 2009;49(1):1–7
 - 48 Schreckinger M, Walker B, Knepper J, et al. Post-operative diabetes insipidus after endoscopic transsphenoidal surgery. *Pituitary* 2013;16(4):445–451
 - 49 De Witte O, Carlot S, Devuyst E, Choufani G, Hassid S. Minimally invasive endoscopic unilateral transsphenoidal surgery for pituitary adenomas. *B-ENT* 2011;7(Suppl 17):27–32
 - 50 Gendeh BS, Doi M, Selladurai BM, Khalid BA, Jegan T, Misiran K. The role of endoscopic endonasal approach to pituitary tumours: HUKM experience. *Med J Malaysia* 2006;61(3):343–348
 - 51 Mamelak AN, Carmichael J, Bonert VH, Cooper O, Melmed S. Single-surgeon fully endoscopic endonasal transsphenoidal surgery: outcomes in three-hundred consecutive cases. *Pituitary* 2013;16(3):393–401
 - 52 da Motta LA, de Mello PA, de Lacerda CM, Neto AP, da Motta LD, Filho MF. Pituitary apoplexy. Clinical course, endocrine evaluations and treatment analysis. *J Neurosurg Sci* 1999;43(1):25–36
 - 53 Fanous AA, Quigley EP, Chin SS, Couldwell WT. Giant necrotic pituitary apoplexy. *J Clin Neurosci* 2013;20(10):1462–1464