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Early outcomes of endoscopic endonasal approach pituitary adenomas resection with minimal nasal injury

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Abstract

To report the results of a consecutive series of pituitary adenomas resected through endoscopic endonasal approach (EEA) with minimal nasal injury.

Retrospectively review tumor characteristics and surgical outcomes of a consecutive series of EEA pituitary adenomas resection performed mainly by a single author between March 2018 and June 2019.

A total of 75 endoscopic endonasal approach pituitary adenoma resections were performed by the authors' team. Of the 75 patients, 28 through mononostril EEA, 47 through Binonostril EEA. Hadad-Bassagasteguy vascularized nasoseptal flap was harvested in only 4 (5.3%) patients with a high risk of postoperative cerebrospinal fluid leak, and one side middle turbinate only been resected in 2 (2.7%) patients, other patients preserved bilateral middle turbinate. Of the 75 patients, gross total resection is 74.7%, near-total resection is 16.0%. Endocrinological remission was achieved in 76.9% of GH-secreting adenomas, 61.5% of prolactin-secreting adenomas. The postoperative cerebrospinal fluid leak rate was 2.7%. Two patients had suprasellar hemorrhage, 1 patient had perioperative stroke, 2 patients had permanent diabetes insipidus, no cranial nerve deficits, internal carotid artery injury, anosmia, and death. The sino-nasal function was measured with the Sino-Nasal Outcome Test-22 and visual analog scale for olfaction preoperatively and postoperatively, and there was no statistically significant difference.

The EEA is an effective approach to resect pituitary adenomas, the gross total resection and near-total resection rate and endocrinological remission rate are satisfactory. The EEA is a safe approach, as the complication rate is acceptable compared with those reported in the previous series of microscopic and endoscopic approaches. These results can be achieved with minimal nasal injury.

Abbreviations: CN = cranial nerve, CS = cavernous sinus, CSF = cerebrospinal fluid, EEA = endoscopic endonasal approach, GTR = gross total resection, ICA = internal carotid artery, MRI = magnetic resonance imaging, MTA = microscopic trans-sphenoidal approach, NTR = near-total resection, PRL = prolactin, SNOT-22 = Sino-Nasal Outcome Test-22, VAS = visual analog scale.

Keywords: adenoma, endonasal, endoscopy, pituitary, surgery, transsphenoidal

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The authors have no conflicts of interest to disclose.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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1. Introduction

The modern techniques of endoscopic endonasal approach (EEA) pituitary adenoma resection had been developed in the past several decades and developed rapidly in the past 10 years.[1–5] Compared with the traditional microscopic trans-sphenoidal approach (MTA) pituitary adenoma resection, EEA can provide better visualization and wider exposure,[6,7] but also with resection of middle turbinate and nasal mucosa. Between March 2018 and June 2019, a total of 75 endoscopic endonasal approach (EEA) pituitary adenoma resections were performed mainly by a single author at the first affiliated hospital with Nanjing Medical University Department of Neurosurgery. In this group of patients, we tried to reduce nasal injury when performed EEA pituitary adenoma resection.[1–5] This study respectively reviewed the surgical methods and outcomes of these cases.

2. Methods

2.1. Patients and tumor characteristics

The age range of these patients is between 24 and 81 years old, and the mean age of patients is 50.36 ± 12.87 years old. Of the 75 patient, men is 43 (57.3%), women is 32 (42.7%). According to the size of tumor, 6 (8.0%) patients had a microadenoma (<1 cm), 52 (69.3%) patients had a macroadenoma (>1 cm, <2.5 cm), and 17 patients (22.7%) had a giant adenoma

(>2.5 cm). There are 19 (25.3%) patients suffered from pituitary adenoma with cavernous sinus (CS) and (or) suprasellar invasion. According to endocrine function, 26 (34.7%) patients had a functioning adenoma, 49 (65.3%) patients had a non-functioning adenoma. Of the 26 functioning adenomas, 13 was growth hormone secreting adenoma, 13 was prolactin (PRL) secreting adenoma. A total of 4 patients were suffered from recurrent pituitary adenoma in this series, and these patients all had undertaken microscopic transsphenoidal pituitary adenoma surgery before.

The radiographic evaluation consisted of magnetic resonance imaging (MRI) scan with contrast performed in all the patients before surgical operation. Some patients undertook additional computed tomography scan of the skull base and magnetic resonance angiography of the brain. These imagines were used to evaluate diagnosis, tumor size, invasion, and surgical risk by neurosurgeon and radiologist.

Visual field examination, visual acuity, and fundoscopy were performed by an ophthalmologist before surgery. A total of 16 patients presented with visual loss and visual field defect and 2 patients had a cranial nerve (CN) III palsy preoperatively.

All the patients underwent preoperative pituitary function assessment, which included free thyroxine, thyroid stimulation hormone, serum cortisol, adrenocorticotrophic stimulating hormone, growth hormone, PRL, luteinizing hormone and follicle-stimulating hormone, testosterone and estradiol.

2.2. Surgical technique

The head was elevated above the heart. Cotton patties soaked with 1% lidocaine and 1:100,000 epinephrine were applied to the nasal cavity to decongest mucosa.

In most of the cases, we chose to preserve the middle turbinate of both side, but pushed them laterally. Middle turbinate only been removed when wider exposure of CS was necessary. Endoscopic examination was performed using a 0° endoscope. The ostia of the sphenoid sinus were identified bilaterally.

Removed the ipsilateral mucosa of the posterior nasal septum when the operation was performed through mononostril, and removed bilateral mucosa of the posterior nasal septum when the operation was performed through binonostril. The size of mucosa removed was about 1×1.8 cm. When removing the mucosa, the superior cut should be at least 1 cm below the roof of the nasal cavity. Hadad-Bassagasteguy vascularized nasoseptal flap was harvested only in patients with a high risk of postoperative cerebrospinal fluid leak.

The posterior nasal septum was resected. The face of sphenoid and sphenoid air cells were removed. Enlarged the opening of sphenoid maximally in all directions if it was necessary. Sellar dura was exposed after thinned and removed the bone of sellar floor. When the tumors extended into the suprasellar space, the bone of the tuberculum sella and planum sphenoidale should be removed. When the tumors extended into the CS, the bone of the anterior and medial wall of CS should be removed.

The dura of sellar floor was opened carefully and exposed the tumor, normal pituitary gland should be dissected firstly in some microadenomas. Two-suction technique was used to resect the tumor. After debulking, the inferior tumor should be removed firstly, then the lateral tumor of both sides until the medial wall of CS was identified clearly, the superior tumor was removed at last. If the tumor capsule been found, gross total resection usually can be achieved by stripping the capsule. If the tumor extended into the suprasellar space or CS, the dura of the tuberculum sella and planum sphenoidale and CS should be opened in some cases. Every corner should be examined again before reconstructing the sellar floor.

We used artificial dura to reconstruct sellar floor. If cerebrospinal fluid (CSF) leak existed without visible arachnoid defect, inlayer fat graft and artificial dura were applied. If CSF leak existed with visible arachnoid defect, inlayer fat graft and artificial dura, combined on layer fascial graft were used. If suprasellar space or third ventricle or internal carotid artery (ICA) was exposed, inlayer fat graft and artificial dura, onlayer fascial graft, and pedicled nasoseptal flap were used. The nasal cavity was packed for 3 days usually, 1 week if fascial graft and pedicled nasoseptal flap were used.

The lumbar drain was only used in patients with high risk of postoperative CSF leak, such as the patients had widely suprasellar space or third ventricle exposure, or used in patients had suspicious postoperative CSF leak before removal of nasal packing.

2.3. Assessment of sino-nasal function and statistical analysis

The sino-nasal function was measured with the Sino-Nasal Outcome Test-22 (SNOT-22) and visual analog scale (VAS) for olfaction before and 12 months after surgery respectively.[8,9] The SNOT-22 is a disease-specific questionnaire to measure the quality of life in patients afflicted by sino-nasal problems. The score of SNOT-22 is from 0 to 110, and lower values are associated with a better quality-of-life related to sino-nasal function. Olfactory function was measured using VAS (0–100). Statistical analysis was performed with Microsoft Excel for Mac, version 16.47.1. Independent-sample t tests were used to determine significant differences. All P values were 2-tailed, and a $P < .05$ value was considered statistically significant.

3. Results

As shown in Table 1, mononostril EEA pituitary adenoma resections were performed in all the 6 microadenomas and 22

Table 1

Extent of nasal injury and outcomes of tumor resection.

Tumor size	n	Mononostril EEA	Binonostril EEA	Vascularized nasoseptal flap harvested	Middle turbinates preserved	One side of middle turbinate removed	GTR	NTR	STR	PR
Micro	6	6	0	0	6	0	6	0	0	0
Macro	52	22	30	0	52	0	44	6	2	0
Giant	17	0	17	4	15	2	6	6	4	1
Total	75	28	47	4	73	2	56	12	6	1

EEA = endoscopic endonasal approach, GTR = gross total resection, NTR = near-total resection, PR = partial resection, STR = sub-total resection.

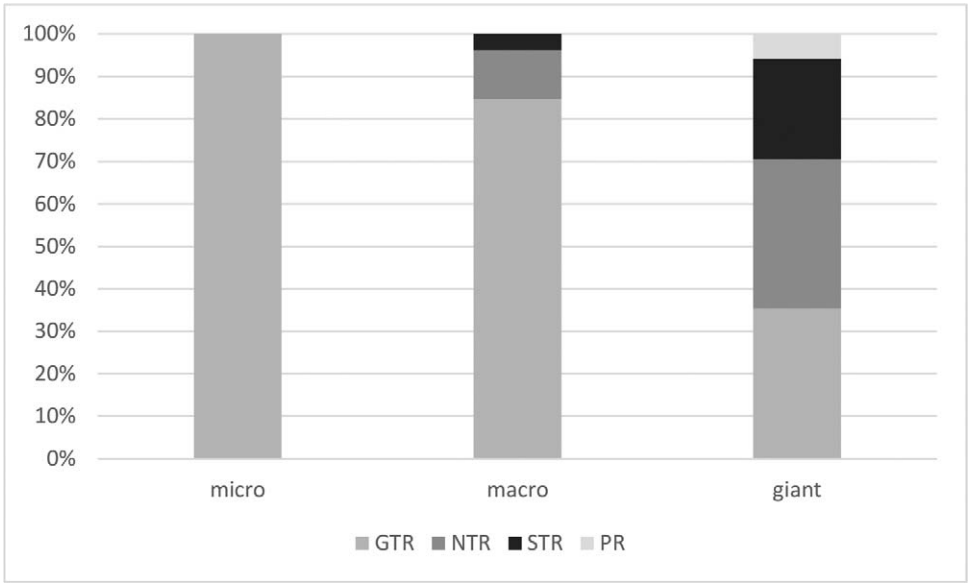

Figure 1. Extent of resection in different size of tumors.

macroadenomas. Binonostril EEA pituitary adenoma resections were performed in all the 17 giant adenomas and other 30 macroadenomas. Hadad-Bassagasteguy vascularized nasoseptal flap was harvested in only 4 (5.3%) patients with a high risk of postoperative CSF leak, and one side of middle turbinate only been removed in 2 (2.7%) patients.

All the patients underwent postoperative pituitary function assessments on the first postoperative day. MRI scan with contrast was performed within 3 days or after 3 months. Complete removal of the tumor was considered to be gross total resection (GTR), >95% removal was considered to be near-total resection (NTR), 80% to 95% removal was considered to be sub-total resection, and when <80% removal was considered to be partial resection.

Of the 75 patients, GTR is 74.7%, NTR is 16.0%. All the microadenomas had achieved gross total resection. Of the 6 cases confirmed as Knosp grade 4 adenomas, only 1 achieved NTR, 4 sub-total resection, and 1 partial resection. Extent of resection in different size of tumors was shown in Fig. 1.

Of the 26 functioning adenomas, 13 was GH-secreting adenoma, 13 was PRL-secreting adenoma. Endocrinological remission was achieved in 76.9% of GH-secreting adenomas, 61.5% of PRL-secreting adenomas. The results of endocrinological remission of functioning adenomas were shown in Table 2 and Fig. 2.

The intraoperative CSF leak rate was 29.3%. The techniques used to reconstruct sellar floor were shown in Table 3. After removal of nasal packing, only 2 (2.7%) patients had postoperative CSF leak. One patient was cured by placing a lumbar drain, one underwent operative repair twice and had meningitis, but the final outcome was good.

A total of 16 patients presented with visual loss and visual field defect preoperatively, 13 of them improved after operation, 3 of them unchanged. No patients had postoperative visual deterioration. Two patients had CN III palsy, and both of them recovered after operation.

One patient with giant non-functioning adenoma presented anterior pituitary insufficiency after surgery. No syndrome of inappropriate antidiuretic hormone secretion, ICA injury and CN deficits were observed in this study. A total of 9 patients complained about anosmia after removed nasal packing, but all recovered in different degree within 3 weeks after surgery. Postoperative complications in this study were shown in Table 4.

The score of SNOT-22 was 18.48 ± 10.99 preoperatively, and 20.85 ± 10.74 at 12 months after surgery. The score of VAS was 90.53 ± 12.95 preoperatively, and 88.00 ± 13.27 at 12 months after surgery. These differences were not statistically significant ($P = .10$ and .15, respectively; Independent-sample t test).

Table 2

Endocrinological remission of functioning adenomas.

Size	GH	PRL
Micro	2 (2)	4 (4)
Macro	7 (10)	4 (6)
Giant	1 (1)	0 (3)
Total	10 (13)	8 (13)

PRL = prolactin.

4. Discussion

The visualization afforded by straight and angled endoscopes makes it possible to get more exposure through EEA. Since the identification of critical neurovascular structures and arachnoid violations of tumor, we can dissect and resect pituitary adenomas using microsurgical technique, thereby improving the extent of tumor resection and decreasing the rate of complications.[10] There are a lot of worldwide studies and literature reviews that came to this conclusion.

The authors have plenty of experience in MTA pituitary adenoma resection, and began to use EEA from March 2018. The first stage experience with these 75 patients is satisfactory and encouraged.

Better visualization and wider exposure are the most important advantage of EEA pituitary tumor surgery compared with MTA.

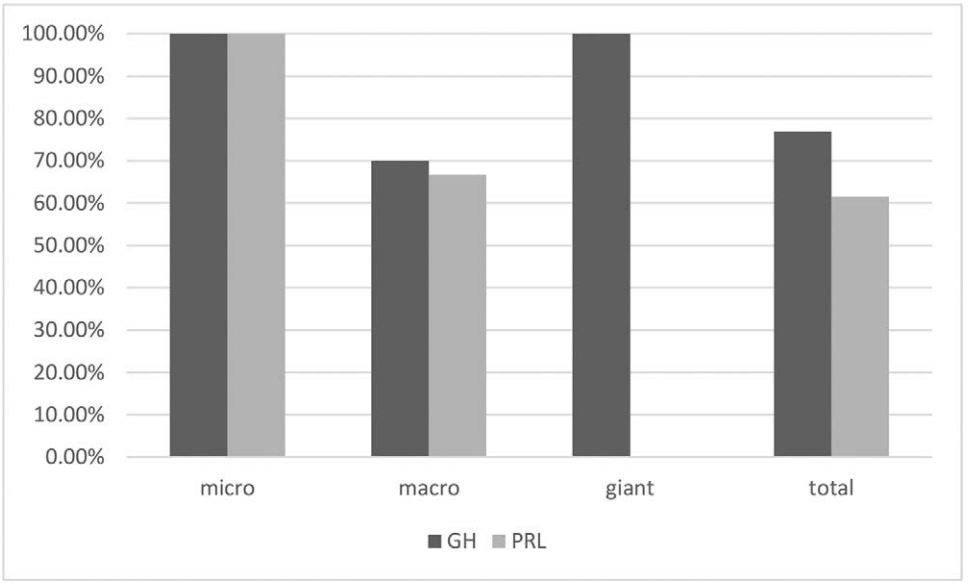

Figure 2. Endocrinological remission rate in different size functioning of tumors.

But on the other side, more exposure means more surgical injury. Higher gross total resection rate and less surgical injury both are the pursue of neurosurgeons. Considering the different tumor characteristics among different patients, we think we can use different tumor resection strategies.

Enough exposure must be considered at first, because exposure is the key to achieve satisfactory gross total resection rate and reasonable postoperative complications rate.[11] For this reason, binonostril EEA pituitary adenoma resections were performed in all the 17 giant adenomas and other 30 macroadenomas. More flexibility of operation can be achieved via binonostril EEA. But in these patients with microadenoma and macroadenoma without invasion, we have opportunity to limit surgical injury, especially in the nasal cavity. In this study, mononostril EEA pituitary adenoma resections were performed in all the 6 microadenomas and 22 macroadenomas. The space of operation was limited, compared with binonostril approach, but enough in these patients. If we found it was difficult to operate vis mononostril, it was easy to remove contralateral mucosa of posterior nasal septum intraoperatively. The middle turbinate is regularly resected reported in some studies. Removal middle turbinate is in the purpose of exposing the bone of the anterior and medial wall of CS. In the cases without this purpose, we pushed the middle turbinate laterally before tumor resection and pushed them medially after tumor resection. Hadad-Bassagasteguy vascularized nasoseptal flap is a revolutionary technique to reconstruct sellar floor.[5] But in this study, the pedicled vascularized nasoseptal flap was harvested in only 4 (5.3%) patients with a high risk of postoperative CSF leak. Our principle is to limit surgical injury, in advance to provide adequate exposure for tumor resection. The SNOT-22 and VAS were used to assess sino-nasal function preoperatively and postoperatively. The score of SNOT-22 was a little higher, and the score of VAS was a little lower after surgery. But these differences were not statistically significant. We can conclude that the surgical technique applied in these patients did not affect sino-nasal function significantly.

The gross total and near-total resection rate and endocrinological remission rate are encouraged in this study compared with previous reports.[4,5,12–15] And the rate of postoperative complications is at a low level.[4,5,12–20] The GTR rate and postoperative complications rate reported by different authors had obvious differences. It is hard to compare with these outcomes, because the patients and tumor characteristics in different studies have great differences, such as the proportion of invasive tumor. The postoperative images were evaluated by authors, and lack of third-party evaluation. The outcomes of long term follow-up may be more convincing. This is also the

Table 3

Sellar floor reconstruction techniques.

Method	Number	Percentage
Artificial dura	53	70.7%
Fat graft and artificial dura	14	18.7%
Fat graft, artificial dura, and fascial graft	4	5.3%
Fat graft, artificial dura, fascial graft, and pedicled nasoseptal flap	4	5.3%

Table 4

Postoperative complications.

	Number	Percentage
Anterior pituitary insufficiency	1	1.3%
Meningitis	1	1.3%
Hemorrhage	2	2.7%
ICA injury	0	0
Intraoperative CSF leak	22	29.3%
Postoperative CSF leak	2	2.7%
Permanent DI	2	2.7%
Visual deterioration	0	0
Cranial nerve deficits	0	0
Perioperative stroke	1	1.3%
Anosmia	0	0
Death	0	0

CSF = cerebrospinal fluid, DI = diabetes insipidus, ICA = internal carotid artery.

limitation of this study, so the results we provide are just early experience.

A total of 22 patients had been found intraoperative CSF leak. The sellar floor reconstruction strategy had been taken as shown in Table 3. The pedicled vascularized nasoseptal flap has a great contribution to sellar floor reconstruction, especially in the complex case with large skull base defect. The application of pedicled vascularized nasoseptal flap had really decreased the postoperative CSF leak rate in these patients. But it should not be applied to all the patients with pituitary tumors. Although the pedicled vascularized nasoseptal flap was applied in only 4 (5.3%) patients in our study, only 2 (2.7%) of the total 75 patients had postoperative CSF leak, the other one underwent operative repair twice and had meningitis, but the ultimate outcome was good. No patient had meningitis without postoperative CSF leak in this study.[21–25]

The role of the lumbar drain in sellar floor reconstruction is still controversial.[26] We placed a lumbar drain in patients with a high risk of postoperative CSF leak, or had suspicious postoperative CSF leak before removal of nasal packing.

The excellent visualization and wide exposure made it possible to apply microsurgical techniques in pituitary adenoma resection especially in giant and invasive tumors. These techniques include 2-suction technique, stripping tumor capsule, and dissect tumor from critical neurovascular structures. As shown in Fig. 3A and B, sella enlarged, diaphragm, and optic chiasm had been pushed upwards, but this tumor did not invade into suprasellar space. In this case, 2-suction technique was applied to resect tumor gross totally according to the postoperative MRI. As shown in Fig. 3C–H, this patient with a giant pituitary tumor extended into suprasellar space and third ventricle. In this case, the pedicled vascularized nasoseptal flap was harvested before tumor removal. Removed the bone of the tuberculum sella and planum sphenoidale was removed, opened dura of sellar floor, resected intrasella tumor, then open the dura of the tuberculum sella and planum sphenoidale, dissected suprasella tumor from critical neurovascular structure, and totally resected. The structure inside the third ventricle was seen clearly. As shown in Fig. 3I–K, this patient with a giant Knosp grade 4 pituitary adenoma, diaphragm, and optic chiasm were pushed upwards, left side ICA was encased by tumor. After debulking the intrasella tumor, we resected the tumor intrasella and extended suprasella by stripped tumor capsule. Then opened the medial wall of CS, and removed tumor intracavernous sinus by using 2 suction

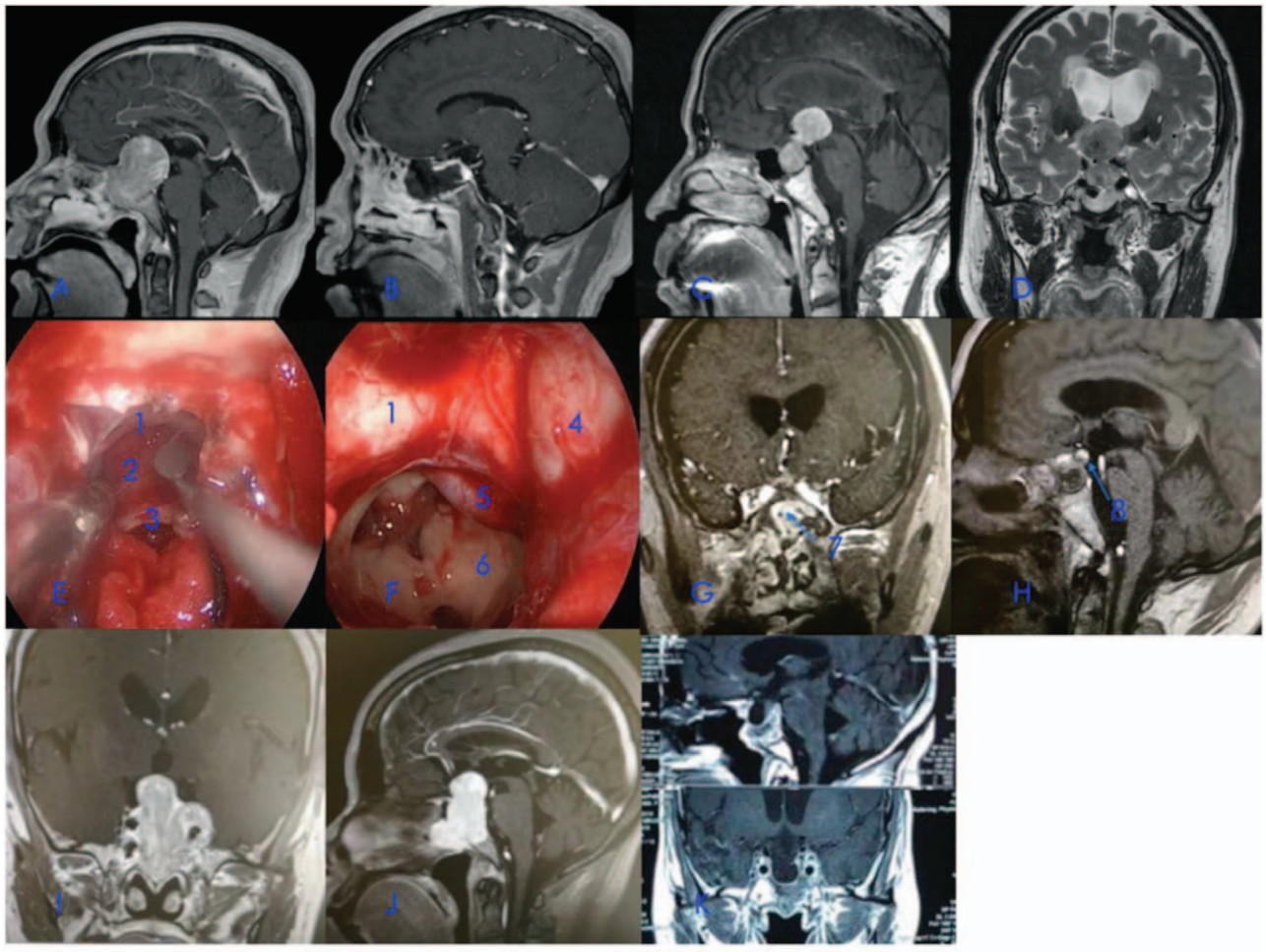

Figure 3. (A, B) Patient 1. Preoperative (A) and postoperative (B) sagittal enhanced T1-weighted MRI. (C–H) Patient 2. Preoperative sagittal enhanced T1-weighted MRI (C) and T2-weighted MRI (D). Endoscopic pictures during surgery (E, F). (I–K) Patient 3. Preoperative coronal (I) and sagittal (J) enhanced T1-weighted MRI. Postoperative sagittal and coronal enhanced T1-weighted MRI (K). 1, Optic chiasm; 2, suprasella tumor; 3, diaphragm; 4, supraclinoidal ICA (left); 5, anterior cerebral artery (left); 6, thalamus; 7, pedicled vascularized nasoseptal flap; 8, fat graft.

technique.[27] Small suspicious residual tumor left in the posterior and superior compartment of CS as shown in Fig. 3K. It should be watched after surgery and addressed by radiotherapy or stereotactic radiosurgery if necessary.

A total of 2 patients had postoperative hemorrhage. One is suprasellar subarachnoid hemorrhage, recovered by placing a lumbar drain. Another patient was spotted hemorrhage in the third ventricle through postoperative computed tomography scan, and accepted external ventricular drainage. Postoperative hemorrhage is one of the most serious complications in EEA pituitary resection.[12,28] According to a study including 2679 cases of endoscopic pituitary surgery performed in the United States, intracranial hemorrhage and hematoma in 1.83% and 0.45% of patients, respectively.[12]

The EEA is an effective and safe approach to resect pituitary adenomas. The technique of EEA pituitary tumor resection is continually evolving. Considering the learning curve, the outcomes reported worldwide in recent years are better than before, and must be better in the future.[5,29–31]

Author contributions

Conceptualization: Weixing Hu.
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Formal analysis: Chao Tao, Weixing Hu.
Investigation: Chao Tao, Weixing Hu.
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Supervision: Gang Cheng, Weixing Hu.
Writing – original draft: Chao Tao.
Writing – review & editing: Weixing Hu.

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