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Original Investigation

Surgical Outcome of Endoscopic Endonasal Surgery for Non-Functional Pituitary Adenoma by a Team of Neurosurgeons and Otolaryngologists

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ABSTRACT

AIM: This study aimed to assess the efficacy of endoscopic endonasal surgery, conducted by a team of neurosurgeons and otolaryngologists.

MATERIAL and METHODS: We studied 40 patients who were undergoing surgery for primary non-functional pituitary adenomas with Knosp grades 1 to 3, at Keio University Hospital between 2005 and 2012. We compared the endoscopic endonasal transsphenoidal approach (team-eTSS; T-eTSS), with a microscopic transsphenoidal approach (mTSS). Analyses were conducted for differences between the two groups in tumor resection rates, operating durations, and complications from the non-functional pituitary adenomas. We also compared the heminostril and binostril approaches for T-eTSS.

RESULTS: Tumor resection rates were higher when the surgeries were conducted by T-eTSS than mTSS. In particular, when the maximum tumor diameter was more than 25 mm, resection rates were significantly higher for T-eTSS than for mTSS. There were no unexpected complications in either group. There was no significant difference in resection rates between the heminostril and binostril approaches when T-eTSS was performed.

CONCLUSION: T-eTSS is an efficacious surgical option for non-functional pituitary adenomas, particularly when the adenoma is of large size. Benefits of the heminostril approach are evident.

KEYWORDS: Endoscopic endonasal surgery, Pituitary adenoma, Heminostril approach, Transsphenoidal

INTRODUCTION

Pituitary adenoma accounts for approximately 10–15% of all primary brain tumors (3,19), and clinically non-functioning pituitary adenoma (NFPA) comprises approximately one third of pituitary adenomas. At diagnosis, most of these tumors are macroadenomas, and clinical manifestations are the result of compression of the surrounding structures, resulting in symptoms such as hypopituitarism, headache, visual disturbances, and oculomotor palsy (3). The preferred initial therapy for NFPA is surgical removal, and the goals of treatment include removal of the pituitary adenoma as completely as possible in order to avoid recurrence, decompress the nervous structures, and manage hormonal deficiencies. Unfortunately, the pooled recurrence rate for patients with postoperative residual tumor is 46% (3). Postoperative radiotherapy is considered for residual tumor, but side effects in relation to pituitary and visual function have not been characterized. Therefore, safe and efficacious maximum tumor resection is critical to the initial treatment.

Transsphenoidal surgery is the treatment of choice for initial therapy. It was introduced in the early 1900s, and restored by Hardy in the 1960's using microscopes and X-ray fluoroscopy

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to create a standardized microscopic transsphenoidal surgery for pituitary adenomas (11).

Endoscopic endonasal pituitary surgery was reported by Jho (13), and has become increasingly more common. The endoscopic endonasal transsphenoidal approach (eTSS) allows more panoramic visualization (21) and wider access to the skull base compared to the microscopic transsphenoidal approach (mTSS) (2,15). Technological advances such as angled endoscopes, specialized instrumentation, and image guidance have extended the use of eTSS. This surgery has been described as increasing resection rates, resulting in fewer complications, and restoring hormone values within typical ranges (4). The overall gross total tumor removal rate when surgery is conducted using eTSS for NFPA is 75.2–93% (5,7,9,14), which is higher than for mTSS. Theodosopoulos et al. reported that endoscopy was equally effective compared to operative MRI when tumor resection rates are considered (22). However, the literature does not include detailed resection rates using eTSS to treat NFPA.

We have used the endoscopic endonasal transsphenoidal approach, conducted by a neurosurgical and otolaryngological team (team-eTSS; T-eTSS) since 2008. The purpose of the present study was to assess the efficacy of endoscopic endonasal surgery by a team of neurosurgeons and otolaryngologists.

■ MATERIAL and METHODS

Institutional Review Board approval was obtained. We retrospectively reviewed the pituitary surgeries between November 2005 and December 2012 at the Division of Neurosurgery of Keio University Hospital. Forty surgeries were performed for primary non-functional pituitary adenomas with Knosp grades of 1–3. Patient characteristics are given in Table I and preoperative clinical presentations are given in Table II. Twenty-one surgeries were performed by T-eTSS and 19 by mTSS. Of those undergoing the T-eTSS approach, 11 patients underwent the heminostril approach and 10 patients the binostril approach. All patients underwent preoperative magnetic resonance imaging (MRI) scans. Preoperative tumor volumes were approximated using a modified ellipsoid volume (A*B*C/2). In this approximation, A and B represented the maximum diameter and the orthogonal maximum diameter at the sagittal plane, respectively. C represented the maximum diameter of the tumor at the coronal plane (Figures 1A-D; 2A-D). Postoperative MRIs were performed within 6 months after surgery. The volume of residual adenomas was calculated with the same mathematical formula (A*B*C/2) used for the initial tumor measurement. The resection rate was calculated from the preoperative and postoperative tumor volumes.

Statistical analyses were performed using the SPSS 22.0 software (IBM, Chicago, Illinois, USA). Comparisons of

Table I: Patient Characteristics and Preoperative Tumor Assessments

	T-eTSS (n = 21)		mTSS (n = 19)		p-value
Age (years), mean (range)	56.2	(22-76)	54	(27-72)	0.61
Sex, (male, %)	13	(61.9)	15	(78.9)	0.25
Knosp grade, mean, (range)	2.4	(1-3)	2.1	(1-3)	0.17
Major diameter, mean, mm (range)	27.9	(16-51.5)	25.9	(13-46)	0.47
Minor diameter, mean, mm (range)	20.0	(13-32.2)	18.1	(11-33)	0.28
Width, mean, mm (range)	26.5	(18-37)	23.7	(14-31)	0.11
Tumor volume, mean, cm^3 (range)	8.4	(2.4-28.2)	6.8	(1.2-21.8)	0.40

Table II: Patient Clinical Presentations

Clinical Presentation	No. of Patients			
	T-eTSS (n = 21)	mTSS (n = 19)	total (n = 40)	
Visual impairment	13	10	23	(57.5%)
Pituitary insufficiency	4	0	4	(10%)
Headache	3	2	5	(12.5%)
Apoplexy	1	0	1	(2.5%)
Oculomotor nerve palsy	1	1	2	(5.0%)
Altered mental status	2	0	2	(5.0%)
Incidental	2	7	9	(22.5%)

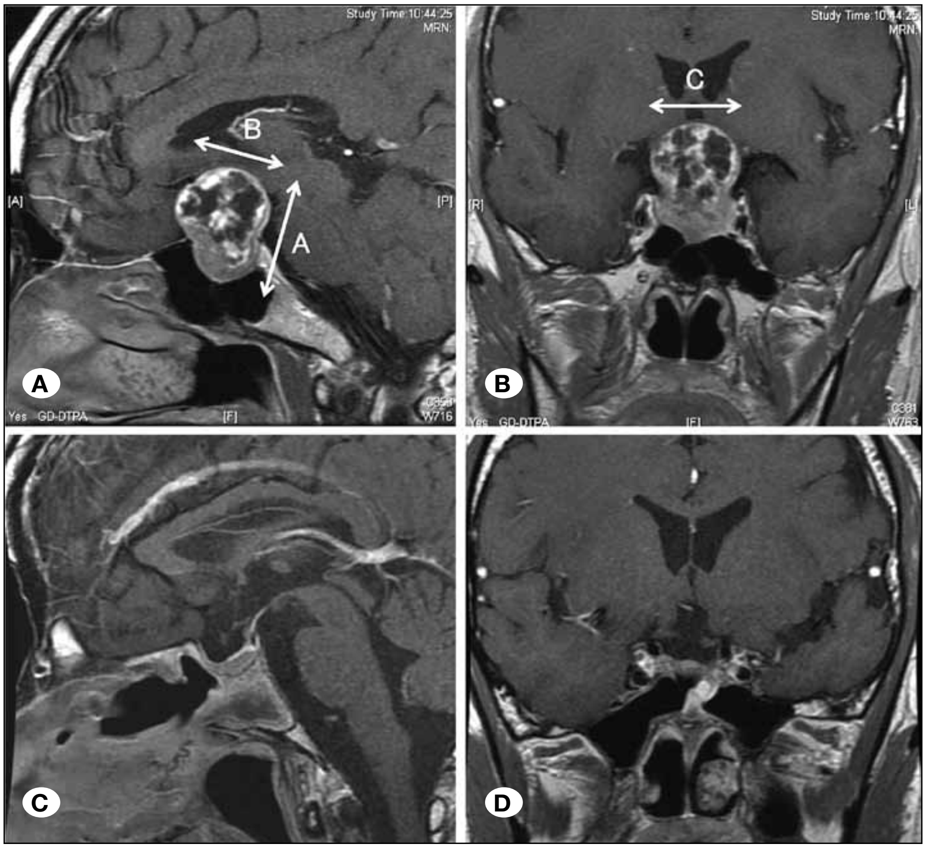

Figure 1: Preoperative and postoperative tumor assessment for T-eTSS. Preoperative sagittal **(A)** and coronal **(B)** contrast-enhanced MRI showing maximum tumor diameter (A) and orthogonal maximum diameter (B) at the sagittal plane, and maximum tumor diameter at the coronal plane (C). A is 29 mm, B is 24 mm, and C is 16 mm in this representative image. Tumor volume was calculated as 9.05 cm^3. Postoperative sagittal **(C)** and coronal **(D)** contrast-enhanced MRI showing no residual tumor. Resection rate was 100%.

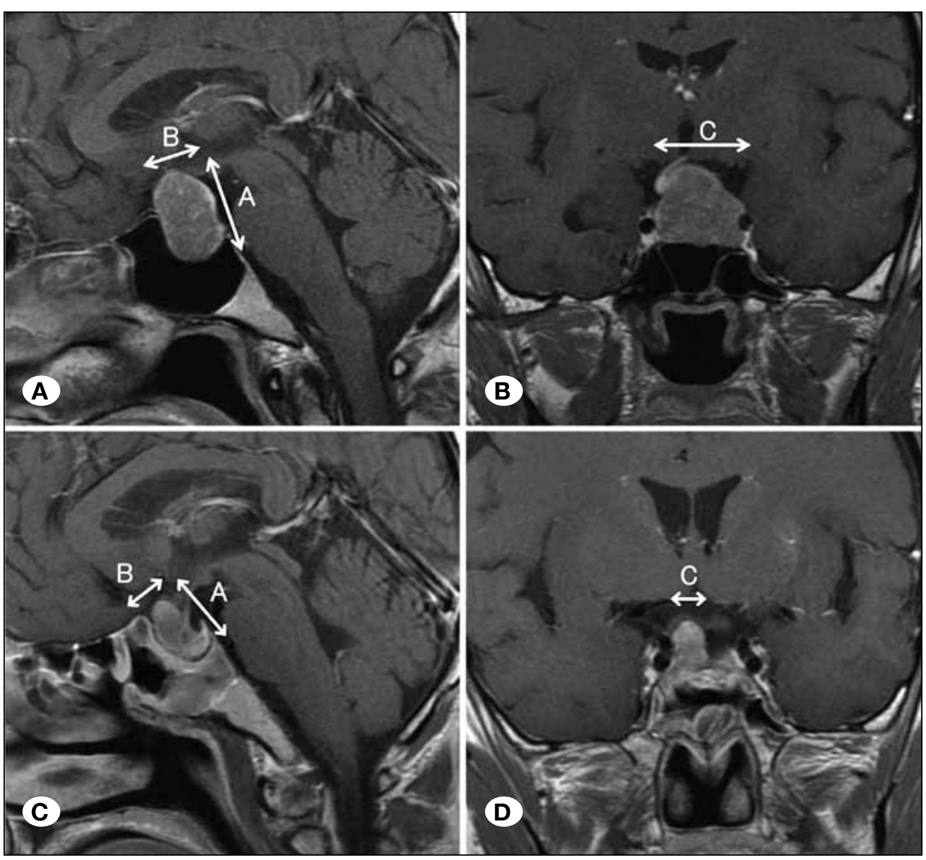

Figure 2: Preoperative and postoperative tumor assessment for mTSS. Preoperative sagittal **(A)** and coronal **(B)** contrast-enhanced MRI showing maximum tumor diameter (A) is 30 mm and orthogonal maximum diameter (B) is 15 mm at the sagittal plane, and maximum tumor diameter at the coronal plane (C) is 27 mm in this representative image. Tumor volume was calculated as 6.08 cm^3. Postoperative sagittal **(C)** and coronal **(D)** contrast-enhanced MRI showed maximum residual tumor diameter (A) is 15 mm, B is 9 mm, and C is 12 mm in this example. The calculated residual tumor volume was 0.81 cm^3 and the resection rate was 86.7%.

preoperative and postoperative tumor sizes, resection rates, and operating durations were made using Student's t-test or the Mann-Whitney nonparametric test, as appropriate. A p value < 0.05 was considered statistically significant.

Surgical Procedure

Nineteen patients underwent mTSS, four through the transendonasal approach and fifteen through the transsublabial approach. Twenty-one patients underwent T-eTSS, using the two surgeons and four hands method. Eleven surgeries were performed via the right nostril, and 10 were conducted using the binostril approach.

When T-eTSS was performed, the otolaryngologist removed the right middle turbinate and harvested the vascularized nasoseptal flap at the beginning of the surgery. For the binostril approach, the right middle turbinate was out-fractured and the posterior cartilaginous septum mucosa was cut to allow binasal access. For the heminostril approach, we preserved the left posterior nasal septum mucosa. Next, the otolaryngologist held and controlled the endoscope and irrigated the operation field during sphenoidotomy and tumor removal. The neurosurgeon manipulated two instruments, using both hands and via both nasal cavities in the binostril approach. In the heminostril approach, the endoscope, irrigation, suction, and instruments were implemented only via the right nasal cavity. After removal of the posterior cartilaginous septum, wide sphenoidotomy was performed. Next, the sellar floor was opened and the dura was cut. The tumor was carefully dissected from the pituitary and removed. If there was cerebrospinal fluid (CSF) leakage during tumor removal, the nasoseptal flap was used for sellar repair. When intraoperative CSF leakage did not occur, the nasoseptal flap was repaired and remained in place.

■ RESULTS

The demographics of both groups are given in Table I. There were no statistical differences in age, sex, maximum tumor diameter, tumor volume, or Knosp grade between T-eTSS and mTSS. The ranges of maximum tumor diameter and tumor volume were 13-46 mm and 1.07-19.44 cm^3, respectively.

Table III gives postoperative tumor diameters, widths, volumes, resection rates, and operating durations. The maximum diameter of residual tumors and residual tumor volume were significantly lower when T-eTSS was performed, than when mTSS was performed. Furthermore, the resection rate was 97.5% by T-eTSS, which is higher than for mTSS. There was no significant difference in the duration of surgeries.

In order to investigate the advantages of T-eTSS for large pituitary tumors, we analyzed the resection rates of pituitary tumors using two categories of tumor diameter. When the maximum tumor diameter was more than 25 mm, resection rates were significantly higher by T-eTSS (98.7%) than by mTSS (66.3%) (Table IV). However, when the maximum tumor diameter was less than 25 mm, resection rates were higher by T-eTSS but the differences between surgical approaches were not statistically significant.

Major surgical complications did not occur in either group (Table V). Although minor intraoperative CSF leaks occurred more frequently during T-eTSS than mTSS, there were no postoperative CSF leaks in either group. There was one

Table III: Postoperative Tumor Assessments

	T-eTSS (n = 21)		mTSS (n = 19)		p-value
Residual major diameter, mean, mm (range)	4.1	(0-16)	11.8	(0-35)	0.01
Residual minor diameter, mean, mm (range)	3.1	(0-14)	11.5	(0-29)	<0.01
Residual width, mean, mm (range)	4.3	(0-17)	12.0	(0-29)	< 0.01
Residual tumor volume, mean, cm^3 (range)	0.3	(0-1.8)	2.1	(0-10.4)	0.02
Resection rate, mean, % (range)	97.0	(80.2-100)	77.6	(25.3-100)	< 0.01
Operating time, mean, min (range)	187	(147-308)	184	(100-270)	0.87

Table IV: Mean Resection Rates According to Maximum Tumor Diameter

Maximum Tumor Diameter of Sagittal Plane	Operating Method	Number of Cases	Mean Resection Rates ±Standard Deviation (%)	p-value
≥ 25mm	T-eTSS	13	97.2 ± 1.7	
	mTSS	10	66.3 ± 7.5	<0.01
< 25mm	T-eTSS	8	96.8 ± 1.7	
	mTSS	9	90.1 ± 4.4	0.20

postoperative tumor hemorrhage following T-eTSS, and the patient developed hypopituitarism. We recorded one event of nasal bleeding shortly after T-eTSS, which required surgical resolution.

Finally, we compared heminostril and binostril approaches to T-eTSS (Table VI). Eleven patients had surgeries using the heminostril approach, and there were no significant differences in tumor volumes and resection rates between groups.

DISCUSSION

eTSS, T-eTSS

Technical and technological advances have extended the applications of eTSS, which allows wide access to the skull base (2,15). Our T-eTSS technique was conducted as described in a previous report on endoscopic skull base surgery (15). An advantage of the two surgeons and four hands technique includes operating with an otolaryngologist, who is highly familiar with the nasal cavities and paranasal sinuses. Additionally, we were able to feel depth by constantly moving the endoscope, two-handed sensitive handling was possible (1), and dura reconstruction was performed using the nasoseptal flap (10).

The present study enabled comparison of pituitary tumor resection rates between T-eTSS and mTSS, which were calculated from tumor volumes based on MRI images. This method enabled detailed comparison and demonstrated that tumor resection rates were significantly increased by T-eTSS, especially for large tumors. Additionally, our approach did not require additional operating time. Our team

Table V: Complications

Surgical complications	No. of Patients	
	T-eTSS (n = 21)	mTSS (n = 19)
Death	0	0
Major vessel injury	0	0
Hypopituitarism (including permanent DI)	1	0
Postoperative CSF leak	0	0
(Minor intraoperative CSF leak)	(9)	(2)
(Massive intraoperative CSF leak)	(3)	(3)
Meningitis	0	0
Postoperative tumor bleeding	1	0
Nasal bleeding requiring surgery	1	0

***DI:** Diabetes insipidus, **CSF:** Cerebrospinal fluid.*

Table VI: Comparison of Heminostril and Binostril Approaches for T-eTSS

	Heminostril Approach (n=11)		Binostril Approach (n=10)		p-value
Knosp grade, mean, n (range)	2.2	(0-3)	2.6	0-3	0.05
Major diameter, mean, mm (range)	25.0	(16.0-37.0)	31.1	(18.0-51.5)	0.11
Minor diameter, mean, mm (range)	19.4	(13.0-28.0)	20.7	(13.0-32.3)	0.57
Width, mean, mm (range)	25.0	(18.0-32.0)	28.1	(22.0-37.0)	0.16
Tumor volume, mean, cm^3 (range)	6.7	(2.4-16.6)	10.2	(3.0-28.2)	0.20
Residual major diameter, mean, mm (range)	3.0	(0.0-12.0)	5.3	(0.0-16.0)	0.40
Residual minor diameter, mean, mm (range)	2.4	(0.0-10.0)	4.0	(0.0-14.0)	0.44
Residual width, mean, mm (range)	3.3	(0.0-12.0)	5.5	(0.0-17.0)	0.44
Residual tumor volume, mean, cm^3 (range)	0.1	(0.0-0.6)	0.4	(0.0-1.7)	0.20
Resection rate, mean, % (range)	98.0	(88.5-100)	96.0	(80.2-100)	0.44
Operating time, mean, min (range)	171.2	(147-221)	204.1	(169-308)	0.04

has previously experienced single-surgeon techniques using a mechanical endoscope holder, but we have found that the result was prolonged interruption time in order to move the endoscope and achieve a clear lens. Our use of endoscopic visualization and collaboration between neurosurgeons and otolaryngologists resulted in more complete tumor extraction, thus indicating the usefulness of T-eTSS.

Complications

Intraoperative CSF leak rates were higher for T-eTSS than for mTSS. This can be explained by the aggressive tumor resection. We added a vascularized nasoseptal flap for sellar floor repair during T-eTSS in cases where high volume intraoperative CSF leaks occurred. In other patients, we used a combination of abdominal fat grafts and mucosa of the middle concha. Using a combination of these techniques, there were no cases of postoperative CSF leakage or meningitis.

One T-eTSS patient had a postoperative tumor hemorrhage and developed hypopituitarism. The maximum diameter of this tumor was 36 mm and the tumor volume was 15.5 cm^3. Tumor hemorrhage is relatively common for pituitary adenomas after partial resection, and has been described in 2.1% of giant pituitary adenoma cases (16). Therefore, postoperative apoplexy is an important complication in giant pituitary adenoma, and differences between mTSS with open craniotomy or open craniotomy alone is the more appropriate comparison than comparison between T-eTSS and mTSS.

Only one T-eTSS patient experienced nasal bleeding after the surgery, and nasal bleeding has previously been described in 0.7–7% of surgeries (8). The right middle turbinate is removed during T-eTSS, and bleeding originated from the resection stump of the middle concha in this case. Thus, coagulation of the cut end of the turbinate is important.

Heminostril Approach or Binostril Approach

We compared a heminostril approach with a binostril approach for T-eTSS surgeries (Table VI) and found no significant differences between tumor volumes or resection rates. Tissue handling was restricted by the instrument interface and the camera in the heminostril approach. Therefore we adopted a binostril approach if surgery was not possible via the heminostril approach. The heminostril method did not require the other nostril to be packed after the surgery, which decreases postoperative discomfort for patients. Therefore, this approach is useful when a localized tumor can be reached via one nostril.

A limitation of this study is that recent conceptual changes in the approach to NFPA treatment have altered the internal decompression model of removing NFPAs (17,20). However, these new concepts also developed with advancements in endoscopic techniques. Therefore, this concept alteration does not contraindicate use of T-eTSS. T-eTSS has not been commonly used in Japan thus far, and many neurosurgeons use a mechanical or pneumatic endoscope holder, as described in previous reports (6,12,18). Mamelak et al. reported that endoscopic outcomes were better than those reported in microscope-based studies, regardless of whether one or two surgeon techniques were applied (18). During a one surgeon, two-handed surgery, the surgeon is required to move the endoscope and irrigate. It is not possible to directly compare one- and two-surgeon techniques, but we postulate that T-eTSS requires a shorter operating duration than single surgeon techniques and also enables more sensitive instrument handling.

■ CONCLUSION

In this retrospective study, the T-eTSS technique produced higher tumor resection rates, especially for tumors with maximum diameters over 2.5 cm. The present study demonstrated applications of T-eTSS for large pituitary adenomas and described the benefits of the heminostril approach.

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