

# Evaluating the Effectiveness of Endoscopic and Transcranial Techniques in Pituitary Tumor Resection: A Single-Institution Study

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## Abstract

**Background:** Transsphenoidal pituitary operations are conducted using microscopic and endoscopic techniques. The microscopic technique provides three-dimensional visualization and follows established procedures based on transsphenoidal approaches. This study compared the clinical efficacy and safety of endoscopic transnasal-transsphenoidal surgery (ETTS) with that of traditional transcranial/microscopic methods for pituitary adenoma.

**Methods:** Eighty patients were divided into two groups: the ETTS ( $n = 40$ ) and transcranial surgery (TCS) ( $n = 40$ ) groups. The evaluation criteria included the extent of tumor removal, hormonal remission in functioning tumors, visual outcomes, perioperative complications, surgery duration, and length of hospital stay. **Results:** The ETTS group demonstrated significantly smaller residual tumor volumes (6.6% vs. 24.6%,  $P = 0.002$ ) and higher remission rates for functioning adenomas (94% vs. 57%,  $P = 0.018$ ) than the TCS group. Visual outcomes were not significantly correlated with tumor size or residual volume in either group. The ETTS group had a lower incidence of post-operative diabetes insipidus (4 vs. 11 patients,  $P = 0.025$ ) and shorter hospital stays for patients with hormonally active tumors ( $3.7 \pm 2.0$  vs.  $7.1 \pm 3.5$  days,  $P = 0.005$ ). However, the ETTS required longer surgery times ( $202 \pm 34$  vs.  $169 \pm 50$  min,  $P = 0.001$ ). The rates of post-operative cerebrospinal fluid leakage and repeat surgeries did not differ significantly between the groups. **Conclusion:** These findings suggest that ETTS is a safe and effective method for treating pituitary adenomas, offering better tumor removal, hormonal remission, and post-operative recovery than traditional methods. However, larger multicenter studies with extended follow-up are required to validate these results.

**Key words:** Adenoma, endoscopic, microscopic, pituitary, remission, transsphenoidal

## INTRODUCTION

Transsphenoidal pituitary operations are conducted using microscopic and endoscopic techniques. The microscopic technique provides three-dimensional visualization and follows established procedures based on transsphenoidal approaches.<sup>[1]</sup> The endoscopic endonasal approach offers broader visualization and superior lighting to access the parasellar, suprasellar, and retrosellar areas, which are challenging with the microscopic method.<sup>[2]</sup> Virtual endoscopy improves intraoperative orientation and enhances the safety of endoscopic techniques, particularly for training surgeons.<sup>[3]</sup>

Multicenter studies have established standards for morbidity, mortality, and tumor control following

transsphenoidal surgery for both methods, providing a reference for evaluating newer techniques.<sup>[4]</sup> These benchmarks confirmed low rates of reoperation, cerebrospinal fluid (CSF) leaks, and hypopituitarism in expert centers, without showing an advantage of either method.<sup>[5]</sup> Prospective data show that both endoscopic and endoscope-assisted microscopic surgeries achieve similar tumor control and long-term outcomes, although endoscopic inspection may detect hidden residual tumors and enhance surgical goals and anterior pituitary function.<sup>[6]</sup>

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Epidemiological studies indicate a trend toward endoscopic transsphenoidal pituitary surgeries, with varying findings on safety and complications. United States claims data show a growing preference for endoscopic surgery but reveal increased rates of diabetes insipidus, electrolyte imbalances, and CSF leaks, leading to longer hospital stays.<sup>[7]</sup> Cost analyses indicate higher overall costs for endoscopic versus microscopic surgery, with length of stay driving the costs.<sup>[8]</sup> Meta-analyses show endoscopy achieves similar remission rates in Cushing's disease and may benefit macroadenomas.<sup>[9]</sup> Broader analyses have revealed no significant differences between the techniques for gross total resection or hormonal remission but have reported lower rates of diabetes insipidus with endoscopy.<sup>[10]</sup> Learning curve analyses have demonstrated improvements in operative time and resection rates with increased endoscopic experience, although complex tumors require longer learning periods.<sup>[11]</sup> A recent large-scale meta-analysis found no significant differences between approaches in resection rates or major complications, with lower mortality in the endoscopic groups, suggesting that patient selection and expertise matter more than the optical system.<sup>[12]</sup>

While endoscopic surgery provides benefits in terms of visualization and is increasingly preferred, the evidence does not conclusively establish its superiority across all settings. The benefits and risks depend on tumor characteristics, surgeon experience, and center-specific factors. This uncertainty and study variability necessitate further research comparing endoscopic and microscopic techniques, forming the basis for this study.

This study compared the clinical efficacy and safety of endoscopic transnasal-transsphenoidal surgery (ETTS) with traditional transcranial/microscopic methods for pituitary adenoma. The evaluation criteria included the extent of tumor removal, hormonal remission in functioning tumors, visual outcomes, perioperative complications, surgery duration, and length of hospital stay. With the increasing use of endoscopic techniques but uncertainty about their superiority, this study aimed to determine whether enhanced visualization provides benefits in surgical radicality, endocrine control, and post-operative recovery within a single institution.

## MATERIALS AND METHODS

Clinical data were gathered from patients who underwent surgery for pituitary adenomas at the neurosurgery departments of the National Hospital of the Ministry of Health of the Kyrgyz Republic and at the Koi-Tash and Zdorovye medical centers. Until November 2013, all surgeries were conducted using the traditional neurosurgical method involving craniotomy. After this date, an endoscopic transnasal technique was adopted. The endoscopic procedures employed the "two nasal passages – four hands" method, executed by a neurosurgeon with the assistance of an assistant.

This study focused on patients who underwent pituitary surgery from November 2013 onwards. The endoscopic group included only those patients who had magnetic resonance imaging (MRI) results available at 6 months post-surgery. All patients who underwent the conventional neurosurgical approach were monitored from the time endoscopic techniques were introduced into clinical practice.

Before surgery, patients underwent brain MRI, a thorough endocrinological evaluation by a specialist, and an ophthalmological assessment, which included checking visual acuity and visual fields. After surgery, data on the duration of hospital stay, complications, and visual function parameters were collected. Endocrinological assessments were conducted at 2 weeks, 6 weeks, and 6 months postoperatively, and follow-up MRI with gadolinium contrast was performed 6 months later.

For hormonally active adenomas, data were gathered on thyroid function, prolactin, cortisol (measured fasting at 8:00 a.m.), insulin-like growth factor-1 levels, and daily growth hormone secretion patterns were charted using an oral glucose tolerance test when necessary [Figure 1].

The volume of tumor formations was estimated based on MRI data performed by two independent consultant neuroradiologists using the generally accepted calculation method:  $V = 0.5 \times \text{craniocaudal max} \times \text{anteroposterior max} \times \text{mediolateral max}.$ <sup>[6,13]</sup> The measurements were performed under blinded conditions, and the specialists were unaware of the patients' clinical information. All scans were analyzed simultaneously and in a random order, minimizing the likelihood of systematic errors and subjective influence by the researcher.

All data were collected prospectively and processed using Microsoft Excel. A preliminary analysis of the variable distribution determined the type of statistical test used (parametric or nonparametric). The Mann–Whitney U-test was used to compare tumor volumes, while the Pearson  $\chi^2$  test was used to compare remission rates for hormonally active adenomas, diabetes insipidus, and post-operative CSF leaks. In all other cases, the Student's t-test for independent samples was used.

The Bioethics Committee of I.K. Akhunbaev Kyrgyz State Medical Academy approved this study (Approval no. 01/24, dated September 01, 2024). All procedures followed the Declaration of Helsinki, and the participants provided written consent. Consent for surgery and study involvement was obtained from all patients or their legal representatives before the study.

## RESULTS

Each study group comprised 40 patients. In the transcranial surgery (TCS) group, there were more male participants ( $n =$

22; 55%) than female participants ( $n = 18$ ; 45%), with a mean age of 49.3 years (range, 23–73 years). In the ETTS group, the sex distribution was 19 men and 21 women, with a mean age of 47.4 years (range, 9–75 years).

The TCS group included 26 non-functioning macroadenomas and 14 functioning tumors, whereas the ETTS group included 24 non-functioning and 16 functioning neoplasms. Within the functioning adenomas, the TCS group identified five macroadenomas and nine microadenomas, while the ETTS group found 11 macroadenomas (including one with parasellar extension) and five microadenomas.

### Operation duration

The mean time for surgery using transcranial access was  $169 \pm 50$  min, which was significantly shorter than that of the ETTS procedure, which has a mean of  $202 \pm 34$  min ( $P = 0.001$ ).

### Tumor volume

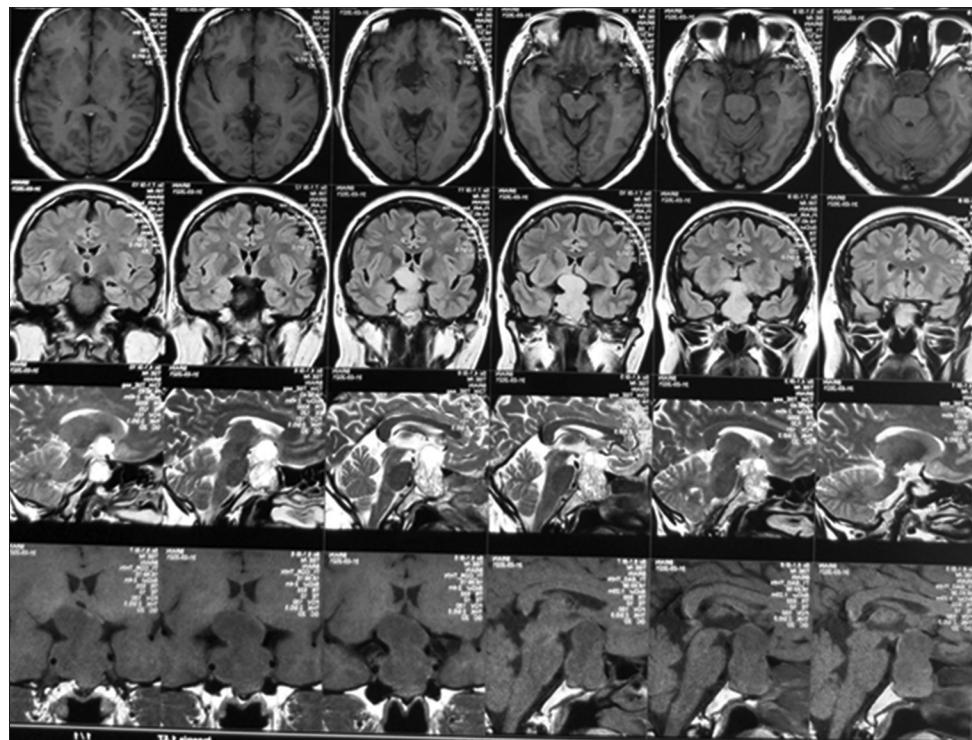
According to neuroradiological analysis, the mean pre-operative and post-operative volumes of non-functioning tumors were determined in both groups. In the TCS group, the mean pre-operative tumor volume was  $7.28 \text{ cm}^3$  (median; interquartile range:  $5.65$ – $5.81 \text{ cm}^3$ ), whereas in the ETTS group, it was  $11.66 \text{ cm}^3$  ( $7.69$ – $13.42 \text{ cm}^3$ ). Postoperatively, the mean tumor volume was  $2.26 \text{ cm}^3$  in the TCS group and  $0.97 \text{ cm}^3$  in the ETTS group [Table 1].

The mean residual tumor volume post-surgery, as a percentage of the initial volume (median; interquartile range), was 6.6% (0%; 8.40%) for the ETTS group, compared to 24.6% (14.0%; 15.6%) for the TCS group, showing a statistically significant difference ( $P = 0.002$ ).

On examining the morphometric characteristics of the tumors, we found that the mean anteroposterior and axial diameters were notably larger in male patients. However, there was no significant link between tumor size and pre-operative visual acuity ( $P = 0.249$ , 0.201, and 0.053 for horizontal, anteroposterior, and axial diameters, respectively) or with post-operative visual acuity ( $P = 0.665$ , 0.543, and 0.408 for the same dimensions).

Patients with larger tumors exhibited poorer visual field indices before surgery ( $r^2 = 0.042$ ; 0.043; 0.091;  $P = 0.007$ ; 0.007;  $<0.001$  for horizontal, anteroposterior, and axial orientations, respectively). However, post-operative analysis did not show a significant relationship between tumor size and visual field improvement ( $r^2 = 0.007$ , 0.009, 0.014;  $P = 0.272$ , 0.232, 0.121, respectively).

There was no statistically significant association between the volume of residual tumor and post-operative visual acuity ( $r^2 = 0.002$ ,  $P = 0.637$ ) or visual field parameters ( $r^2 = 0.001$ ,  $P = 0.781$ ). Similarly, the presence of residual tumor did not significantly affect post-operative visual function parameters ( $P = 0.724$  for visual acuity and  $P = 0.844$  for visual field).



**Figure 1:** Magnetic resonance imaging of the patient with pituitary adenoma

**Table 1:** Distribution of TCS and ETTS groups patients considering main characteristics

Parameters	TCS group	ETTS group	P-value
Surgery duration	169±50 min	202±34 min	0.001
Tumor size			0.002
Pre-operative (mean)	7.28 cm <sup>3</sup>	11.7 cm <sup>3</sup>	
Post-operative (mean)	2.26 cm <sup>3</sup>	0.97 cm <sup>3</sup>	
Residual (mean) (%)	24.6	6.6	
Secreting tumors			
Remission (%)	57	94	0.018
Hospital stays	8±6.7	6±7.5	0.400
Hospital stays in secreting tumors	7.1±3.5	3.7±2.0	0.005
Complications			
Cerebrospinal fluid leakage (%)	14.1	9.4	0.74
Diabetes insipidus	11	4	0.025
Repeat surgery	4	0	0.12

Data presented as *n* (%), *n*=number of patients, % = percentage of patients, mean±standard deviation (M±m). \**P*<0.05. ETTS: Endoscopic transnasal-transsphenoidal surgery, TCS: Transcranial surgery

## Secreting tumors

Endocrine parameters were evaluated before and after surgery using the institution's laboratory reference values. Remission was defined as post-operative normalization of the laboratory parameters.

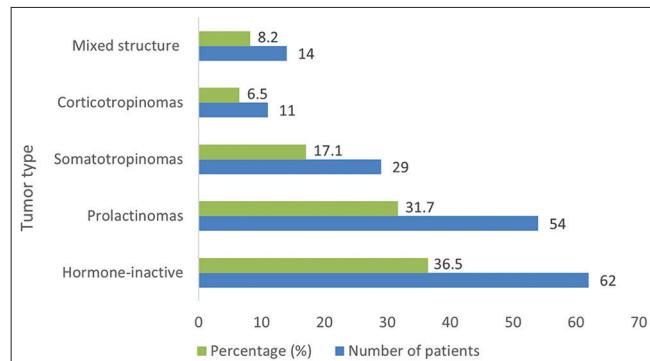
The remission rate was 57% (8 out of 14 patients) in the TCS group and 94% (15 out of 16 patients) in the ETTS group, with a statistically significant difference (*P*=0.018). Figure 2 illustrates the distribution of patients with hormonally active adenomas.

## Duration of hospitalization

The mean duration of hospitalization was 6±7.5 days for the ETTS group and 8±6.7 days for the TCS group (*P*=0.400). Subgroup analysis revealed that for non-functioning adenomas, both groups had a mean hospital stay of 8 days, with a standard deviation of 9.2 in the ETTS group and 7.9 in the TCS group (*P*=0.975). Conversely, for patients with hormonally active tumors, the ETTS group experienced a significantly shorter average stay of 3.7±2.0 days compared to 7.1±3.5 days in the TCS group (*P*=0.005) (Table 1).

## Post-operative complications

The rate of post-operative CSF leakage showed no statistically significant difference between the groups. In the TCS group, 12 patients (14.1%) experienced post-operative CSF leakage compared to 8 patients (9.4%) in the ETTS group (*P*=0.74). Notably, none of the CSF leakage cases in the ETTS group required a vascularized nasoseptal flap to repair skull base defects.



**Figure 2:** Distribution of patients due to hormonal activity

In the early post-operative phase, diabetes insipidus occurred in 11 patients following TCS and in four patients after ETTS (*P*=0.025). Four patients in the TCS group required reoperation shortly after the initial procedure: two due to bleeding and two due to residual tumors causing ongoing visual problems. In one patient, surgery was halted due to bleeding during the operation, necessitating a second surgery 14 days later.

Three patients were removed from the TCS group as they were unsuitable for this procedure; they underwent craniotomy as their primary surgical method and were thus excluded from the microscopic surgery subgroup. In the ETTS group, no conversion to craniotomy was necessary. However, in the TCS group, one patient required craniotomy to remove a residual or recurrent tumor. Although the TCS group had a slightly higher rate of conversion to craniotomy, this difference was not statistically significant (*P*=0.12) [Table 1].

A fatality occurred in the ETTS group on the 4<sup>th</sup> day after surgery. The patient was admitted in a critical state with

symptoms of pituitary apoplexy and did not survive despite surgical and endocrinological treatment. Post-surgery, the patient developed hypothalamic ischemia, which led to cerebral infarction and ultimately resulted in death.

### Duration of symptoms

The mean duration of general clinical symptoms such as headache, galactorrhea, amenorrhea, acromegaly, and infertility was  $19.0 \pm 31.3$  months, with a range from 0 to 156 months. In contrast, the mean duration of visual impairment was  $7.5 \pm 21.4$  months (range, 0–156 months). Patients who regained normal vision after surgery had a notably shorter history of systemic symptoms ( $P = 0.049$ ) than those who continued to experience visual impairment. Statistical analysis showed no significant link between the duration of systemic symptoms and post-operative visual acuity ( $r^2 = 0.013$ ;  $P = 0.143$ ) or visual field evaluation ( $r^2 = 0.001$ ;  $P = 0.746$ ). Similarly, the duration of visual impairment was not significantly correlated with post-operative visual acuity ( $r^2 = 0.017$ ;  $P = 0.094$ ) or visual field recovery ( $r^2 = 0.012$ ;  $P = 0.148$ ).

## DISCUSSION

Contemporary pituitary surgery has shifted toward endoscopic procedures in clinical settings. Despite the broad adoption of endoscopic techniques, a consensus on their superiority over traditional microsurgical approaches remains unclear.<sup>[14]</sup>

Systematic reviews of 10 or more clinical studies have shown that endoscopic and microscopic methods are similarly effective for tumor removal and hormonal remission rates. However, researchers have noted that ETTS is associated with lower rates of post-operative diabetes insipidus and nasal complications, with reduced hospital stays. There is no consensus on the frequency of post-operative CSF leakage.

The ETTS group demonstrated lower residual tumor volumes and higher hormonal remission rates than the transcranial methods, supporting the effectiveness of endoscopic techniques in pituitary adenoma management. Meta-analyses indicate that ETTS is as effective as microscopic or transcranial methods for resection extent and complications, while offering better parasellar visualization and endocrine outcomes. Pooled analyses have shown higher gross total resection rates and lower diabetes insipidus risk with endoscopic surgery,<sup>[15]</sup> with meta-analyses demonstrating comparable hormonal remission and visual improvement between techniques.<sup>[10]</sup> Visual improvement rates remain similar across methods, although endoscopic approaches may better access complex extensions.<sup>[16]</sup> Our findings showed that tumor size did not strongly correlate with post-operative visual outcomes, suggesting that the surgical technique is more important than tumor size. Endoscopic

resection achieves positive endocrine outcomes even in complex cases, supporting its use in patients with expertise. These results indicate that the endoscopic transsphenoidal approach provides comparable or superior outcomes to traditional techniques, particularly for endocrine remission and tumor reduction, while emphasizing individualized surgical planning.

This study compared patient groups who underwent pituitary surgery using microscopic or endoscopic techniques. The results showed that the endoscopic group had higher rates of complete non-functioning adenoma removal and functioning tumor remission. The endoscopic approach required a longer surgery time, consistent with the literature.<sup>[17]</sup> The ETTS requires two surgical consultants due to its technical demands.

CSF leakage remains the main post-operative complication of pituitary surgery, with a similar incidence between the groups. Microsurgical dural defects were treated with fat grafts, tissue adhesives, and lumbar drainage. Endoscopic skull base reconstruction uses vascularized nasoseptal flaps,<sup>[18]</sup> except when prior surgery prevents flap formation. In these cases, microsurgical sealing techniques were employed.

In patients who underwent plastic surgery with a nasoseptal flap, there were no cases of CSF leakage after surgery in the endoscopic group, demonstrating the effectiveness of the method in sealing skull base defects.

The intraoperative opening of the dura mater is constrained superiorly by its plane, which risks CSF leakage. Laterally, it is limited by the internal carotid arteries and anteriorly by the sella turcica floor. These constraints reduce microscopic visibility, hindering tumor excision, particularly in the case of larger lesions. Surgeons often rely on tactile sensation rather than direct vision.

Endoscopic technology, with different viewing angles, enables surgeons to inspect difficult areas, including the lateral and superior tumor parts, allowing a thorough evaluation of boundaries and facilitating radical resection. This accounts for the improved resection completeness and hormonal remission rates in our study, with lower post-operative diabetes insipidus.<sup>[19]</sup>

Extended endoscopic approaches enable the safe removal of large tumors through the transsphenoidal route. No patient in the ETTS group required a craniotomy, despite the larger average pre-operative tumor size.

In this study, the “Pittsburgh model” was used, involving two surgeons (“two heads, four hands” model). This ensures better instrument control and safety during the procedure.<sup>[20]</sup> This technique enhances pituitary region access and allows effective sealing of skull base defects using vascularized nasoseptal flaps. Two experienced surgeons improved the readiness to manage complications, especially significant bleeding.

To leverage the benefits of endoscopic technology, avoiding fixed endoscope holders is recommended. Manual control allows for flexible viewing angle adjustment and thorough examination of the pituitary cavity through the dural window.

The analysis showed that the ETTS by two surgeons yielded better short-term outcomes at 6 months post-surgery. Further research is required to assess long-term outcomes. With growing experience, this technique could be widely applied to anterior cranial fossa procedures, as adopted in several international clinics.

Despite the significant benefits of the endoscopic technique, the sample size was relatively small, requiring caution in the interpretation of the results and confirmation in larger clinical samples.<sup>[21]</sup>

## CONCLUSION

This comparative analysis revealed that ETTS is a secure and effective method for treating pituitary adenomas, offering significant benefits over traditional TCS. The ETTS led to smaller residual tumor volumes and higher hormonal remission rates in functioning adenomas, even with larger pre-operative tumors. These results indicate that improved endoscopic visualization enables more thorough tumor removal and better endocrine management.

Visual outcomes were similar between the surgical methods, and post-operative recovery was not significantly affected by tumor size or residual volume, suggesting that sufficient decompression may be crucial for visual improvement. The endoscopic method showed lower post-operative diabetes insipidus rates and shorter hospital stays in patients with hormonally active tumors. Although the ETTS required longer surgery times, this reflects its technical complexity rather than decreased efficiency.

These findings endorse ETTS as a dependable surgical option for pituitary adenomas when performed in well-equipped centers with experienced teams. While microscopic and transcranial methods remain appropriate in certain cases, endoscopic techniques provide superior short-term outcomes for tumor control and endocrine remission. Larger multicenter studies with extended follow-up are needed to validate these findings.

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