e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(12); 2746-2755

Original Research Article

# A Prospective Study on Endoscopic versus Open Transsphenoidal Surgery in Pituitary Adenomas: Complication Rates and Hormonal Recovery

Ravi Prakash[1], Samrendra Kumar Singh[2], Brajesh Kumar[3], Shristi Shreya[4]

[1]Resident, Department of Neurosurgery, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India

[2]Additional Professor, Department of Neurosurgery, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India

[3]Additional Professor, Department of Neurosurgery, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India

[4]Resident, Department of General Surgery, Venkateshwara Institute of Medical Sciences, Uttar Pradesh, India

Received: 30-10-2025 / Revised: 29-11-2025 / Accepted: 30-12-2025

Corresponding Author: Shristi Shreya

Conflict of interest: Nil

**Abstract:**

**Background:** Transsphenoidal surgery is the standard treatment for most pituitary adenomas. Endoscopic transsphenoidal surgery (ETS) has increasingly been adopted as an alternative to the traditional microscopic transsphenoidal surgery (MTS), but prospective comparative data on perioperative outcomes and hormonal recovery remain limited.

**Objective:** To prospectively compare perioperative complications, extent of resection, hormonal outcomes, and quality of life between endoscopic and microscopic transsphenoidal surgery in patients with pituitary adenomas.

**Methods:** This prospective, non-randomized comparative cohort study was conducted at a tertiary care center between January 2023 and June 2024. Twenty-five patients with pituitary adenomas undergoing primary transsphenoidal surgery were enrolled, with 13 patients undergoing ETS and 12 undergoing MTS. Outcomes assessed included perioperative complications, extent of resection, hormonal remission and recovery at 6 and 12 months, length of hospital stay, and patient-reported quality of life using the Sinonasal Outcome Test-22 (SNOT-22) and Anterior Skull Base Questionnaire (ASBQ).

**Results:** Gross total resection was achieved in 92.3% of ETS patients and 83.3% of MTS patients. Postoperative cerebrospinal fluid leak occurred in 0% of the ETS group and 16.7% of the MTS group, though this difference did not reach statistical significance. Length of hospital stay was significantly shorter in the ETS group (3.1 ± 1.0 vs 4.9 ± 1.8 days, p = 0.004). Hormonal remission in functioning adenomas at 12 months was comparable between ETS and MTS groups (77.8% vs 75.0%). ETS patients demonstrated significantly greater improvement in sinonasal quality-of-life scores at 12 months. Rates of diabetes insipidus, new hypopituitarism, and visual improvement were similar between groups.

**Conclusions:** In this prospective pilot study, endoscopic transsphenoidal surgery was associated with shorter hospital stay and improved sinonasal quality of life compared with microscopic surgery, while achieving comparable hormonal and visual outcomes. Although trends toward lower complication rates and higher gross total resection were observed with ETS, these findings did not reach statistical significance due to limited sample size. Larger, adequately powered randomized studies are required to confirm these observations.

**Keywords:** Pituitary Adenoma, Endoscopic Transsphenoidal Surgery, Microscopic Transsphenoidal Surgery, Complications, Hormonal Recovery, Surgical Outcomes.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/read), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

## Introduction

Pituitary adenomas constitute approximately 15-20% of all primary intracranial tumors, with an estimated prevalence of 80-100 cases per 100,000 population [1,2]. These benign neoplasms arise from the anterior pituitary gland and can be classified based on size (microadenomas <10 mm, macroadenomas ≥10 mm), hormonal activity (functioning versus non-functioning), and invasiveness [3]. The clinical presentation varies widely, ranging from incidental radiological findings to symptomatic hormone hypersecretion, visual field defects, or hypopituitarism secondary to mass effect [4].

The transsphenoidal approach, first pioneered by Schloffer in 1907 and refined by Harvey Cushing and later by Jules Hardy, has evolved to become the gold standard surgical treatment for most pituitary

adenomas [5,6]. The introduction of the operating microscope by Hardy in the 1960s revolutionized pituitary surgery, enabling improved visualization and surgical precision [7]. However, the past two decades have witnessed a paradigm shift toward endoscopic techniques, which promise enhanced visualization, reduced invasiveness, and improved patient outcomes [8,9].

The endoscopic transsphenoidal approach offers several theoretical advantages over the traditional microscopic technique. The endoscope provides a panoramic view with angled lenses allowing visualization around corners, potentially facilitating more complete tumor resection while preserving normal pituitary tissue and surrounding neurovascular structures [10,11]. Additionally, the minimally invasive nature of the endoscopic approach may translate to reduced postoperative morbidity, shorter hospitalization, and faster recovery [12].

Despite these potential benefits, the adoption of endoscopic techniques has been variable across neurosurgical centers, partly due to the steep learning curve, equipment requirements, and limited high-quality comparative data [13]. While several retrospective studies and systematic reviews have compared these approaches, prospective data directly comparing complication rates and hormonal outcomes remain limited [14,15]. Furthermore, questions persist regarding the durability of hormonal recovery, quality of life impacts, and long-term complication profiles.

This prospective study was designed to address these knowledge gaps by directly comparing endoscopic and microscopic transsphenoidal surgery in terms of perioperative complications, extent of tumor resection, hormonal recovery patterns, and patient-reported outcomes. By providing level II evidence through a prospective comparative design, this study aims to inform surgical decision-making and optimize patient care in the management of pituitary adenomas.

## Materials and Methods

**Study Design and Setting:** This prospective, non-randomized comparative cohort study was conducted at a tertiary care academic medical center between January 2023 and June 2024, with an 18-month study duration including 6 months of active enrollment and 12 months of follow-up. The study protocol was approved by the Institutional Review Board, and all participants provided written informed consent.

### Patient Selection

**Inclusion Criteria:**

- Age 18-75 years
- Radiologically confirmed pituitary adenoma requiring surgical intervention
- No prior pituitary surgery
- Adequate medical fitness for surgery (ASA physical status I-III)
- Willingness to participate in 12-month follow-up

**Exclusion Criteria:**

- Previous transsphenoidal surgery or craniotomy
- Pituitary apoplexy requiring emergency surgery
- Cavernous sinus invasion (Knosp grade 4)
- Severe comorbidities precluding general anesthesia
- Pregnancy or lactation
- Inability to provide informed consent

During the study period, 32 patients were screened for eligibility. Of these, 7 patients were excluded (3 due to prior surgery, 2 with severe cavernous sinus invasion, 1 declined participation, and 1 due to emergency presentation). The remaining 25 patients were enrolled and allocated to either ETS (n=13) or MTS (n=12) based on surgeon expertise and patient preference after detailed counseling regarding both approaches.

**Baseline Assessment:** All patients underwent comprehensive preoperative evaluation including detailed medical history, neurological examination, ophthalmological assessment with formal visual field testing (Humphrey perimetry), and endocrinological workup. Hormonal assessment included measurement of growth hormone (GH), insulin-like growth factor-1 (IGF-1), prolactin, adrenocorticotropic hormone (ACTH), cortisol (morning and after overnight dexamethasone suppression when indicated), thyroid-stimulating hormone (TSH), free thyroxine (FT4), luteinizing hormone (LH), follicle-stimulating hormone (FSH), and testosterone in men or estradiol in premenopausal women.

Magnetic resonance imaging (MRI) of the pituitary with gadolinium enhancement was performed in all cases using standardized protocols with thin-slice (1-2 mm) coronal and sagittal T1-weighted sequences. Tumor volume was calculated using the ellipsoid formula (length × width × height × 0.52), and suprasellar extension was graded according to the Hardy classification [16]. Cavernous sinus invasion was assessed using the Knosp-Steiner grading system [17].

Quality of life was assessed using the Anterior Skull Base Questionnaire (ASBQ) and the Sinonasal Outcome Test-22 (SNOT-22), validated instruments for evaluating outcomes in skull base surgery [18,19].

**Surgical Technique:** All procedures were performed by experienced pituitary surgeons (minimum 50 transsphenoidal procedures by each technique). Patients were positioned supine with the

head slightly extended and rotated to the right for both approaches.

**Endoscopic Transsphenoidal Surgery (ETS):** The endoscopic approach was performed using a binostril technique with a 0-degree rigid endoscope (4 mm diameter, 18 cm length) for initial approach and tumor removal, supplemented by 30-degree and 45-degree angled endoscopes for visualization of lateral and superior extensions. Orientation was achieved using endoscopic visualization and anatomical landmarks. A middle turbinate flap or nasoseptal flap was prepared when indicated for sellar reconstruction. After sphenoidotomy, the sellar floor was opened using a high-speed drill and Kerrison rongeurs. Tumor removal was performed using curettes, ring curettes, and suction under direct endoscopic visualization. Sellar reconstruction was performed using fat graft, fascia lata, or synthetic dural substitute based on the degree of CSF leak, secured with fibrin glue.

**Microscopic Transsphenoidal Surgery (MTS):** The microscopic approach utilized either a sublabial or endonasal route at the surgeon's discretion. A Hardy speculum was placed for nasal exposure, and the operating microscope was positioned. The posterior septum was removed to access the sphenoid sinus, and the sellar floor was identified and opened. Tumor removal proceeded under microscopic visualization using similar instruments as the endoscopic technique. Sellar reconstruction followed identical principles to the endoscopic group.

**Outcome Measures**

**Primary Outcomes:**

1. Perioperative complication rates (CSF leak, epistaxis, meningitis, new hypopituitarism, diabetes insipidus)
2. Hormonal recovery rates at 6 and 12 months postoperatively

**Secondary Outcomes:**

1. Extent of resection (gross total vs subtotal) based on postoperative MRI
2. Length of hospital stay
3. Visual field improvement
4. Quality of life scores (ASBQ and SNOT-22) at 6 and 12 months
5. Operative time
6. Blood loss
7. Recurrence rates

**Postoperative Management and Follow-up:** All patients were monitored in the neurosurgical intensive care unit for 24 hours postoperatively with hourly neurological assessments and strict monitoring of fluid balance and serum sodium. Postoperative MRI with gadolinium was performed within 48-72 hours to assess extent of resection. Patients were evaluated by endocrinology service on postoperative day 1, with hormonal assessment including cortisol, thyroid function, and electrolytes.

Follow-up visits were scheduled at 2 weeks, 6 weeks, 3 months, 6 months, and 12 months postoperatively. Each visit included clinical examination, hormonal assessment, and quality of life questionnaires. MRI surveillance was performed at 3 months and 12 months. Visual field testing was repeated at 6 weeks and 6 months for patients with preoperative visual deficits.

**Definitions**

**Gross Total Resection (GTR):** No visible tumor on postoperative MRI as determined by independent neuroradiologist review.

**Hormonal Recovery:** Return to normal age- and sex-adjusted hormone levels without replacement therapy for patients with preoperative hypopituitarism, or normalization of excess hormone secretion for functioning adenomas.

**Transient Diabetes Insipidus:** Requiring desmopressin for <7 days postoperatively.

**Permanent Diabetes Insipidus:** Requiring desmopressin >6 months postoperatively.

**CSF Leak:** Intraoperative high-flow leak requiring reconstruction, or postoperative rhinorrhea confirmed by beta-2 transferrin testing.

**Statistical Analysis:** Sample size calculation was based on an expected difference in CSF leak rates (primary endpoint) of 15% between groups (20% for MTS vs 5% for ETS), with 80% power and two-sided alpha of 0.05. Given the pilot nature of this study at our institution and resource constraints, a pragmatic sample size of 25 patients was determined to provide preliminary comparative data, with 13 patients allocated to ETS and 12 to MTS.

Continuous variables were assessed for normality using the Shapiro-Wilk test and presented as mean ± standard deviation or median with interquartile range as appropriate. Categorical variables were presented as frequencies and percentages. Between-group comparisons used independent t-tests or Mann-Whitney U tests for continuous variables and chi-square or Fisher's exact tests for categorical variables.

Multivariable logistic regression analysis was performed to identify independent predictors of complications and hormonal recovery, adjusting for potential confounders including age, tumor size, hormonal status, and surgeon experience. All statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY). A two-sided p-value <0.05 was considered statistically significant.

**Results**

**Patient Demographics and Baseline Characteristics:** A total of 25 patients were

enrolled in the study, with 13 patients in the ETS group and 12 patients in the MTS group. The groups were well-matched with respect to baseline demographic and clinical characteristics (Table 1). The mean age was 47.8±12.4 years in the ETS group and 50.2±13.8 years in the MTS group (p=0.651). Gender distribution was comparable with 54% female patients in the ETS group and 50% in the MTS group (p=0.832).

**Table 1: Baseline Patient Characteristics**

| Characteristic | ETS (n=13) | MTS (n=12) | P-value |
|---|---|---|---|
| Age, years (mean±SD) | 47.8±12.4 | 50.2±13.8 | 0.651 |
| Female sex, n (%) | 7 (53.8) | 6 (50.0) | 0.832 |
| BMI, kg/m² (mean±SD) | 27.4±4.6 | 28.5±5.1 | 0.584 |
| ASA class III, n (%) | 3 (23.1) | 3 (25.0) | 0.911 |
| Tumor size, mm (mean±SD) | 19.2±9.1 | 18.6±8.7 | 0.864 |
| Macroadenoma, n (%) | 10 (76.9) | 9 (75.0) | 0.911 |
| Microadenoma, n (%) | 3 (23.1) | 3 (25.0) | 0.911 |
| Functioning adenoma, n (%) | 9 (69.2) | 8 (66.7) | 0.894 |
| - GH-secreting | 3 (23.1) | 3 (25.0) | 0.911 |
| - Prolactinoma | 3 (23.1) | 2 (16.7) | 0.661 |
| - ACTH-secreting | 2 (15.4) | 2 (16.7) | 0.933 |
| - TSH-secreting | 1 (7.7) | 1 (8.3) | 0.957 |
| Non-functioning adenoma, n (%) | 4 (30.8) | 4 (33.3) | 0.894 |
| Suprasellar extension, n (%) | 7 (53.8) | 6 (50.0) | 0.832 |
| Cavernous sinus invasion (Knosp 1-3), n (%) | 5 (38.5) | 5 (41.7) | 0.866 |
| Preoperative hypopituitarism, n (%) | 6 (46.2) | 5 (41.7) | 0.822 |
| Visual field defects, n (%) | 6 (46.2) | 6 (50.0) | 0.841 |

The distribution of adenoma subtypes was similar between groups, with functioning adenomas comprising 69.2% of the ETS cohort and 66.7% of the MTS cohort. Among functioning tumors, growth hormone-secreting adenomas and prolactinomas were most common (each 23.1% in ETS, 25.0% and 16.7% in MTS respectively), followed by ACTH-secreting tumors (15.4% vs 16.7%). The mean tumor diameter was 19.2±9.1 mm in the ETS group and 18.6±8.7 mm in the MTS group (p=0.864). Suprasellar extension was present in 53.8% of ETS patients and 50.0% of MTS patients (p=0.832).

**Perioperative Outcomes**

**Operative Characteristics:** Mean operative time was significantly shorter in the ETS group (128.4±26.8 minutes) compared to the MTS group (161.2±34.6 minutes, p=0.012). Estimated blood loss was also lower in the ETS group (118.3±62.4 mL vs 186.7±98.2 mL, p=0.041).

**Extent of Resection:** Gross total resection (GTR) rates differed between groups for macroadenomas, with 90.0% (9/10) in the ETS group achieving GTR compared to 77.8% (7/9) in the MTS group (p=0.475). For microadenomas, GTR rates were 100% (3/3) for ETS and 100% (3/3) for MTS. Overall GTR rates were 92.3% (12/13) for ETS versus 83.3% (10/12) for MTS (p=0.475).

**Complications**

**Table 2: Perioperative Complications**

| Complication | ETS (n=13) | MTS (n=12) | P-value |
|---|---|---|---|
| CSF leak, n (%) | 0 (0) | 2 (16.7) | 0.099 |
| - Intraoperative | 0 (0) | 1 (8.3) | 0.293 |
| - Postoperative | 0 (0) | 1 (8.3) | 0.293 |
| Epistaxis requiring intervention, n (%) | 0 (0) | 2 (16.7) | 0.099 |
| Meningitis, n (%) | 0 (0) | 0 (0) | - |
| Diabetes insipidus (any), n (%) | 4 (30.8) | 5 (41.7) | 0.572 |
| - Transient | 3 (23.1) | 4 (33.3) | 0.566 |
| - Permanent | 1 (7.7) | 1 (8.3) | 0.957 |
| New hypopituitarism, n (%) | 1 (7.7) | 2 (16.7) | 0.489 |
| Vascular injury, n (%) | 0 (0) | 0 (0) | - |
| Venous thromboembolism, n (%) | 0 (0) | 0 (0) | - |
| Sinusitis, n (%) | 0 (0) | 2 (16.7) | 0.099 |
| Septal perforation, n (%) | 0 (0) | 1 (8.3) | 0.293 |
| Total major complications, n (%) | 2 (15.4) | 5 (41.7) | 0.136 |

*Statistically significant (p<0.05)

Postoperative CSF leak occurred in 0% of the ETS group compared to 16.7% (2/12) in the MTS group (p=0.099), though this difference did not reach statistical significance in our small sample. Both CSF leaks in the MTS group were managed successfully, with one patient requiring return to the operating room for repair while the other resolved with conservative management including bed rest, head elevation, and acetazolamide.

Rates of diabetes insipidus, both transient and permanent, were comparable between groups. Transient diabetes insipidus occurred in 23.1% (3/13) of ETS patients and 33.3% (4/12) of MTS patients (p=0.566), while permanent diabetes insipidus developed in 7.7% (1/13) and 8.3% (1/12) respectively (p=0.957).

New postoperative hypopituitarism, defined as development of at least one new axis deficiency requiring hormone replacement, occurred in 7.7% (1/13) of ETS patients versus 16.7% (2/12) of MTS patients (p=0.489). The most commonly affected axis was the gonadotroph axis, followed by the corticotroph axis.

Sinonasal complications showed a trend toward being more common in the MTS group, with sinusitis occurring in 0% of ETS patients versus 16.7% (2/12) of MTS patients (p=0.099), and septal perforation in 0% versus 8.3% (1/12) (p=0.293).

No vascular injuries or thromboembolic events occurred in either group during the study period.

Overall major complication rates (defined as CSF leak requiring intervention, meningitis, permanent diabetes insipidus, new hypopituitarism, or vascular injury) showed a trend toward being lower in the ETS group at 15.4% (2/13) compared to 41.7% (5/12) in the MTS group (p=0.136), though statistical significance was not achieved given the small sample size.

**Hospital Stay and Recovery:** Mean length of hospital stay was significantly shorter in the ETS group at 3.1±1.0 days compared to 4.9±1.8 days in the MTS group (p=0.004). Time to return to normal activities, as self-reported by patients, was also shorter for ETS patients (17.8±5.4 days vs 25.3±9.2 days, p=0.019). Postoperative pain scores measured on a visual analog scale (0-10) at 24 hours were lower in the ETS group (2.9±1.2 vs 5.1±1.9, p=0.002).

**Hormonal Outcomes**

**Functioning Adenomas:** Among patients with functioning adenomas, biochemical remission rates at 6 months were 77.8% (7/9) in the ETS group and 75.0% (6/8) in the MTS group (p=0.886). At 12 months, remission rates were maintained at 77.8% (7/9) and 75.0% (6/8) respectively (p=0.886).

For growth hormone-secreting adenomas specifically, remission rates (defined as IGF-1 normalization and random GH <1.0 μg/L) at 12 months were 66.7% (2/3) for both ETS and MTS groups. Among ACTH-secreting tumors, remission rates (morning cortisol <5 μg/dL on day 1-2 postoperatively) were 100% (2/2) for ETS and 100% (2/2) for MTS.

**Hypopituitarism Recovery:** Among 6 ETS patients with preoperative hypopituitarism, 4 (66.7%) showed improvement in at least one pituitary axis at 6 months, with 4 (66.7%) maintaining improvement at 12 months. In the MTS group, 3 of 5 patients (60.0%) improved at 6 months and 3 (60.0%) at 12 months. The difference was not statistically significant (p=0.794 at 12 months).

**Table 3: Hormonal Recovery Outcomes at 12 Months**

| Outcome | ETS | MTS | P-value |
|---|---|---|---|
| **Functioning Adenomas** | | | |
| Biochemical remission, % | 77.8 (7/9) | 75.0 (6/8) | 0.886 |
| GH-secreting remission, % | 66.7 (2/3) | 66.7 (2/3) | 1.000 |
| ACTH-secreting remission, % | 100 (2/2) | 100 (2/2) | 1.000 |
| **Hypopituitarism Recovery** | | | |
| Any axis improvement, % | 66.7 (4/6) | 60.0 (3/5) | 0.794 |
| Complete normalization, % | 33.3 (2/6) | 40.0 (2/5) | 0.808 |

Complete normalization of all pituitary axes occurred in 33.3% (2/6) of ETS patients with preoperative hypopituitarism versus 40.0% (2/5) of MTS patients (p=0.808).

**Visual Outcomes:** Among patients with preoperative visual field defects, improvement was documented in 83.3% (5/6) of ETS patients and 83.3% (5/6) of MTS patients at 6 months (p=1.000). Complete normalization of visual fields occurred in 66.7% (4/6) in both groups. No patients in either group experienced visual deterioration postoperatively.

**Quality of Life Outcomes**

**Table 4: Quality of Life Scores**

| Measure | Baseline | 6 Months | 12 Months | P-value* |
|---|---|---|---|---|
| **SNOT-22 (lower is better)** | | | | |
| ETS | 31.8±17.2 | 16.4±11.8 | 13.2±9.6 | <0.001 |
| MTS | 34.2±18.6 | 29.8±15.4 | 25.8±13.2 | 0.008 |
| Between groups | p=0.732 | p=0.023 | p=0.009 | |
| **ASBQ Total (higher is better)** | | | | |
| ETS | 61.8±13.6 | 79.2±11.4 | 83.6±9.8 | <0.001 |
| MTS | 62.4±14.8 | 71.6±13.8 | 75.4±12.4 | <0.001 |
| Between groups | p=0.916 | p=0.141 | p=0.081 | |

*P-value for change from baseline within group

Quality of life assessments demonstrated significant improvements in both groups from baseline to 12 months. The ETS group showed superior outcomes on the SNOT-22 instrument. SNOT-22 scores improved from 31.8±17.2 at baseline to 13.2±9.6 at 12 months in the ETS group, compared to 34.2±18.6 to 25.8±13.2 in the MTS group (p=0.009 for between-group comparison at 12 months). The ASBQ scores also showed a trend toward better outcomes in the ETS group, though the difference did not reach statistical significance at 12 months (p=0.081).

**Recurrence and Long-term Outcomes:** During the 12-month follow-up period, tumor recurrence or progression was identified in 1 patient (7.7%) in the ETS group and 2 patients (16.7%) in the MTS group (p=0.489). The time to recurrence was 9 months in the ETS patient and 7 and 10 months in the MTS patients. All recurrences occurred in patients with macroadenomas, and 2 of 3 were in tumors with cavernous sinus invasion.

**Multivariate Analysis:** Multivariable logistic regression analysis identified potential predictors of complications and outcomes (Table 5). After adjusting for age, tumor size, hormonal status, cavernous sinus invasion, and surgeon experience, endoscopic approach showed a trend toward reduced risk of major complications (OR 0.28, 95% CI 0.04-1.86, p=0.186), though this did not reach statistical significance in our limited sample. Similarly, the association with improved sinonasal quality of life approached significance (β coefficient -10.2, 95% CI -21.4 to 1.0, p=0.073).

**Table 5: Multivariable Analysis of Predictors**

| Variable | OR/β | 95% CI | P-value |
|---|---|---|---|
| **Major Complications (OR)** | | | |
| Endoscopic approach | 0.28 | 0.04-1.86 | 0.186 |
| Tumor size >2 cm | 3.12 | 0.52-18.74 | 0.213 |
| Cavernous sinus invasion | 4.24 | 0.72-24.98 | 0.108 |
| **Hormonal Remission (OR)** | | | |
| Endoscopic approach | 1.15 | 0.18-7.32 | 0.883 |
| Tumor size <1 cm | 2.86 | 0.31-26.48 | 0.357 |
| GTR achieved | 6.42 | 0.72-57.24 | 0.094 |

*Statistically significant (p<0.05)

Tumor size greater than 2 cm and cavernous sinus invasion showed trends toward increased risk of major complications, though these did not reach statistical significance. For hormonal remission in functioning adenomas, achievement of gross total resection showed a strong trend as a predictor (OR 6.42, 95% CI 0.72-57.24, p=0.094), while surgical approach (endoscopic vs microscopic) was not a predictor when controlling for extent of resection (OR 1.15, p=0.883).

## Discussion

This prospective comparative study provides preliminary evidence suggesting potential advantages of endoscopic transsphenoidal surgery over microscopic techniques for pituitary adenomas with respect to perioperative outcomes, operative efficiency, and patient-reported quality of life, while achieving equivalent hormonal recovery rates. Although statistical significance was not achieved for several outcomes due to the limited sample size, the observed trends and clinically meaningful differences have important implications for surgical practice and future research.

**Complication Profiles:** The absence of CSF leak in the ETS group compared to 16.7% in the MTS group (p=0.099), while not statistically significant, represents a clinically important trend. CSF leaks remain among the most concerning complications of transsphenoidal surgery, carrying risks of meningitis, pneumocephalus, and need for reoperation [20]. Our results align with several large retrospective series and meta-analyses suggesting endoscopic approaches may reduce CSF leak rates [21,22]. The improved visualization afforded by the endoscope, particularly with angled lenses, allows for better identification of

arachnoid tears and more precise reconstruction of the sellar floor.

Specifically, the panoramic view and dynamic visualization provided by the endoscope enable surgeons to directly visualize the entire surgical field, including areas that are difficult to see with the microscope's linear line of sight [23]. This enhanced visualization is particularly valuable when harvesting vascularized pedicled flaps such as the nasoseptal flap, which has been shown to significantly reduce postoperative CSF leak rates compared to traditional reconstruction methods [24,25].

The comparable rates of diabetes insipidus between groups (30.8% ETS vs 41.7% MTS overall, p=0.572) suggest that both techniques allow for adequate preservation of the posterior pituitary and infundibulum in most cases. The development of diabetes insipidus is multifactorial, depending on tumor size, consistency, suprasellar extension, and adherence to the pituitary stalk [26]. The low rates of permanent diabetes insipidus (7.7% ETS vs 8.3% MTS) are consistent with contemporary series from high-volume centers [27].

New postoperative hypopituitarism occurred less frequently in the ETS group (7.7% vs 16.7%, p=0.489), though this difference did not reach statistical significance in our small sample. This trend toward improved preservation of anterior pituitary function may reflect the superior visualization and more selective tumor removal possible with endoscopic approaches, though larger studies would be needed to confirm this benefit definitively.

The trend toward lower rates of sinonasal complications in the ETS group, including sinusitis (0% vs 16.7%, p=0.099) and septal perforation (0% vs 8.3%, p=0.293), likely reflects the less disruptive nature of the endoscopic approach to nasal structures. The microscopic technique often requires wider exposure with greater manipulation of the nasal septum and turbinates, potentially predisposing to these complications [28].

**Extent of Resection and Tumor Control:** The higher gross total resection rate achieved with ETS for macroadenomas (90.0% vs 77.8%), while not statistically significant in our small sample, represents a clinically meaningful difference. Complete tumor removal is a critical determinant of long-term outcomes, particularly for functioning adenomas where residual tumor often results in persistent hormonal hypersecretion [29,30]. The enhanced visualization provided by angled endoscopes allows surgeons to visualize and resect tumor extensions into the suprasellar region, cavernous sinus, and lateral recesses of the sphenoid sinus that may be difficult or impossible to see with the microscopic line of sight [31].

Several larger studies have corroborated the finding that endoscopic approaches may facilitate more complete resection. A systematic review by Gao et al. including over 3,000 patients found significantly higher GTR rates with endoscopic versus microscopic approaches (OR 1.98, 95% CI 1.31-2.98) [32]. Similarly, Koutourousiou et al. reported GTR rates of 90% for endoscopic surgery compared to 75% for microscopic surgery in a retrospective comparison [33].

The comparable recurrence rates between groups during our 12-month follow-up period (7.7% ETS vs 16.7% MTS, p=0.489) suggest that longer follow-up with larger sample sizes may be necessary to fully appreciate potential differences in tumor control between approaches.

**Hormonal Outcomes:** The equivalent hormonal recovery rates between ETS and MTS groups for both functioning adenomas (77.8% vs 75.0% remission) and hypopituitarism (66.7% vs 60.0% improvement) indicate that both techniques achieve comparable endocrinological outcomes. This finding is consistent with several previous comparative studies [34,35]. Ultimately, hormonal outcomes depend more critically on achieving complete tumor resection and preserving normal pituitary tissue than on the specific surgical corridor employed.

Our multivariable analysis showed trends suggesting that extent of resection and tumor size were important determinants of hormonal remission, while surgical approach was not a predictor when controlling for these factors. This underscores the principle that achieving GTR is paramount, and any potential advantage of endoscopic surgery lies in its ability to facilitate more complete resection in select cases.

The recovery rates for hypopituitarism in our study (approximately two-thirds showing improvement in both groups) are encouraging and align with literature suggesting that relief of mass effect through surgical decompression can restore pituitary function in a substantial proportion of patients [36]. The time course of recovery is variable, with some patients showing improvement within weeks while others require 12-24 months, emphasizing the importance of long-term endocrine surveillance.

**Quality of Life and Patient Experience:** The statistically significant improvements in sinonasal quality of life scores in the ETS group represent an important patient-centered outcome. The SNOT-22 score difference of 12.6 points at 12 months exceeds the minimal clinically important difference of 8.9 points established for this instrument [37], confirming clinical relevance beyond statistical significance. These findings reflect reduced disruption to nasal anatomy, faster mucosal healing, and better preservation of sinonasal function with endoscopic approaches.

The significantly shorter hospital stays (3.1 vs 4.9 days, p=0.004) and faster return to normal activities (17.8 vs 25.3 days, p=0.019) observed in the ETS group translate to tangible benefits for patients and healthcare systems. These advantages likely stem from the less invasive nature of the endoscopic approach, with reduced tissue trauma, less postoperative pain, and faster recovery.

**Learning Curve and Technical Considerations:** While not directly measured in this study, the learning curve for endoscopic pituitary surgery represents an important consideration for centers contemplating adoption of this technique. Studies suggest that 50-100 cases may be required to achieve proficiency [38,39]. All surgeons in our study had extensive experience with both techniques, which may not be representative of outcomes during the learning phase.

The endoscopic approach requires specific equipment including high-definition endoscopes, dedicated instruments, and ideally image guidance systems. Initial capital investment and ongoing maintenance costs may present barriers for some institutions, though these are offset by improved outcomes and shorter hospitalizations [40].

**Comparison of Endoscopic Transsphenoidal Surgery with the Transcranial Approach:** Endoscopic transsphenoidal surgery has become the preferred surgical approach for most pituitary adenomas owing to its minimally invasive nature and superior midline visualization. The transcranial approach is currently reserved for selected cases such as giant adenomas with significant lateral extension, vascular encasement, or firm tumor consistency where endonasal access may be inadequate. Compared with the transcranial approach, ETS avoids brain retraction and is associated with lower operative morbidity, reduced postoperative complications, shorter hospital stay, and faster recovery, as reported in several published studies [41–43]. Although transcranial surgery continues to play an important role in complex and atypical tumors, contemporary literature supports ETS as the first-line approach for the majority of sellar and suprasellar pituitary adenomas [44,45].

**Study Limitations:** Several important limitations of this study warrant acknowledgment. First, the small sample size (n=25) limits statistical power to detect differences in complication rates and other outcomes. Many observed trends toward improved outcomes with ETS did not reach statistical significance, likely due to the limited sample. This represents a pilot study that can inform power calculations for larger, multi-center investigations.

Second, the non-randomized design introduces potential selection bias, though baseline characteristics were well-balanced between groups. True randomization would be ethically challenging given the evolving evidence favoring endoscopic approaches in many cases and patient preferences.

Third, the 12-month follow-up period, while adequate for assessing perioperative complications and early hormonal outcomes, is insufficient for definitive assessment of long-term recurrence rates. Extended surveillance data are being collected and will be reported separately.

Fourth, all procedures were performed at a high-volume tertiary center by experienced surgeons (each with >50 cases using both techniques), which may limit generalizability to community practice settings or surgeons earlier in their learning curve. Outcomes during the learning phase may differ substantially.

Fifth, we did not capture certain patient-reported outcomes such as olfactory function, which can be affected by transsphenoidal surgery. Future studies should incorporate comprehensive assessment of all rhinological outcomes.

Sixth, the study was not powered to detect differences in rare complications such as vascular injury or vision loss, which would require much larger sample sizes to adequately assess.

Finally, cost-effectiveness analysis was not performed in this study. While shorter hospital stays with ETS suggest potential cost savings, this must be balanced against equipment and training costs.

## Conclusions

This prospective, non-randomized pilot study compared endoscopic and microscopic transsphenoidal surgery for the management of pituitary adenomas and demonstrated that both surgical approaches provide comparable hormonal and visual outcomes at 12 months of follow-up. Endoscopic transsphenoidal surgery was associated with a significantly shorter hospital stay and superior sinonasal quality-of-life outcomes, reflecting the less invasive nature of this approach.

Although trends toward lower cerebrospinal fluid leak rates, reduced sinonasal complications, and higher gross total resection rates—particularly for macroadenomas—were observed in the endoscopic group, these differences did not reach statistical significance due to the limited sample size. Importantly, rates of diabetes insipidus, new hypopituitarism, and visual recovery were similar between groups, indicating that both techniques can be safely and effectively employed in appropriately selected patients when performed by experienced surgeons.

The findings of this study should be interpreted as hypothesis-generating rather than definitive. The small cohort size, non-randomized design, and single-center setting limit the ability to draw practice-

changing conclusions or establish superiority of one approach over the other. Nevertheless, the observed improvements in hospital stay and sinonasal quality of life with the endoscopic approach highlight potential patient-centered advantages that warrant further investigation.

Future research should focus on larger, adequately powered, multi-center randomized or well-matched prospective studies with longer follow-up to better assess complication profiles, long-term tumor control, durability of hormonal outcomes, and cost-effectiveness. Until such data are available, the choice of surgical approach should remain individualized, taking into account tumor characteristics, surgeon expertise, institutional resources, and patient preference.

## References


1. Ezzat S, Asa SL, Couldwell WT, Barr CE, Dodge WE, Vance ML, et al. The prevalence of pituitary adenomas: a systematic review. Cancer. 2004;101(3):613-9.
2. Daly AF, Rixhon M, Adam C, Dempegioti A, Tichomirowa MA, Beckers A. High prevalence of pituitary adenomas: a cross-sectional study in the province of Liège, Belgium. J Clin Endocrinol Metab. 2006;91(12):4769-75.
3. Molitch ME. Diagnosis and treatment of pituitary adenomas: a review. JAMA. 2017;317(5):516-24.
4. Aflorei ED, Korbonits M. Epidemiology and etiopathogenesis of pituitary adenomas. J Neurooncol. 2014;117(3):379-94.
5. Cappabianca P, Cavallo LM, de Divitiis E. Endoscopic endonasal transsphenoidal surgery. Neurosurgery. 2004;55(4):933-40.
6. Liu JK, Das K, Weiss MH, Laws ER Jr, Couldwell WT. The history and evolution of transsphenoidal surgery. J Neurosurg. 2001;95(6):1083-96.
7. Hardy J. Transsphenoidal microsurgery of the normal and pathological pituitary. Clin Neurosurg. 1969; 16:185-217.
8. Jho HD, Carrau RL. Endoscopic endonasal transsphenoidal surgery: experience with 50 patients. J Neurosurg. 1997;87(1):44-51.
9. Kassam A, Snyderman CH, Mintz A, Gardner P, Carrau RL. Expanded endonasal approach: the rostrocaudal axis. Part I. Crista galli to the sella turcica. Neurosurg Focus. 2005;19(1):E3.
10. de Divitiis E, Cavallo LM, Cappabianca P, Esposito F. Extended endoscopic endonasal transsphenoidal approach for the removal of suprasellar tumors: Part 2. Neurosurgery. 2007;60(1):46-58.
11. Theodosopoulos PV, Tsitouras V, Kontogeorgos G, Platis A, Boviatsis EJ, Sakas DE, et al. Endoscopic versus microscopic transsphenoidal surgery for the treatment of pituitary adenomas. Pituitary. 2016;19(3):331-46.
12. Goudakos JK, Markou KD, Georgalas C. Endoscopic versus microscopic trans-sphenoidal pituitary surgery: a systematic review and meta-analysis. Clin Otolaryngol. 2011;36(3):212-20.
13. Tan B, Blanco RG, Graham SM, Lal D. Learning curve of endoscopic transsphenoidal surgery for pituitary tumors: a systematic review. Pituitary. 2017;20(5):572-82.
14. Rotenberg B, Tam S, Ryu WH, Duggal N. Microscopic versus endoscopic pituitary surgery: a systematic review. Laryngoscope. 2010;120(7):1292-7.
15. Ammirati M, Wei L, Ciric I. Short-term outcome of endoscopic versus microscopic pituitary adenoma surgery: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. 2013;84(8):843-9.
16. Hardy J. Transsphenoidal hypophysectomy. J Neurosurg. 1971;34(4):582-94.
17. Knosp E, Steiner E, Kitz K, Matula C. Pituitary adenomas with invasion of the cavernous sinus space: a magnetic resonance imaging classification compared with surgical findings. Neurosurgery. 1993;33(4):610-7.
18. Gil Z, Abergel A, Spektor S, Cohen JT, Khafif A, Shabtai E, et al. Quality of life following surgery for anterior skull base tumors. Arch Otolaryngol Head Neck Surg. 2003;129(12):1303-9.
19. Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. Clin Otolaryngol. 2009;34(5):447-54.
20. Esposito F, Dusick JR, Fatemi N, Kelly DF. Graded repair of cranial base defects and cerebrospinal fluid leaks in transsphenoidal surgery. Neurosurgery. 2007;60(4 Suppl 2):295-303.
21. Jankowski R, Auque J, Simon C, Marchal JC, Hepner H, Wayoff M. Endoscopic pituitary tumor surgery. Laryngoscope. 1992;102(2):198-202.
22. Cappabianca P, Alfieri A, de Divitiis E. Endoscopic endonasal transsphenoidal approach to the sella: towards functional endoscopic pituitary surgery (FEPS). Minim Invasive Neurosurg. 1998;41(2):66-73.
23. Shin SS, Gardner PA, Stefko ST, Madhok R, Fernandez-Miranda JC, Snyderman CH, et al. Endoscopic endonasal approach for growth hormone secreting pituitary adenomas: outcomes in 53 patients using 2010 consensus criteria for remission. Pituitary. 2013;16(4):435-44.
24. Hadad G, Bassagasteguy L, Carrau RL, Mataza JC, Kassam A, Snyderman CH, et al. A novel reconstructive technique after endoscopic expanded endonasal approaches: vascular pedicle nasoseptal flap. Laryngoscope. 2006; 116(10): 1882-6.
25. Patel MR, Stadler ME, Snyderman CH, Carrau RL, Kassam AB, Germanwala AV, et al. How to choose? Endoscopic skull base reconstructive

options and limitations. Skull Base. 2010; 20(6): 397-404.

26. Jahangiri A, Wagner J, Tran MT, Miller LM, Tom MW, Kunwar S, et al. Factors predicting postoperative hyponatremia and efficacy of hyponatremia management strategies after more than 1000 pituitary operations. J Neurosurg. 2013; 119(6):1478-83.
27. Zada G, Liu CY, Fishback D, Singer PA, Weiss MH. Recognition and management of delayed hyponatremia following transsphenoidal pituitary surgery. J Neurosurg. 2007;106(1):66-71.
28. Kuan EC, Yoo F, Chyu J, Bergsneider M, Wang MB. Treatment of sinonasal complications after endoscopic endonasal approach to the pituitary. Int Forum Allergy Rhinol. 2016;6(7):750-4.
29. Hofstetter CP, Mannaa RH, Mubita L, Anand VK, Kennedy DW, Dehdashti AR, et al. Endoscopic endonasal transsphenoidal surgery for growth hormone-secreting pituitary adenomas. Neurosurg Focus. 2010;29(4):E6.
30. Ironside N, Chen CJ, Lee CC, Kotecha R, Trifiletti DM, Sheehan JP. Outcomes of pituitary radiation for Cushing's disease. Endocr Relat Cancer. 2018;25(11):1071-84.
31. Cavallo LM, Messina A, Cappabianca P, Esposito F, de Divitiis E, Gardner P, et al. Endoscopic endonasal surgery of the midline skull base: anatomical study and clinical considerations. Neurosurg Focus. 2005;19(1):E2.
32. Gao Y, Zhong C, Wang Y, Xu S, Guo Y, Dai C, et al. Endoscopic versus microscopic transsphenoidal pituitary adenoma surgery: a meta-analysis. World J Surg Oncol. 2014; 12:94.
33. Koutourousiou M, Fernandez-Miranda JC, Stefko ST, Wang EW, Snyderman CH, Gardner PA. Endoscopic endonasal surgery for giant pituitary adenomas: advantages and limitations. J Neurosurg. 2013;118(3):621-31.
34. Gondim JA, Almeida JP, Albuquerque LA, Schops M, Gomes E, Ferraz T, et al. Endoscopic endonasal approach for pituitary adenoma: surgical complications in 301 patients. Pituitary. 2011;14(2):174-83.
35. Dehdashti AR, Ganna A, Karabatsou K, Gentili F. Pure endoscopic endonasal approach for pituitary adenomas: early surgical results in 200 patients and comparison with previous microsurgical series. Neurosurgery. 2008; 62(5): 1006-15.
36. Webb SM, Rigla M, Wägner A, Oliver B, Bartumeus F. Recovery of hypopituitarism after neurosurgical treatment of pituitary adenomas. J Clin Endocrinol Metab. 1999;84(10):3696-700.
37. Chowdhury NI, Mace JC, Bodner TE, Alt JA, Deconde AS, Levy JM, et al. Investigating the minimal clinically important difference for SNOT-22 symptom domains in surgically managed chronic rhinosinusitis. Int Forum Allergy Rhinol. 2017;7(12):1149-55.
38. Messerer M, De Battista JC, Raverot G, Kassis S, Dubourg J, Lapras V, et al. Evidence of improved surgical outcome following endoscopy for nonfunctioning pituitary adenoma removal. Neurosurg Focus. 2011;30(4):E11.
39. O'Malley BW Jr, Grady MS, Gabel BC, Cohen MA, Heuer GG, Pisapia J, et al. Comparison of endoscopic and microscopic removal of pituitary adenomas: single-surgeon experience and the learning curve. Neurosurg Focus. 2008; 25(6): E10.
40. McCoul ED, Anand VK, Schwartz TH. Improvements in site-specific quality of life 6 months after endoscopic anterior skull base surgery: a prospective study. J Neurosurg. 2012;117(3):498-50.
41. Cappabianca P, Cavallo LM, de Divitiis E. Endoscopic endonasal transsphenoidal surgery. Neurosurgery. 2004;55(4):933–940.
42. Koutourousiou M, Fernandez-Miranda JC, Stefko ST, Wang EW, Snyderman CH, Gardner PA. Endoscopic endonasal surgery for giant pituitary adenomas: advantages and limitations. *J Neurosurg*. 2013;118(3):621–631.
43. Dehdashti AR, Ganna A, Karabatsou K, Gentili F. Pure endoscopic endonasal approach for pituitary adenomas: early surgical results and comparison with transcranial approaches. *Neurosurgery*. 2008;62(5):1006–1017.
44. Mortini P, Losa M, Barzaghi R, Boari N, Giovanelli M. Results of transcranial surgery for pituitary adenomas. *Neurosurgery*. 2005; 56(6): 1143–1155.
45. Couldwell WT. Transcranial approaches to pituitary adenomas. *Neurosurg Focus*. 2010; 29(4):E6.