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*Original Article*

# The learning curve and outcomes of 1038 endoscopic endonasal transsphenoidal pituitary tumor surgeries – A single surgical team experience

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## ABSTRACT

**Background:** Pituitary adenomas rank third among adult intracranial tumors, with an incidence of 3.9–7.4 cases/per 100,000 annually. Transsphenoidal surgery has evolved to include endoscopic endonasal surgery (EEA) in many centers due to technological and surgical advancements over the past two decades. We aim to analyze a 12-year cohort of pituitary adenomas operated through EEA, highlighting the evolution of surgical techniques and outcomes.

**Methods:** A retrospective review of patients undergoing EEA was conducted. A team of an otolaryngologist and neurosurgeon performed surgeries. The cohort was divided into three groups: Phase 1 (P1, 2012–2015), Phase 2 (P2, 2016–2019), and Phase 3 (P3, 2020–2023). Patient demographics, clinical data, and outcomes were collected from electronic medical records and compared over time.

**Results:** The mean age was 54.2 years, with 53.5% being female. The gross total resection rate was 75.6%, increasing from 62.3% in P1 to 76.3% in P3 ($P = 0.003$). The mean operative duration was 274.61 min, with no significant correlation to case number. Complication rates, excluding cerebrospinal fluid (CSF) leaks, were similar between the groups, with no statistically significant differences observed for complications such as visual deficit, cranial nerve palsy, and epistaxis. However, meningitis decreased significantly from 3.8% to 0.3% ($P < 0.001$). Intraoperative CSF leaks decreased from 65.1% to 55% ($P = 0.003$). The need for revision surgery was lower in P3 (8.5% vs. 5.4% vs. 2.1, $P < 0.001$). Length of hospitalization decreased from 5.3 days to 3.9 days ($P < 0.001$).

**Conclusion:** Our experience with EEA for pituitary adenomas shows significant improvements in surgical outcomes, reduced complications, and better postoperative management, underscoring the importance of experience, technical refinement, and a multidisciplinary approach.

**Keywords:** Adenoma, Endonasal, Endoscopic, Learning curve, Pituitary

## INTRODUCTION

Pituitary adenomas are the third most common intracranial tumor in adults, with an incidence rate between 3.9 and 7.4 cases/100.000/year.[4] The transfacial transsphenoidal approach, initially performed with lateral rhinotomy, was first introduced by Schloeffel in 1907.[27] Hirsch later refined this technique in Vienna in 1910, who developed the transseptal submucosal approach, and Harvey Cushing in Boston in 1910, who employed the sublabial submucosal approach.[1] However, by 1929, Cushing abandoned the transsphenoidal approach, returning to frontal craniotomy due to the challenges of poor illumination and a high mortality rate. The transnasal approach was revived decades later, first by Guiot in 1958 using fluoroscopy and later by Hardy in 1967 with the introduction of the operating microscope.[15] The use of endoscopy for pituitary adenomas was pioneered by Jankowski *et al*. in 1992.[6] Over the past two decades, many centers have gradually transitioned to endoscopic endonasal surgery (EEA).[5,7,28,29] Recent advancements in endoscopic technology, including improved endoscopes, monitors, and stereotactic instruments, alongside the evolution of extended endonasal approaches and robust closure techniques, have propelled the field to the forefront of contemporary skull base surgery. As the technique has improved, the focus has been on evaluating the safety and effectiveness of the endoscopic approach compared to the microscopic and open transcranial approach.[10-13,22] This technique has many clear advantages, including a broader and more panoramic visual field, enhanced illumination, increased maneuverability of instruments, and the capability to explore anatomical corners by employing angled lenses.[5,25] Little *et al*. showed that hospital fees decreased slightly when the endoscopic technique was used compared to the microscopic approach.[17] Despite the numerous advantages, acquiring proficiency in this technique necessitates a substantial time commitment. Less experienced surgeons in endoscopic surgery should proceed cautiously in patient selection, considering the inherent learning curves associated with this approach.

The objective of this study is to analyze our historical 12-year cohort of pituitary adenomas operated through EEA to describe how surgical technical variables and clinical outcomes have evolved and experienced.

## MATERIALS AND METHODS

We retrospectively reviewed all pituitary tumor patients who were operated on with EEA between 2012 and 2023 at our institution. A 2-surgeon approach was employed for all operations, involving the same neurosurgeon and otolaryngologist. The study was conducted with the Institutional Review Board approval (20160437), and patient consent was not required due to the retrospective nature of the study and the removal of all identifying patient information.

Electronic medical records were reviewed for patient demographics, preoperative clinical deficits, diagnosis, preoperative and postoperative magnetic resonance imaging (MRI) scans, and lesion characteristics, including location, volume, extent of resection, postoperative complications, and postoperative deficits.

### Radiologic assessment

All patients underwent high-resolution MRI scans with and without contrast, specifically focusing on thin sections through the sella. Adenoma volume was calculated using the formula (length × width × height)/2, assessed based on the greatest dimensions in axial, coronal, and sagittal planes from MRI scans. Adenomas were categorized based on the maximum tumor diameter into two groups: Microadenomas (≤10 mm) and macroadenomas (>10 mm). The Knosp classification was utilized to assess the relationship of adenoma with the cavernous sinus.[9,19] Tumors were analyzed using contrast-enhanced MR images on postoperative day 1, 3 months after surgery, and then at a yearly interval. The absence of any detectable tumor on postoperative imaging was defined as "Gross-total resection (GTR)." Progression was characterized by a more than 25% increase in the volume of residual tumor post-STR compared to its dimensions observed on early postoperative imaging. Regression was defined as a minimum 25% reduction in volume during subsequent follow-ups after STR.

### Endocrinologic evaluation

Patients received comprehensive evaluation at a specialized multidisciplinary pituitary center, comprising neurosurgeons and endocrinologists. Each patient underwent an initial assessment involving baseline pituitary hormone profiling encompassing serum cortisol, free thyroxine, thyroid-stimulating hormone, adrenocorticotropic hormone (ACTH), growth hormone (GH), insulin-like growth factor, prolactin (PRL), luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone (in men), and estradiol (in women). Endocrine outcomes were assessed based on specific criteria for defining complete biochemical remission in different tumor types. This included the normalization of serum PRL levels (<20 µg/L) for prolactinomas, the normalization of serum GH (<1 µg/L) or nadir GH after an oral glucose tolerance test (≤0.4 µg/L) for GH-producing tumors, and morning serum cortisol levels (<3 µg/dL) 3–5 days postsurgery for ACTH-producing tumors.

### Statistical analysis

A comparison of categorical variables was conducted using Chi-square and Fisher exact tests where appropriate. Comparison of continuous variables was conducted using the independent samples *t*-test and one-way analysis of variance test, and pairwise comparisons were conducted using *post hoc* testing. Spearman correlation and regression analyses were conducted to assess the relationships between the operation duration and preoperative volume, as well as the number of cases and cerebrospinal fluid (CSF) leaks. A $P < 0.05$ was considered statistically significant. Statistical analyses were performed using the Statistical Package for the Social Sciences 23.0 software (IBM, New York) and GraphPad Prism software (Version 10.1.2, GraphPad Software Inc., San Diego, California).

## RESULTS

### Patient characteristics

We included 1038 consecutive patients treated over 12 years. The cohort was divided into three groups: Phase 1 (P1, 2012–2015), Phase 2 (P2, 2016–2019), and Phase 3 (P3, 2020–2023). There were 106 patients in P1, 350 patients in P2, and 582 patients in P3, indicating an increase in case volume as the surgeon gained experience. The demographic characteristics of the cohort are summarized in Table 1. The mean age of the cohort was 54.2 ± 16.2 years, with 53.5% women. 50.3% ($n = 522$) of the patients had visual deficits preoperatively. Sixty-seven (6.5%) patients had apoplexy. The median preoperative KPS was 90 (50–100). Among the patients, 523 (50.4%) had normal endocrine function preoperatively. In contrast, 515 (49.6%) had endocrine dysfunction, such as panhypopituitarism, hypo- or hypercortisolism, hypogonadism, and hypothyroidism. Except for the prevalence of preoperative visual deficit, which was significantly higher in the first phase (67% vs. 50%, 47.4%, $P = 0.001$), and preoperative endocrine dysfunction, which was significantly higher in the third phase (49.1% vs. 43.7% vs. 53.3%, $P = 0.018$), there were no statistically significant differences between the groups regarding patient characteristics [Table 1].

Among 1038 pituitary adenomas, 387 (37.3%) were functional, and functional adenomas were more frequent in Phase 3 (25.5% vs. 28.6% vs. 44.7%, $P < 0.001$). Of the functional adenomas, 31% ($n = 120$) were ACTH-secreting, 29.5% ($n = 114$) were prolactinoma, 18.9% ($n = 73$) were GH-secreting, and 12.4% ($n = 48$) were FSH/LH-secreting adenomas. The majority of the adenomas (87%, $n = 903$) were located in the sellar region, while 56 (5.4%) were found in the suprasellar region, and 72 (6.9%) were located in both sellar and suprasellar region. According to the Knosp classification, there were 217 (20.9%) Grade 0 adenomas, 247 (23.8%) Grade 1, 172 (16.6%) Grade 2, 256 (24.7%) Grade 3A, 61 (5.9%) Grade 3B, and 85 (8.2%) Grade 4 adenomas. Grade 3–4 adenomas were more frequent in the first group (70.8% vs. 31.4% vs. 37.3%, $P < 0.001$). Optic chiasm compression was present in 64.9% ($n = 674$) of the cases and more prevalent in the first group (86.2% vs. 63.5%, $P < 0.001$). The mean preoperative volume was 6.04 ± 10.49 $cm^3$. Smaller lesions (<3 $cm^3$) were more prevalent in the second and third phases (38.8% vs. 54.8% vs. 54.4%, $P = 0.032$) [Table 1].

### Operative characteristics and outcomes

The data on operative duration were available for 785 consecutive cases and were not available for the first 240 cases. Operative duration is defined as the time elapsed from the initial incision to completion of reconstruction. The mean operative duration was 274.61 ± 77.83 min, and there was no correlation between operative duration and the number of cases ($r = -0.05$, $P = 0.16$) [Figure 1]. Knosp grade 3–4 adenomas were associated with a longer operative time ($P < 0.0001$), with a mean duration of 283.87 min, compared to 261.27 min for Grade 0–2 adenomas. A positive correlation was found between preoperative volume and operative time ($r = 0.33$, $P < 0.0001$). Usage of lumbar drain was 29.2% ($n = 19$) in the first group and significantly reduced to 1.1% ($n = 11$) in the latter group ($P < 0.001$). The overall rate of GTR was 75.6% (62.3% in Phase 1, 76.3% in Phase 2, 77.7% in Phase 3, $P = 0.003$). The rate of GTR in nonfunctional adenomas significantly increased to 76.7% in Phase 3 from 62% in Phase 1 ($P = 0.003$). While a similar trend was observed in the rates of GTR for functional adenomas, this increase did not reach statistical significance (62.3% vs. 79.4% vs. 78.8%, $P = 0.152$). As shown in Table 2, the use of Alloderm along with other substitutes, such as amniotic membrane or Cygnus, was the primary choice for closure in the first group of cases. In contrast, no substitute was used for closure in 52% of the cases in the second group and 43.6% of the cases in the third group ($P < 0.001$). The septal flap was used in 9.4% of the cases in the first group, 8.6% of the cases in the second group, and 8.8% of the cases in the third group for closure.

The mean length of hospitalization was 4.06 ± 3.47 days and significantly shorter in the second group (5.3 days vs. 3.8 days vs. 3.9 days, $P < 0.001$). The intraoperative CSF leak rate was significantly higher in the first group compared to the rest of the cases (65.1% vs. 47.1% vs. 55%, $P = 0.003$). The mean preoperative volume was significantly greater in the patients with intraoperative CSF leak (6.75 $cm^3$ vs. 5.2 $cm^3$, $P < 0.001$) [Figure 2a]. Similarly, intraoperative CSF leak was more common in Knosp grade 3–4 adenomas (61.7%) [Figure 2b]. Univariable logistic regression analyses revealed a significant association between intraoperative CSF leak and preoperative

**Table 1:** Cohort overview and tumor characteristics.

| Variable | Phase I (2012–2015) | Phase II (2016–2019) | Phase III (2020–2023) | *P*-value |
|---|---|---|---|---|
| Patient demographics | | | | |
| Number of cases | 106 | 350 | 582 | |
| Age, years | 54.3±15.5 | 53.4±16.5 | 54.6±16.3 | 0.533 |
| Gender, female | 52 (49.1) | 189 (54) | 314 (54) | 0.63 |
| Median preop. KPS | 90 (70–100) | 90 (70–100) | 90 (70–100) | 0.06 |
| Preop. endocrine status | | | | |
| Normal function | 54 (50.9) | 197 (56.3) | 272 (46.7) | 0.018 |
| Dysfunction | 52 (49.1) | 153 (43.7) | 310 (53.3) | |
| Preop. visual deficits | 71 (67) | 175 (50) | 276 (47.4) | 0.001 |
| Apoplexy | 5 (4.7) | 24 (6.9) | 38 (6.5) | 0.73 |
| History of radiotherapy | 0 (0) | 6 (1.7) | 9 (1.5) | 0.412 |
| Is it revision surgery? | 4 (3.8) | 27 (7.7) | 47 (8.1) | 0.298 |
| Adenoma characteristics | | | | |
| Location | | | | |
| Sellar | 96 (90.6) | 334 (95.4) | 473 (81.3) | <0.001 |
| Suprasellar | 3 (2.8) | 11 (3.1) | 42 (7.2) | |
| Sellar+suprasellar | 6 (5.7) | 1 (0.3) | 65 (11.2) | |
| Parasellar | 1 (0.9) | 4 (1.1) | 1 (0.2) | |
| Sellar+infrasellar | 0 (0) | 0 (0) | 1 (0.2) | |
| Knosp grade | | | | <0.001 |
| Grade 0–2 | 31 (29.2) | 240 (68.6) | 365 (62.7) | |
| Grade 0 | 6 (5.7) | 135 (38.6) | 76 (13.1) | |
| Grade 1 | 8 (7.5) | 63 (18) | 176 (30.2) | |
| Grade 2 | 17 (16) | 42 (12) | 113 (19.4) | |
| Grade 3–4 | 75 (70.8) | 110 (31.4) | 217 (37.3) | |
| Grade 3A | 55 (51.9) | 62 (17.7) | 139 (23.9) | |
| Grade 3B | 9 (8.5) | 9 (2.6) | 43 (7.4) | |
| Grade 4 | 11 (10.4) | 39 (11.1) | 35 (6) | |
| Chiasm compression | 86 (81.1) | 234 (66.9) | 354 (60.8) | <0.001 |
| Macroadenoma | 97 (91.5) | 317 (90.6) | 500 (85.9) | 0.054 |
| Adenoma function | | | | |
| Nonfunctional | 79 (74.5) | 250 (71.4) | 322 (55.3) | <0.001 |
| Functional | 27 (25.5) | 100 (28.6) | 260 (44.7) | |
| ACTH | 11 (10.4) | 36 (10.3) | 73 (12.5) | |
| GH | 3 (2.8) | 24 (6.9) | 46 (7.9) | |
| Prolactin | 7 (6.6) | 25 (7.1) | 82 (14.1) | |
| FSH/LH | 0 (0) | 4 (1.1) | 44 (7.6) | |
| Mixed | 6 (5.6) | 11 (3.1) | 15 (2.5) | |
| Preop. volume ($cm^3$) | 6.9±8.4 (0.1–50) | 5.8±9.3 (0.1–137.7) | 6.02±11.5 (0.1–137.7) | 0.687 |
| Small (<3 $cm^3$) | 40 (38.8) | 190 (54.8) | 313 (54.4) | 0.032 |
| Medium (3–8 $cm^3$) | 32 (31.1) | 88 (25.4) | 152 (26.4) | |
| Large (>8 $cm^3$) | 31 (30.1) | 69 (19.9) | 110 (19.1) | |

KPS: Karnofsky performance scale, ACTH: Adrenocorticotropic hormone, GH: Growth hormone, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone

volume (OR: 1.013 [1–1.02], *P* = 0.048), Knosp grade 3-4 (OR: 1.59 [1.24–2.05], *P* < 0.001), chiasm compression (OR: 2.25 [1.73–2.91], *P* < 0.001), and macroadenomas (OR: 2.81 [1.88–4.2], *P* < 0.001). Knosp grade, chiasm compression, and macroadenomas were the only factors found to be associated with intraoperative CSF leak in multivariable regression analysis [Table 3].

Epistaxis (7.3%), transient postoperative visual deficits (4.9%), and CSF leak (4.04%) were the three most common postoperative complications. There were no statistically significant differences in rates of complications between the groups, except for the rate of meningitis, which significantly reduced to 0.3% in the third phase from 3.8% in the first phase (*P* < 0.001). Complications are summarized in Table 2.

The rate of postoperative permanent deficits, such as visual disturbances or cranial nerve deficits, was 5.7%, 7.4%, and 9.5 in the first, second, and third groups, respectively ($P = 0.316$). Among the patients, 67.7% had normal endocrine function postoperatively, with 72.6% in the first group, 60.9% in the second group, and 71% in the third group ($P = 0.003$). Among the patients who had functional adenomas, the percentage of patients with normal endocrine function in the postoperative period was 63% in the first group, 58.8% in the second group, and 63.2% in the third group ($P = 0.737$). The need for revision surgery was significantly lower in Phase 3 (8.5% vs. 5.4% vs. 2.1%, $P < 0.001$). There was a significant association between the risk of the need for revision surgery and case volume (r = −0.131, OR: 0.997 [95% CI: 0.996–0.999], $P < 0.001$) [Figure 3].

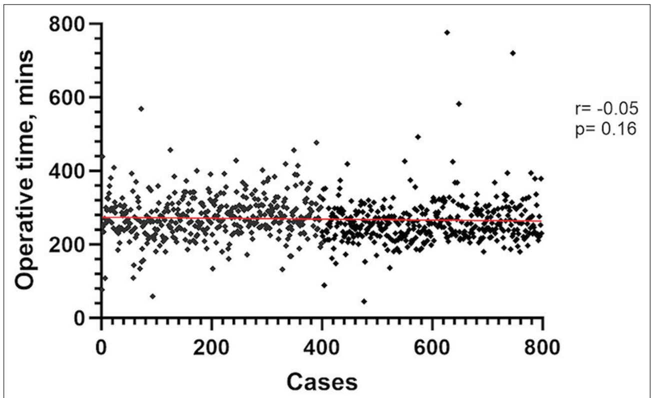


**Figure 1:** Relationship between operation duration and number of cases.

## DISCUSSION

The steep initial learning curve in endoscopic transsphenoidal surgery cases has been reported in the literature.[3,14,21,23,29] Our retrospective study involving 1038 patients sheds light on the learning curve and outcomes associated with endoscopic transsphenoidal surgery for pituitary adenomas and highlights the importance of neurosurgery and ENT collaboration for enhanced patient outcomes. The analysis of these cases demonstrates a higher rate of GTR and reduction in the rates of CSF leaks and the need for revision surgery in the latter group of cases.

**Table 2:** Operative characteristics and treatment outcomes.

| Variable | Phase I (2012–2015) | Phase II (2016–2019) | Phase III (2020–2023) | *P*-value |
|---|---|---|---|---|
| Operative characteristics | | | | |
| Lumbar drain | 19 (17.9) | 4 (1.1) | 7 (1.2) | <0.001 |
| Postoperative volume (cm$^3$) | 0.73±2.4 (0–16.3) | 0.48±2.5 (0–31.2) | 0.47±1.9 (0–23.04) | 0.527 |
| GTR* | | | | |
| Overall | 66 (62.3) | 267 (76.3) | 452 (77.7) | 0.003 |
| Functional adenomas | 17 (63) | 81 (79.4) | 212 (78.8) | 0.152 |
| Nonfunctional adenomas | 49 (62) | 186 (75) | 240 (76.7) | 0.027 |
| Intraoperative CSF leak | 69 (65.1) | 165 (47.1) | 320 (55) | 0.003 |
| Closure technique | | | | |
| Alloderm only | 1 (0.9) | 51 (14.6) | 143 (24.6) | <0.001 |
| Alloderm+other substitutes** | 57 (53.8) | 87 (24.9) | 110 (23) | |
| Septal flap±other substitutes*** | 10 (9.4) | 30 (8.6) | 51 (8.8) | |
| None | 38 (35.8) | 182 (52) | 254 (43.6) | |
| Complications and outcomes | | | | |
| Length of stay, days (median, range) | 4 (2–54) | 3 (1–49) | 3 (0–41) | <0.001 |
| Postoperative CSF leak | 2 (1.9) | 13 (3.7) | 27 (4.6) | 0.387 |
| Vascular injury | 0 (0) | 2 (0.6) | 0 (0) | 0.14 |
| Septal perforation | 1 (0.9) | 7 (2) | 25 (4.3) | 0.717 |
| Meningitis | 4 (3.8) | 1 (0.3) | 2 (0.3) | <0.001 |
| Epistaxis | 9 (8.5) | 20 (5.7) | 47 (8.1) | 0.362 |
| Transient postop. visual deficit | 1 (0.9) | 15 (4.3) | 35 (6) | 0.068 |
| Permanent deficit | 6 (5.7) | 26 (7.4) | 55 (9.5) | 0.316 |
| Postop. endocrine status | | | | |
| Normal function | 77 (72.6) | 213 (60.9) | 413 (71) | 0.003 |
| Dysfunction | 29 (27.4) | 137 (39.1) | 169 (29) | |
| Readmission to neurosurgery | 4 (3.8) | 16 (5.7) | 23 (4) | 0.49 |
| Need for revision surgery | 9 (8.5) | 19 (5.4) | 12 (2.1) | <0.001 |

*Data on operative data were available for 785 consecutive cases. **Cygnus or amniotic membrane ***Alloderm, Cygnus, fat, or amniotic membrane. GTR: Gross total resection, CSF: Cerebrospinal fluid, DI: Diabetes insipidus

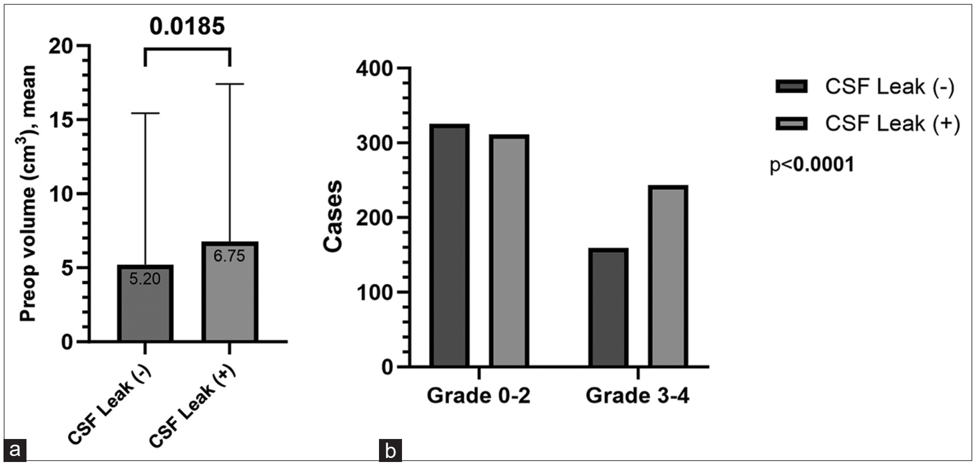


**Figure 2:** (a) Comparison of mean operative volumes for cases with and without intraoperative CSF leak. (b) Comparison of Knosp grade for cases with and without intraoperative CSF leak.

**Table 3:** Univariable and multivariable logistic regression analysis of factors affecting intraoperative CSF leak.

| Variable | Univariable | | Multivariable | |
|---|---|---|---|---|
| | OR (95% CI) | *P*-value | OR (95% CI) | *P*-value |
| Case volume | 0.99 (0.99–1) | 0.871 | 1 (0.99–1) | 0.446 |
| Age | 1.008 (0.99–1) | 0.05 | 1 (0.99–1.01) | 0.7 |
| Gender, female | 0.908 (0.71–1.15) | 0.438 | 1.08 (0.83–1.4) | 0.549 |
| Preop volume | 1.013 (1–1.02) | 0.048 | 0.99 (0.98–1.01) | 0.725 |
| Knosp grade 3–4 | 1.59 (1.24–2.05) | <0.001 | 1.33 (1–1.76) | 0.043 |
| Chiasm compression | 2.25 (1.73–2.91) | <0.001 | 1.86 (1.38–2.52) | <0.001 |
| Macroadenoma | 2.81 (1.88–4.2) | <0.001 | 1.81 (1.14–2.89) | 0.012 |
| History of radiotherapy | 0.57 (0.2–1.63) | 0.301 | 0.72 (0.24–2.12) | 0.558 |
| Revision surgery | 0.86 (0.54–1.37) | 0.535 | 0.86 (0.53–1.39) | 0.556 |

CSF: Cerebrospinal fluid, OR: Odds ratio, CI: Confidence interval

The traditional learning curve exhibits an S-shaped progression comprising three distinct stages. The initial phase encompasses a gradual acquisition of new skills, followed by a phase characterized by rapid proficiency enhancement. The final stage marks a plateau, signifying the attainment of mastery.[29] The essential variables in examining the surgical learning curve usually involve operative length and rates of complications.[8,29] In our study, the mean operative duration was 274.61 ± 77.83 min, and there was no correlation between operative duration and the number of cases ($r = -0.05$, $P = 0.16$). As several studies noted previously, the evaluation based on operation length has been subject to scrutiny due to its inherent limitations and may not always reflect the classic S-shaped learning curve adequately; it may plateau with increased experience.[24,29] As surgeons attain proficiency, they often undertake more intricate cases and allocate additional time to teaching, leading to a potential increase in operative duration toward the later stages of the learning curve.

The significant improvement in the rate of GTR, particularly for nonfunctional adenomas, from 62% in the first group to 76.7% in the third group ($P = 0.027$), underscores the significant advancement in surgical skills and experience. Nonfunctional adenomas tend to be larger and more invasive due to their slower growth and later presentation. The primary surgical goal for nonfunctional adenomas is to resect as much of the tumor as possible while minimizing harm to surrounding structures, especially given their proximity to critical areas such as the optic chiasm and cavernous sinus. The significant improvement in GTR rates for nonfunctional adenomas reflects enhanced surgical techniques, better preoperative planning, and refined intraoperative strategies over time.

The rate of intraoperative CSF leaks was notably higher in Phase 1 (65.1% vs 47.1% vs 55%, $P = 0.003$), which aligns with the learning curve associated with mastering endoscopic techniques and reflects the refinement of our skills in preserving the integrity of the diaphragma sella while ensuring GTR. Several studies noted a similar reduction in CSF leaks with increased case volume.[3,14,16,29] Our analysis revealed significant associations between intraoperative

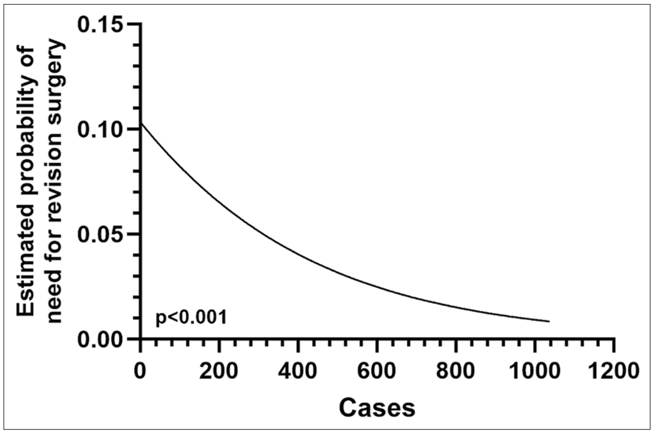


**Figure 3:** Change of estimated risk of the need for revision surgery with increased number of cases.

CSF leaks and factors such as preoperative tumor volume, Knosp grade 3–4, optic chiasm compression, and the presence of macroadenomas. These findings underscore the complexity of managing larger and more invasive tumors and highlight the importance of surgical experience in reducing intraoperative complications.

Intraoperative CSF leak was more common in Knosp grade 3–4 adenomas (61.7%) because these adenomas often invade the cavernous sinus and have a higher likelihood of involving the diaphragma sellae. Although parasellar invasion typically does not involve the diaphragma sellae directly, the adenoma's lateral extension and displacement of surrounding structures increase the risk of dural tears, especially during resection. In such cases, inadvertent rupture or thinning of the diaphragm or adjacent sellar dura can lead to a CSF leak. In addition, in high-grade adenomas, the tumor's proximity to the suprasellar cisterns increases this risk. To address adenoma invasion into the cavernous sinus, we utilized a transsellar approach, following the tumor from the sella into the cavernous sinus. This technique allows gradual tumor debulking and minimizes trauma to surrounding neurovascular structures. We did not rely solely on diaphragmatic rupture; instead, we improved exposure by lateralizing the pituitary gland and selectively resecting the medial wall of the cavernous sinus where needed.[20,26]

While overall complication rates remained comparable between the two groups, the incidence of meningitis significantly decreased from 3.8% in the first group to 0.3% in the remaining cohort ($P < 0.001$). This reduction likely reflects improvements in surgical technique, aseptic protocols, and perioperative management. The need for revision surgeries was also significantly lower in the latter cohort (8.5% vs. 5.4% vs. 2.1%, $P < 0.001$), suggesting enhanced initial surgical efficacy and better long-term outcomes. Moreover, a significant reduction in the length of hospitalization was observed, decreasing from an average of 5.3 days in the first group to 3.9 days in the third group ($P < 0.001$). This reduction can be attributed to more efficient surgical procedures, enhanced postoperative care, and the benefits of a minimally invasive approach.

The postoperative endocrine function was another measure of success. Although a higher percentage of patients in the first phase retained normal endocrine function postoperatively (72.6% vs 60.9% vs. 71%, $P = 0.003$), this discrepancy might be influenced by the selection of less complex cases during the initial phase of the learning curve. Notably, functional adenomas were more frequent in the third group (25.5% vs 28.6% vs 44.7%, $P < 0.001$), and the surgical resection of these hormone-secreting adenomas is often a more complex procedure associated with higher complication rates and a strict necessity for GTR.[2] For patients with functional adenomas, the rates of postoperative normalization of endocrine function did not significantly differ between the groups (63% vs. 58.8% vs. 63.2, $P = 0.737$), indicating consistent endocrine management throughout the study period.

A critical aspect contributing to the success of these surgeries and the mitigation of complications, especially intraoperative and postoperative CSF leaks, is the consistent involvement of the same surgical team, comprised of the same neurosurgeon and otolaryngologist, throughout all 1038 cases. This collaboration facilitates a seamless working relationship, allowing for refined coordination and shared expertise, ultimately contributing to the positive outcomes observed in our study. Likewise, Lofrese *et al*. emphasized the significance of collaboration with otolaryngologists in endoscopic pituitary surgery.[18] This collaboration is valued for their expertise in skillfully maneuvering the endoscope through safer nasal recesses, providing an expanded view facilitated by their precise knowledge of nasal corridors and anatomy.[18] Furthermore, they highlighted that the reduction in operative duration within their cohort, where 89% of cases involved macroadenomas with suprasellar and parasellar involvement, was attributed to their collaboration with otolaryngologists. Further studies that compare outcomes between a single neurosurgeon and multiple neurosurgeons, as well as neurosurgeons collaborating with and without otolaryngologists in endoscopic pituitary surgeries, will corroborate our findings.

## Limitations

A significant limitation of our study is its retrospective design, inherently carrying the risk of selection bias and the inability to control or standardize data collection methods. The observed decrease in the operative duration between the two halves may have limited clinical relevance. In addition, the surgeries were conducted at a single center, potentially limiting the generalizability of the findings to other institutions. Moreover, the process of assimilating a new surgical technique, akin to any cognitive endeavor, is shaped by a multitude of influences. The expertise of the surgeon, accumulated experience, team dynamics, and the impact of emerging tools and technological advancements collectively contribute to the outcome. Whether this trajectory will persist or reach a stabilization phase remains uncertain, awaiting further observation over time. Notably, existing literature implies that the surgical learning curve might extend beyond a decade of ongoing refinement.[29]

## CONCLUSION

In summary, our extensive experience with endoscopic endonasal transsphenoidal surgery for pituitary adenomas demonstrates a clear learning curve, with significant improvements in surgical outcomes, reduction in complications, and enhanced postoperative management over time. This study underscores the importance of experience, technical refinement, and a multidisciplinary approach in optimizing the outcomes for patients undergoing this complex surgical procedure.

### Ethical approval

The research/study was approved by the Institutional Review Board at the University of Miami, number 20160437, dated 2022.

### Declaration of patient consent

Patient's consent is not required as there are no patients in this study.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

### Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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