



# TUMOR RESECTION RATE AND POSTOPERATIVE COMPLICATIONS OF TRANSSPHEOIDAL SURGERY FOR PITUITARY ADENOMAS

Rojas, Héctor Pablo;<sup>1</sup> José, Pablo Horacio;<sup>1</sup> Miralles, Sabrina;<sup>1</sup> Barrenechea, Ignacio;<sup>1</sup> Schwarzstein, Diego;<sup>2</sup> Feldman, Rodolfo Néstor;<sup>1</sup> Moloeznik, Laura;<sup>1</sup> Ramírez Stieben, Luis Agustín<sup>1</sup>

1. Pituitary and Skull Base Surgery Department of Grupo Gamma (Rosario, Argentina).  
2. Clínica ServiDigest (Barcelona, España).

## ARTICLE INFO

### Keywords:

Pituitary adenomas, endoscopic transsphenoidal surgery, cerebrospinal fluid leak.

## ABSTRACT

Pituitary adenomas (PA) are benign tumors arising from anterior pituitary cells and account for 8-15% of intracranial tumors. Surgery remains the primary treatment for most PA, particularly for non-functioning pituitary adenomas (NFPA). The aim of this study was to describe the outcomes of a consecutive series of patients undergoing pure endoscopic transsphenoidal surgery (ETSS) and to assess the efficacy and safety of this procedure. Materials and methods: We conducted a retrospective review of medical records from 2010 to 2022. Clinical, biochemical, and radiological data were collected preoperatively. The extent of tumor resection was classified as gross total resection (GTR), subtotal resection (STR), and partial resection (PR). Histopathological findings and perioperative complications were also recorded. Results: A total of 59 patients underwent ETSS for PA. NFPA represented most cases (57.1%), while growth hormone (GH)-secreting adenomas were the most common functioning subtype. GTR was achieved in 47 patients (79.7%) and PR in 9 (15.3%). Only 44.4% of giant adenomas ( $\geq 40$  mm) were completely resected. Postoperative cerebrospinal fluid leak occurred in 3 patients (5.1%), and permanent diabetes insipidus in 2 patients (3.4%). No perioperative deaths were observed. Discussion: Endoscopic transsphenoidal surgery is a safe and effective treatment for PA, achieving satisfactory resection rates, favorable clinical outcomes, and low complication rates in this consecutive series.

**Received:** August 12, 2025

**Accepted:** September 30, 2025

**Autor de correspondencia:** Héctor Pablo Rojas. [hrojas@grupogamma.com](mailto:hrojas@grupogamma.com)

**Doi:** Copyright © 2025 FASEN - CC-BY-NC 4.0

## TASA DE RESECCIÓN TUMORAL Y COMPLICACIONES POSOPERATORIAS DE LA CIRUGÍA TRANSENFENOIDAL EN ADENOMAS HIPOFISARIOS

### INFO DEL ARTÍCULO

**Palabras clave:** Adenomas hipofisarios, cirugía transesfenoidal endoscópica, fístula de líquido cefalorraquídeo

### RESUMEN

Los adenomas hipofisarios (AH) son tumores benignos originados en las células de la hipófisis anterior y representan entre el 8 y el 15% de los tumores intracraneales. La cirugía continúa siendo el tratamiento de elección para la mayoría de los AH, en particular para los adenomas hipofisarios no funcionantes (AHNF). El objetivo de este estudio fue describir los resultados de una serie consecutiva de pacientes sometidos a cirugía transesfenoidal endoscópica pura (CTE) y evaluar la eficacia y seguridad de este procedimiento. **Materiales y métodos:** Se realizó una revisión retrospectiva de historias clínicas entre 2010 y 2022. Se recolectaron datos clínicos, bioquímicos y radiológicos preoperatorios. La extensión de la resección tumoral se clasificó como resección total macroscópica (RTM), resección subtotal (RST) y resección parcial (RP). También se registraron los hallazgos histopatológicos y las complicaciones perioperatorias. **Resultados:** Un total de 59 pacientes fueron sometidos a CTE por AH. Los AHNF representaron la mayoría de los casos (57,1%), mientras que los adenomas secretores de hormona de crecimiento (GH) fueron el subtipo funcionante más frecuente. Se logró RTM en 47 pacientes (79,7%) y RP en 9 (15,3%). Solo el 44,4% de los adenomas gigantes ( $\geq 40$  mm) fueron completamente resecados. Se observaron fístulas de líquido cefalorraquídeo posoperatorias en 3 pacientes (5,1%) y diabetes insípida permanente en 2 pacientes (3,4%). No se registraron muertes perioperatorias. **Discusión:** La cirugía transesfenoidal endoscópica constituye un tratamiento seguro y eficaz para los adenomas hipofisarios, con tasas satisfactorias de resección, resultados clínicos favorables y baja frecuencia de complicaciones en esta serie consecutiva.

**Recibido:** 12 de agosto 2025

**Aceptado:** 30 de septiembre 2025

### INTRODUCTION

Pituitary adenomas (PA) are benign tumors that originate from cells of the anterior pituitary and account for approximately 8-15% of intracranial tumors [1]. While most PA are histologically benign, a subset of tumors (34-60%) are invasive [2,3]. They are classified as non-functioning PA (NFPA) or clinically functional PA (FPA), such as prolactin-secreting tumors (PRL), adrenocorticotropin hormone (ACTH)-secreting tumors, growth hormone (GH)-producing tumors or thyrotropin (TSH)-producing tumors [4]. PA can exert pressure on adjacent structures, leading to impaired field of vision, hypopituitarism, and ophthalmoplegia [5].

Surgery remains the main treatment for NFPA and some FPA; however, complete tumor resection is often challenging, which can result in tumor regrowth or recurrence. Transsphenoidal surgical approach of PA has the advantages of endoscopic surgery, including improved illumination and visualization of the lesions. The integration of neurophysiological monitoring, neuronavigation, Doppler ultrasound, high-speed drill, and other technologies and equipment has significantly enhanced surgical quality and patient prognosis in endoscopic skull base surgery. However, as the application of endoscopic

transsphenoidal surgery expands, certain limitations have become evident, such as the two-dimensional visual field, the long and narrow corridor, difficulties in hemostasis, cerebrospinal fluid leaks (CSF), and potential damage to nasal structures [6-8].

Although most of the published series on endoscopic transsphenoidal surgery (ETSS) come from large international reference centers, reports from Latin American institutions remain scarce. The variability in health systems, access to technology, and availability of experienced multidisciplinary teams makes it essential to document local experiences. Reporting the outcomes of an Argentine tertiary center provides valuable information not only to compare with international benchmarks but also to highlight the feasibility, safety, and effectiveness of this surgical approach in our regional context. This contribution can help strengthen local expertise, guide training programs, and promote collaborative networks in pituitary and skull base surgery within Latin America.

In the present study, we aimed to summarize our 12 years of experience in ETSS and analyze clinical, biochemical, and radiological characteristics, short-term structural response, and the incidence of early postoperative complications.

## MATERIALS AND METHODS

### *Study design*

We conducted a retrospective analysis of fifty-nine patients with a confirmed diagnosis of PA who underwent ETSS at our institution between January 2010 and January 2022. Exclusion criteria were patients with other sellar or parasellar lesions (e.g., craniopharyngiomas, Rathke's cleft cysts, meningiomas), incomplete clinical or radiological data, and those who did not have a minimum follow-up of three months with postoperative magnetic resonance imaging (MRI). These criteria ensured a homogeneous cohort, allowing us to specifically evaluate surgical and postoperative outcomes in PA.

### *Preoperative evaluation*

Preoperative data included age, sex, presenting symptoms, visual status, and the use of cabergoline or somatostatin analogues (SSA). All patients underwent a comprehensive preoperative evaluation, including radiological, endocrinological, and neuro-ophthalmological assessments. MRI with gadolinium contrast was performed to evaluate the tumor, using a 3.0 Tesla spin echo-weighted MRI on T1 and T2 sequences. The size of the PA was categorized as microadenoma ( $\leq 10$  mm), macroadenoma (10-40 mm), or giant adenoma ( $\geq 40$  mm). The degree of tumor invasion was assessed based on the Knosp classification, and the presence of suprasellar extension was determined. Neuro-ophthalmological evaluations included formal visual field tests and assessment of visual acuity. The endocrinological diagnosis was based on hormonal levels, clinical symptoms, and histopathological findings.

### *Surgical procedure*

All procedures were performed by the same surgical team (1 neurosurgeon and 1 otolaryngologist), using the same surgical technique. The patients were positioned in supine position with reverse Trendelenburg. Using the Mayfield clamp, the head was fixed with 15° extension and slight rotation to the right. After aseptic preparation with 5% povidone-iodine, the nasal cavity was decongested using topical oxymetazoline (50 mg/100 mL). The surgical approach was initiated through the right nasal cavity using a 0° endoscope. The "two surgeons - 4 hands - 2 nostrils" technique was employed in most cases. At the beginning of our series, we proceeded with the resection of a middle turbinate; however, in the last 8 years we have only displaced them laterally through dislocation, with the aim of avoiding smell disorders and minimizing the impact of surgery on nasal physiology. The nasoseptal flap was raised selectively when subarachnoid dissection was planned, while preserving the pedicles on both sides ("rescue flap"). An extended sphenoidotomy was performed to access the sphenoid sinus,

which served as the common point of entry for most procedures. Mucosal preservation of the sphenoid sinus was attempted. The transellar craniotomy was performed in all patients, with possible extension superiorly (transtuberculum, transplanum) or laterally (transcavernous, transpterygoid) in specific cases. The dura was meticulously opened layer by layer. En bloc peripseudocapsular dissection along a 360° path between the pseudocapsule of the adenoma and the normal pituitary was attempted whenever possible. Tumor decompression and subsequent peripseudocapsular dissection were performed in larger PA.

#### *Reconstruction of the base of the skull*

Three different techniques for skull base reconstruction were employed based on the presence and characteristics of intraoperative CSF leak: (1) in cases where the dura or arachnoid mater remained intact without any CSF leak during surgery, oxidized cellulose, non-suturable collagen matrix, dural sealant, and absorbable hemostatic gelatin sponge were used; (2) for arachnoid defects  $\leq 1$  cm with a low-output fistula, a sequential approach was followed. It involved the use of oxidized cellulose, non-suturable collagen matrix as an inlay inside the dura mater, and another layer of superimposed material known as overlay; (3) if the arachnoid defect was  $> 1$  cm or if a high-output CSF leak was found during surgery, the nasoseptal pedicled flap was added to the above.

#### *Postoperative evaluation*

All patients underwent the immediate postoperative period (first 24 hours) in the intensive care unit (ICU). A cranial computed tomography (CT) scan was routinely conducted within the first day after surgery. The extent of tumor resection was determined based on both contrast-enhanced MRI findings obtained three months after the surgery and the surgeon's intraoperative assessment. Gross total resection (GTR) was considered when surgical observation, along with postoperative imaging, confirmed the absence of any visible

tumor. Subtotal resection (STR) was defined as removing more than 90% of the tumor but not achieving complete removal. Partial resection (PR) was defined as excising less than 90% of the lesion.

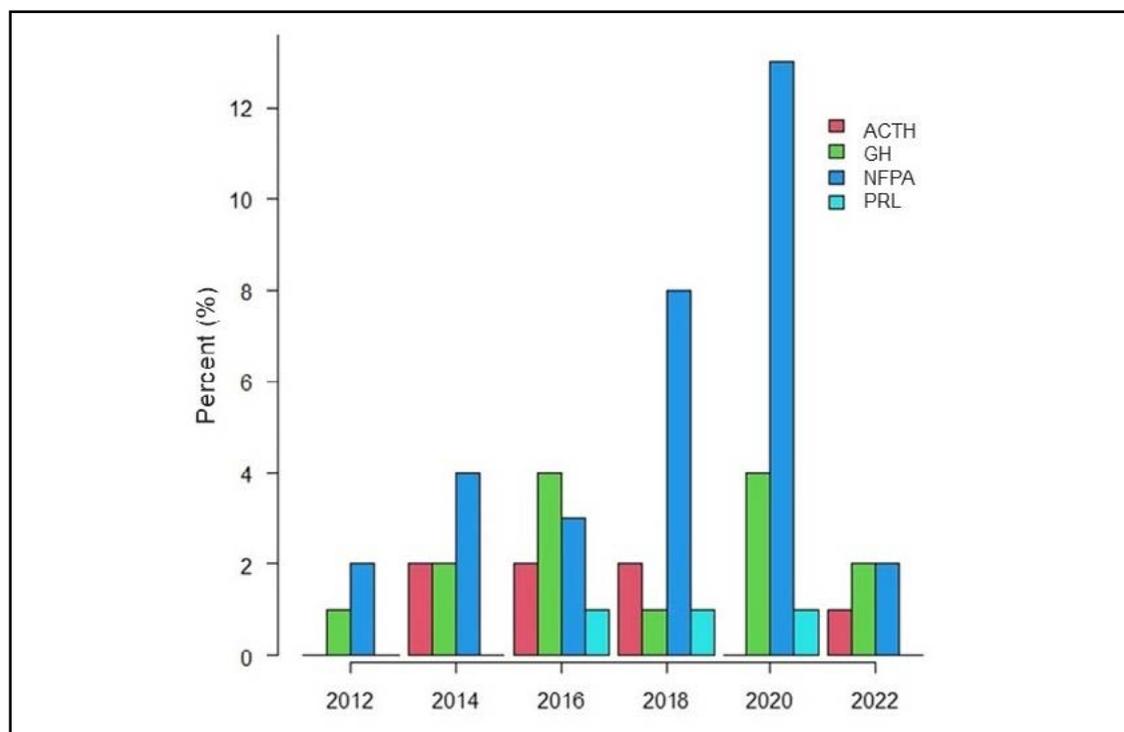
#### *Statistical analysis*

The R program version 4.1.0 was used. Continuous variables were first tested for normality using the Shapiro–Wilk test and for homogeneity of variance with Bartlett's test. Parametric data were analyzed using Student's t-test (two groups) or ANOVA (more than two groups). For non-parametric data, the Mann–Whitney U test (two groups) or Kruskal–Wallis test with Bonferroni post-hoc correction (more than two groups) were applied. Categorical variables were compared using chi-square or Fisher's exact test, as appropriate. Results are expressed as mean  $\pm$  standard deviation (SD) or median with interquartile range (IQR). A p-value  $< 0.05$  was considered statistically significant.

## **RESULTS**

From January 2010 to January 2022, a total of 59 patients underwent surgical treatment for PA at our center. Among these surgeries, 32 (54.2%) have been performed since 2018. Among the patients, 35 (59.3%) were women. The mean age of the study population was  $45.68 \pm 15.38$  years. Most of the PA were NFPA, accounting for 34 cases (57.6%), while FPA represented 25 cases (42.4%). Eight patients (13.6%) had undergone previous pituitary surgery. Figure 1 shows the relative frequency of surgeries based on their date of performance.

The most common preoperative symptom reported was altered visual acuity and/or visual field, observed in 16 cases (27.1%). Headache was another frequent symptom, reported by 9 cases (15.2%). Patients with visual disturbances were found to have larger PA [31 mm (25–37.5) vs. 17.5 mm (10–24.5),  $p=0.0003$ ], a higher percentage of giant adenomas (26.7% vs. 4.8%; Fisher's test,  $p=0.0001$ ), and a higher prevalence of suprasellar extension (84.6% vs. 44.4%;



**Figure 1.** Distribution of surgeries according to type of adenoma and date of completion  
*Abbreviations:* ACTH: adrenocorticotropin hormone-secreting tumors, GH: growth hormone-producing tumors, NFPA: non-functioning pituitary adenomas, PRL: prolactin-secreting tumors

Fisher’s test,  $p=0.002$ ). Among patients with NFPA, 42.4% had visual field defects, while only one patient with FPA experienced visual disturbances (chi-square test,  $p=0.0007$ ). Additionally, there were 2 cases of pituitary apoplexy and 2 cases of panhypopituitarism.

The most frequent FPA were GH-secreting (14 adenomas, 56%), followed by ACTH-secreting (8 adenomas, 32%). Among all patients who underwent surgery, 16 individuals received pre-surgical treatment with cabergoline, with no differences depending on whether they were NFPA or FPA (24.24% vs. and 34.78%, chi-square test,  $p=0.52$ ). In the subgroup of patients with acromegaly, 8 (57.14%) received preoperative treatment with SSA. Ki-67 was higher in patients with giant adenomas ( $5\pm 2.58\%$  vs.  $2\pm 2.99\%$ ), although the difference was not significant ( $p=0.09$ ).

A total of 81.3% of the tumors were macroadenomas, with a mean size of 20 mm (range: 12-28), and 10.3% were giant

adenomas. Among the cases, 31.9% were classified as Knosp grade 2, 17.0% as Knosp grade 3, and 8.5% as Knosp grade 4. Suprasellar extension was observed in 28 cases (54.9%). Table 1 provides a summary of the radiological characteristics based on the hormonal status of the adenomas.

PA with suprasellar extension were found to be larger tumors [23 mm (18-31.5) vs. 11.5 mm (6.25-16);  $p=0.0002$ ], as well as PA with a Knosp grade  $\geq 3$  [ $\geq 3$ : 29.5 mm (25.75-34.25) vs.  $\leq 2$ : 17 mm (10-22.5);  $p=0.0002$ ].

The average hospital stay was 5 days (4-6.25). GTR was achieved in 47 patients (79.7%), STR in 6 (10.2%), and PR in 5 patients (8.5%). In one patient with Cushing’s disease, resection could not be performed as the PA was not found. Patients with previous pituitary surgeries had a lower frequency of GTR (50% with prior surgery vs. 84.3% without prior surgery; Fisher’s test,  $p=0.07$ ). There were no significant differences in the surgical outcomes based on whether the

**Table 1.** Radiological characteristics according to hormonal status

	<b>GH-secreting (n=14)</b>	<b>Prolactinoma (n=3)</b>	<b>ACTH- secreting (n=8)</b>	<b>NFPA (n=34)</b>	<b>p-value</b>
<b>Size, mm, median [IQR]</b>	11.5 (8.25-15.75)	21 (17-23)	6.5 (5.25-7)	25 (18.5-31)	<0.001*
<b>Microadenoma, n (%)</b>	4 (28.6)	0 (0)	7 (87.5)	0 (0)	
<b>Macroadenoma, n (%)</b>	9 (64.3)	3 (100)	1 (12.5)	29 (85.3)	0.0001**
<b>Giant adenoma (%)</b>	1 (7.1)	0 (0)	0 (0)	5 (14.7)	
<b>Knosp <math>\geq</math>3, n (%)</b>	1 (7.14)	1 (33.33)	0 (0)	10 (38.5)	0.10**
<b>Suprasellar extension, n (%)</b>	2 (18.2)	1 (33.33)	2 (25)	23 (79.3)	0.001**
<b>Visual fields defects, n (%)</b>	1 (7.14)	0 (0)	0 (0)	14 (42.4)	0.01**

*Abbreviations:* GH, growth hormone; ACTH, adrenocorticotropin; NFPA, non-functioning pituitary adenoma. Values are expressed as median [IQR] or n (%). P-values from Kruskal-Wallis test (continuous variables) or Fisher's exact test (categorical variables). Global Fisher's exact test for tumor size across groups:  $p < 0.001$ . Post-hoc Bonferroni:  $p = 0.01$  NFPA vs ACTH;  $p = 0.02$  NFPA vs GH.

PA were functioning or non-functioning. Among macroadenomas, 83.3% were completely resected, while only 33.3% of giant adenomas were completely resected (Table 2).

Patients who achieved GTR had smaller tumor sizes compared to those who did not achieve GTR [20 mm (12-26) vs. 32.5 mm (28.7-47.5),  $p = 0.005$ ]. There were no significant differences in surgical outcomes

based on the hormonal status of the PA. Ki-67 expression was lower in patients who achieved GTR (GTR  $3.0 \pm 2.8$  vs non-GTR  $5.6 \pm 2.9\%$ ). The surgical outcomes were not affected by previous treatment with cabergoline or by prior treatment with somatostatin analogs (SSA) in patients with acromegaly. Table 3 provides a summary of the surgical results based on the radiological characteristics.

**Table 2.** Surgical results according to tumor size

	<b>GTR (n=47)</b>	<b>STR (n=6)</b>	<b>PR (n=5)</b>
Microadenoma (<10 mm, n=10)	10 (100)	0 (0)	0 (0)
Macroadenoma (10–30 mm, n=42)	35 (83.3)	4 (9.5)	3 (7.1)
Giant adenoma ( $\geq$ 40 mm, n=6)	2 (33.3)	2 (33.3)	2 (33.3)

*Abbreviations:* GTR, gross total resection; STR, subtotal resection; PR, partial resection. p-value from Fisher's exact test=0.04.

**Table 3.** Surgical results according to radiological characteristics

	GTR (n=47)	STR (n=6)	PR (n=5)	p
Size, mm, median [IQR]	18 (11-26)	34 (31-43)	31 (24.5-45.5)	0.02*
Suprasellar extension, n (%)	50%	100%	50%	0.07#
Knosp $\geq 3$ , n (%)	14.6%	75%	100%	<0.001**

*Abbreviations:* GTR, gross total resection; STR, subtotal resection; PR, partial resection. p-value from Kruskal–Wallis test (post-hoc Bonferroni: p=0.04 GTR vs. STR). #p-value from Fisher's exact test (post-hoc Bonferroni: p=0.09 GTR vs. STR). \*p-value from Fisher's exact test (post-hoc Bonferroni: p=0.004 GTR vs. PR; p=0.05 GTR vs. PR).

A total of 9 patients (15.8%) were confirmed to have an intraoperative CSF leak. Postoperative CSF leak occurred in 3 patients (5.1%), with 2 of them undergoing additional surgery for repair and 1 resolving with lumbar drainage. There were no significant differences in tumor size or frequency of suprasellar extension based on the presence of a postoperative CSF leak. Transient DI was observed in 8 patients (13.6%), while permanent DI was detected in 2 patients (3.4%). No cases of syndrome of inappropriate secretion of antidiuretic hormone (SIADH) were reported. One patient developed post-surgical panhypopituitarism, while another patient experienced post-neurosurgical meningitis, which resolved without complications following antimicrobial treatment. Unfortunately, there was one postoperative death in a patient with a giant adenoma who developed septic shock.

## DISCUSSION

The development and refinement of ETSS have greatly contributed to the treatment of PA. In 12 years of experience in ETSS, we performed a total of 59 pituitary surgeries using this technique. Notably, 54.2% of these surgeries were performed within the last four years. This can reflect the progress of the medical team involved, both in surgical and post-surgical management.

The growing popularity of ETSS can be attributed to several factors. The advantages of this type of approach include better visualization and, with it, better exposure and understanding

of the anatomy, a better working angle, a lower incidence of lesions in the nasal cavity, and a faster recovery [9,10]. However, ETSS has some limitations, such as a narrow channel into the sellar turcica, the need for special instrumentation, the difficulty of managing bleeding complications, and the need for experience of the surgical team. Although microsurgical vision has the advantage of three-dimensional vision [6-8], this situation can be overcome with knowledge of the anatomy of the sella turcica and the movements of the endoscope [10]. In this regard, in a previous study we demonstrated the rate of complications associated with the endonasal endoscopic approach of different skull base pathologies in a cohort of 120 patients [11].

In our series, the mean age of patients undergoing surgery for PA was 45.7 years, with a higher proportion of female patients (59.3%). NFPA were the most frequently operated tumors, accounting for 57.6% of cases, while GH-secreting adenomas were the most common subtype among FPA. Consistent with previous studies, NFPA were larger in size compared to FPA, with a median of 25 mm, and showed a higher prevalence of macroadenomas, giant adenomas, and suprasellar extension (79.3%) [12,13]. These tumor characteristics explain why patients with NFPA are more often presented with visual disturbances, reported in 42.4% of cases. Overall, visual disturbances were the most common manifestation (27.1%), followed by headache (15.2%). Patients with visual symptoms had larger tumors, a higher frequency of giant adenomas, and more frequent

suprasellar extension. These findings are in line with previous reports [14].

NFPA were the most frequently operated PA in our series (57.6%), while GH-secreting represented the most frequent subtype among FPA. As in previous series [13], NFPA were larger than FPA, with a median of 25 mm, with a higher frequency of macroadenomas, giant adenomas, and suprasellar extension (79.3%). This finding would explain why patients with NFPA had more frequent visual disturbances (42.4%).

In our series, most tumors were macroadenomas, accounting for 81.3% of cases. Among them, 10.3% were classified as giant adenomas. The median tumor size was 20 mm, which is consistent with the sizes reported by other research groups [15,16]. To assess cavernous sinus invasion, we used T1-weighted coronal MRI. The tumors were categorized into five Knosp grades, with 17.0% of cases classified as Knosp grade 3 and 8.5% as Knosp grade 4. Additionally, 54.9% of patients had PA with suprasellar extension.

Large PA are known to be invasive and can infiltrate surrounding structures such as the dura, sinuses, brain, and bone tissue [17]. Therefore, GTR is often technically challenging. In our series, GTR was achieved in 79.7%. Previous studies report a GTR resection between 10-89% [13,15,18-20]. As expected, the tumor size was smaller in those patients in whom GTR was achieved (20 mm vs. 32.5 mm). While 83.3% of macroadenomas could be completely resected, only 33.3% of giant adenomas ( $\geq 40$  mm) were completely removed, consistent with previous reports [21-23]. Tabaei et al. reported that large tumors are associated with longer procedures and longer hospital stay [15]. In our series, although surgical time was not analyzed, we did not find an association between tumor size and length of hospital stay.

In our study, we observed that patients with STR and PR had a higher percentage of adenomas with Knosp grade  $\geq 3$  compared to those who achieved GTR (75%, 100%, and 14.6% respectively). These findings align with the results reported by Li et al [12]. While we observed a trend towards a greater presence

of suprasellar extension in tumors with STR, we did not reach statistical significance ( $p=0.08$ ), possibly due to the limited number of patients in our study. In this sense, Jain et al. demonstrated that the absence of suprasellar extension is a favorable factor for total tumor resection [16].

Patients with aggressive and invasive PA often require multiple surgical interventions, and in some cases, additional treatments such as radiotherapy and chemotherapy may be necessary [17]. In our series, we observed that patients with a history of previous pituitary surgery had a lower rate of GTR compared to those undergoing surgery for the first time (50% vs. 84.3%). This suggests that the complexity and invasiveness of the tumor, as well as the potential scarring and anatomical changes from prior surgeries, may contribute to the challenge of achieving complete tumor removal in these cases. Interestingly, we did not find significant differences in the structural response to surgery based on the hormonal status of the PA (FPA or NFPA). However, our findings indicate that among those patients who achieved GTR, the Ki-67 proliferation index was lower. This observation can be explained by the fact that larger adenomas, particularly giant adenomas, tend to have higher Ki-67 values, and Ki-67 itself is considered an independent risk factor for tumor progression or recurrence [24]. These findings highlight the importance of considering the tumor characteristics, including size and Ki-67 proliferation index, as well as the previous surgical history when planning interventions for aggressive and invasive PA. Future studies with larger sample sizes and longer follow-up periods are needed to further elucidate these relationships and guide treatment decisions for these challenging cases.

Despite previous evidence suggesting the potential benefits of preoperative somatostatin analogs (SSA) in normalizing growth hormone and insulin-like growth factor-1 (IGF-1) levels and reducing postoperative hospitalization [25,26], our study did not find a significant association between the use of SSA and improved structural response or a lower rate of complications. Similarly, we did not observe any benefits with the

use of cabergoline. It is important to note that our study was not specifically designed to evaluate the treatment response to SSA or cabergoline. Further research specifically focusing on the response to these medications is warranted to provide a more comprehensive understanding of their effectiveness in this context.

In our study, a total of 17 patients (28.8%) experienced complications, which is consistent with findings reported in the existing literature [2,27-29]. Although we found the presence of transient DI in 13.56% of patients, a slightly higher percentage than previously reported [13], we observed permanent DI only in 3.4%, a frequency like that reported observed in other series (1–3.4%) [27-29]. None of the patients in our series developed SIADH. We had one patient with macroprolactinoma who experienced postoperative panhypopituitarism, permanent DI, and CSF leak.

Postoperative CSF leak is a significant complication of transsphenoidal surgery, which can lead to meningitis and often requires reconstructive surgery. It is more commonly observed in patients with macroadenomas and suprasellar extension [26,27]. The incidence of postoperative CSF leak reported in the literature ranges from 0.6% to 13.9%. In our series, this complication occurred in 5.1% of the patients. Two patients required endoscopic reoperation for repair, while one patient was managed with lumbar drainage. Intraoperative CSF leak was observed in 15.8% of the patients. These patients were managed with a mucosal flap from the vascularized nasal septum to reduce the risk of postoperative CSF leak. In this sense, only one patient developed a fistula in the postoperative period. We did not find any significant differences in tumor size or frequency of suprasellar extension between patients who experienced CSF leak and those who did not. However, the limited number of patients included in the analysis may have contributed to the lack of statistical significance. None of the cases of postoperative CSF leak were associated with the development of meningitis. However, we did observe one case of meningitis (1.7%) in a patient who underwent surgery for a

GH-secreting PA. This frequency is comparable to previously published results [13,27-29].

Nasal complications, which have been reported in a range of 0.7% to 2.7% in previous studies, were not observed in our patient cohort [13,27-29]. This low prevalence can be attributed to the fact that the endoscopic approach avoids the nasal phase of the surgery and starts directly at the sphenoid ostium. Furthermore, we did not encounter other complications such as sinusitis, ischemia, hematoma, new visual field defects, ophthalmoplegia, intracerebral hemorrhage, or internal carotid artery lesions, which have been reported in a small percentage of patients in previous studies (ranging from 0% to 0.68% for internal carotid artery lesions) [13]. However, we did experience one unfortunate case of postoperative mortality in a patient with an invasive adenoma, a history of previous surgeries, epilepsy, and developmental delay. The cause of death in this case was septic shock of extracranial origin.

Despite the significant findings of this study, it is important to acknowledge several limitations. Firstly, the study design was retrospective, relying on descriptive variables obtained from medical record reviews, which may have led to potential data loss or missing information. Secondly, there was no direct comparison made with the microscopic transsphenoidal technique, making it difficult to establish a definitive superiority of the endoscopic approach. Thirdly, the analysis did not include an evaluation of hormonal response post-surgery, which is an important aspect to consider in assessing treatment outcomes. Lastly, the follow-up period in this series was relatively short, spanning only three months, whereas the recurrence of PA can occur over many years. Therefore, longer-term follow-up and additional research are necessary to address these limitations and provide a more comprehensive understanding of the topic.

In summary, ETSS has emerged as the standard treatment for PA, especially in specialized tertiary care centers. This approach has demonstrated reasonable resection rates, favorable clinical outcomes, and low complication rates. However, certain

preoperative factors such as Knosp grade  $\geq 3$ , tumor size, recurrent tumors, and suprasellar extension may pose challenges to achieving complete tumor resection and successful ETSS outcomes. In such cases, it may be necessary to consider alternative approaches, such as staged surgeries or adjusting goals and expectations to accept partial resection with decompression of the optic pathway as an acceptable option. To further validate these results, more reports based on local institutional experiences, longer follow-up periods, and prospective studies are required.

### Conflicts of interest

The authors declare no conflicts of interest.

### Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or non-profit sectors.

### Author contributions

All authors contributed to the conception of the work, drafted the manuscript, and critically revised the content. All authors approved the final version for publication.

## REFERENCES

- Melmed S. Pathogenesis of pituitary tumors. *Nat Rev Endocrinol* 2011; 7(5): 257-66. doi: 10.1038/nrendo.2011.40.
- 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. doi: 10.1227/01.neu.0000325862.83961.12.
- Woodworth GF, Patel KS, Shin B, Burkhardt JK, Tsiouris AJ, McCoul ED, et al. Surgical outcomes using a medial-to-lateral endonasal endoscopic approach to pituitary adenomas invading the cavernous sinus. *J Neurosurg* 2014; 120(5): 1086-94. doi: 10.3171/2014.1.JNS131228.
- Lopes MBS. The 2017 World Health Organization classification of tumors of the pituitary gland: a summary. *Acta Neuropathol* 2017; 134(4): 521-35. doi: 10.1007/s00401-017-1769-8.
- Barzaghi LR, Medone M, Losa M, Bianchi S, Giovanelli M, Mortini P. Prognostic factors of visual field improvement after trans-sphenoidal approach for pituitary macroadenomas: review of the literature and analysis by quantitative method. *Neurosurg Rev* 2012; 35(3):369-78. doi: 10.1007/s10143-011-0365-y.
- Dehdashti AR, Ganna A, Witterick I, Gentili F. Expanded endoscopic endonasal approach for anterior cranial base and suprasellar lesions: indications and limitations. *Neurosurgery* 2009; 64(4):677-87. doi: 10.1227/01.NEU.0000339121.20101.85.
- de Angelis M, Cappabianca P. Gutta cavat lapidem: the reconstruction of the skull base after endoscopic endonasal surgery. *World Neurosurg* 2015; 83(2):136-7. doi: 10.1016/j.wneu.2014.06.050.
- Constantinidis J, Konstantinidis I. Avoiding complications in endoscopic skull base surgery. *Curr Opin Otolaryngol Head Neck Surg* 2017; 25(1):79-85. doi: 10.1097/MOO.0000000000000327.
- Koren I, Hadar T, Rappaport ZH, Yaniv E. Endoscopic transnasal transsphenoidal microsurgery versus the sublabial approach for the treatment of pituitary tumors: endonasal complications. *Laryngoscope* 1999; 109(11):1838-40. doi: 10.1097/00005537-199911000-00022.
- Cappabianca P, de Divitiis E. Endoscopy and transsphenoidal surgery. *Neurosurgery* 2004; 54(5):1043-8. doi: 10.1227/01neu.0000119325.14116.9c.
- Rojas HP, José PH, Herrera RR, Ledesma JL, Rubín E, Ramírez Stieben LA. Cirugía endoscópica transnasal de base de cráneo: Análisis de las complicaciones en los primeros 120 procedimientos. *Surg Neurol Int* 2022;13:523. doi: 10.25259/SNI\_980\_2022.
- Li C, Zhu H, Zong X, Wang X, Gui S, Zhao P, et al. Experience of trans-nasal endoscopic surgery for pituitary tumors in a single center in China: Surgical results in a cohort of 2032 patients, operated between 2006 and 2018. *Clin Neurol Neurosurg* 2020; 197:106176. doi: 10.1016/j.clineuro.2020.106176.
- Gondim JA, Schops M, de Almeida JP, de Albuquerque LA, Gomes E, Ferraz T, et al. Endoscopic endonasal transsphenoidal surgery:

- surgical results of 228 pituitary adenomas treated in a pituitary center. *Pituitary* 2010; 13(1):68-77. doi: 10.1007/s11102-009-0195-x.
14. Elshazly K, Kshetry VR, Farrell CJ, Nyquist G, Rosen M, Evans JJ. Clinical Outcomes After Endoscopic Endonasal Resection of Giant Pituitary Adenomas. *World Neurosurg* 2018; 114:e447-56. doi: 10.1016/j.wneu.2018.03.006.
  15. Tabae A, Anand VK, Barrón Y, Hiltzik DH, Brown SM, Kacker A, et al. Predictors of short-term outcomes following endoscopic pituitary surgery. *Clin Neurol Neurosurg* 2009; 111(2):119-22. doi: 10.1016/j.clineuro.2008.09.010.
  16. Jain AK, Gupta AK, Pathak A, Bhansali A, Bapuraj JR. Endonasal transsphenoidal pituitary surgery: is tumor volume a key factor in determining outcome? *Am J Otolaryngol* 2008; 29(1):48-50. doi: 10.1016/j.amjoto.2007.01.006.
  17. Cappabianca P, Cavallo LM, Esposito F, De Divitiis O, Messina A, De Divitiis E. Extended endoscopic endonasal approach to the midline skull base: the evolving role of transsphenoidal surgery. *Adv Tech Stand Neurosurg* 2008; 33:151-99. doi: 10.1007/978-3-211-72283-1\_4.
  18. Guvenc G, Kizmazoglu C, Pinar E, Imre A, Kaya I, Bezircioglu H, et al. Outcomes and Complications of Endoscopic Versus Microscopic Transsphenoidal Surgery in Pituitary Adenoma. *J Craniofac Surg* 2016; 27(4):1015-20. doi: 10.1097/SCS.0000000000002684.
  19. Nakao N, Itakura T. Surgical outcome of the endoscopic endonasal approach for non-functioning giant pituitary adenoma. *J Clin Neurosci* 2011; 18(1):71-5. doi: 10.1016/j.jocn.2010.04.049.
  20. Chabot JD, Chakraborty S, Imbarrato G, Dehdashti AR. Evaluation of Outcomes After Endoscopic Endonasal Surgery for Large and Giant Pituitary Macroadenoma: A Retrospective Review of 39 Consecutive Patients. *World Neurosurg* 2015; 84(4):978-88. doi: 10.1016/j.wneu.2015.06.007.
  21. Yano S, Hide T, Shinojima N. Efficacy and Complications of Endoscopic Skull Base Surgery for Giant Pituitary Adenomas. *World Neurosurg* 2017; 99:533-42. doi: 10.1016/j.wneu.2016.12.068.
  22. Gondim JA, Almeida JP, Albuquerque LA, Gomes EF, Schops M. Giant pituitary adenomas: surgical outcomes of 50 cases operated on by the endonasal endoscopic approach. *World Neurosurg* 2014; 82(1-2):e281-90. doi: 10.1016/j.wneu.2013.08.028.
  23. Kuo CH, Yen YS, Wu JC, Chang PY, Chang HK, Tu TH, et al. Primary Endoscopic Transnasal Transsphenoidal Surgery for Giant Pituitary Adenoma. *World Neurosurg* 2016; 91:121-8. doi: 10.1016/j.wneu.2016.03.092.
  24. Chen Y, Cai F, Cao J, Gao F, Lv Y, Tang Y, et al. Analysis of Related Factors of Tumor Recurrence or Progression After Transnasal Sphenoidal Surgical Treatment of Large and Giant Pituitary Adenomas and Establish a Nomogram to Predict Tumor Prognosis. *Front Endocrinol (Lausanne)* 2021; 12:793337. doi: 10.3389/fendo.2021.793337.
  25. Mao ZG, Zhu YH, Tang HL, Wang DY, Zhou J, He DS, et al. Preoperative lanreotide treatment in acromegalic patients with macroadenomas increases short-term postoperative cure rates: a prospective, randomised trial. *Eur J Endocrinol* 2010; 162(4):661-6. doi: 10.1530/EJE-09-0908.
  26. Araujo-Castro M, Pian H, Ruz-Caracuel I, Acitores Cancela A, Pascual-Corrales E, Rodríguez Berrocal V. Presurgical somatostatin receptor ligand treatment does not affect tumor consistency in GH-secreting pituitary macroadenomas. *Endocr Connect* 2021; 10(1):102-9. doi: 10.1530/EC-20-0414.
  27. Frank G, Pasquini E, Farneti G, Mazzatenta D, Sciarretta V, Grasso V, et al. The endoscopic versus the traditional approach in pituitary surgery. *Neuroendocrinology* 2006; 83(3-4):240-8. doi: 10.1159/000095534.
  28. Cappabianca P, Cavallo LM, Colao A, de Divitiis E. Surgical complications associated with the endoscopic endonasal transsphenoidal approach for pituitary adenomas. *J Neurosurg* 2002; 97(2):293-8. doi: 10.3171/jns.2002.97.2.0293.
  29. Magro E, Graillon T, Lassave J, Castinetti F, Boissonneau S, Tabouret E, et al. Complications Related to the Endoscopic Endonasal Transsphenoidal Approach for Nonfunctioning Pituitary Macroadenomas in 300 Consecutive Patients. *World Neurosurg* 2016; 89:442-53. doi: 10.1016/j.wneu.2016.02.059.
  30. Kim JH, Lee JH, Lee JH, Hong AR, Kim YJ, Kim YH. Endoscopic Transsphenoidal Surgery Outcomes in 331 Nonfunctioning Pituitary Adenoma Cases After a Single Surgeon Learning Curve. *World Neurosurg* 2018; 109:e409-e416. doi: 10.1016/j.wneu.2017.09.194.