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Original Article

Comparison of complete resection rate and endocrine function improvement between neuronavigation-assisted neuroendoscopic transnasal transsphenoidal approach and microscopic transcranial approach for giant pituitary adenoma

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Abstract: This study aimed to compare the complete resection rate and endocrine function improvement between the neuronavigation-assisted neuroendoscopic transnasal transsphenoidal approach and the microscopic transcranial approach for giant pituitary adenomas (diameter ≥4 cm). In a retrospective cohort of 300 patients, 132 underwent the transsphenoidal approach and 168 the transcranial approach. Postoperative magnetic resonance imaging revealed a significantly higher complete resection rate in the transsphenoidal group (71.21% vs. 59.52%, $P=0.036$). At two weeks postoperatively, the transsphenoidal group demonstrated significantly better outcomes in endocrine function, visual field parameters, and surgical indicators (shorter operation time, less blood loss, and shorter postoperative stay), with a lower overall complication rate (13.64% vs. 23.21%, $P=0.036$). Multivariate analysis identified the transsphenoidal approach as an independent protective factor against incomplete resection. In conclusion, for selected giant pituitary adenomas, the neuronavigation-assisted neuroendoscopic transnasal transsphenoidal approach may be superior to the microscopic transcranial approach in achieving higher rates of complete resection, better endocrine and visual recovery, and reduced surgical trauma.

Keywords: Pituitary adenoma, neuroendoscopy, neuronavigation, transsphenoidal surgery, transcranial surgery

Introduction

Giant pituitary adenomas, defined as tumors exceeding 4 cm in diameter, present unique challenges in neurosurgery due to their size and anatomical location. These tumors can exert significant mass effect on surrounding structures, leading to compressive symptoms such as visual impairment and endocrine dysfunction [1-3]. Complete resection is crucial for symptom relief and prevention of recurrence, but achieving this goal without compromising normal pituitary function remains a formidable task. Traditional surgical approaches have evolved over time, with each method offering distinct advantages and limitations. The choice between different techniques depends on various factors, including tumor size, extension, and patient-specific considerations [4, 5].

The microscopic transcranial approach has been a mainstay in the management of giant pituitary adenomas, particularly those extending beyond the sellar region into the suprasellar or parasellar spaces. This method involves creating a craniotomy to access the sellar region, providing a wide field of view and extensive exposure of the tumor. Surgeons can manipulate the frontal lobe and other adjacent structures to gain better access to the tumor, facilitating resection of large and complex lesions [6, 7]. However, this approach is associated with greater surgical trauma, including longer operation times, higher intraoperative blood loss, and increased risk of postoperative complications such as brain swelling, infection, and cerebrospinal fluid leakage. Additionally, the necessity to retract brain tissue may result in damage to the hypothalamus-pituitary axis,

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leading to endocrine dysfunction. Despite these drawbacks, the transcranial approach remains valuable for tumors that extend laterally or superiorly, where direct visualization and manipulation are essential [8, 9].

In contrast, the neuroendoscopic transnasal transsphenoidal approach offers a minimally invasive alternative for pituitary adenoma resection. This technique accesses the sellar region via natural nasal passages, minimizing disruption to surrounding structures and reducing the need for brain retraction [10]. Neuronavigation technology further enhances the precision and safety of this approach by providing real-time guidance during surgery. Preoperative imaging data is used to create detailed anatomical maps, allowing surgeons to navigate complex regions with greater accuracy [11, 12]. The transnasal transsphenoidal approach provides direct access to the sellar region, potentially enabling more thorough dissection around the tumor and better preservation of the optic apparatus. By avoiding extensive craniotomy and brain manipulation, this method leads to shorter operation times, reduced intraoperative blood loss, and quicker postoperative recovery. However, its effectiveness may be limited for tumors with significant lateral extension or those involving complex anatomical regions, necessitating careful patient selection and surgical planning [13, 14].

Given the potential benefits and limitations of both approaches, comparative studies are essential to inform clinical decision-making. However, existing literature on giant pituitary adenomas (≥4 cm) often includes heterogeneous cohorts, combines different surgical techniques, or lacks comprehensive comparison across multiple outcome domains, particularly regarding the impact of modern neuronavigation on endoscopic resection outcomes [9, 14]. The present study aims to address these gaps by conducting a focused, head-to-head comparison between the neuronavigation-assisted neuroendoscopic transnasal transsphenoidal approach and the established microscopic transcranial approach in a relatively large, well-matched cohort of patients with strictly defined giant pituitary adenomas. Our investigation not only evaluates the primary endpoints of complete resection rate and endocrine function improvement but also provides a multidimensional assessment encompassing visual outcomes, key surgical parameters, and complication profiles. By doing so, we seek to delineate the specific advantages and trade-offs associated with each technique in the contemporary management of these complex tumors, thereby offering evidence to refine surgical strategy selection. Through this comparison, we hope to provide valuable insights that will guide future clinical practice and improve outcomes for patients with giant pituitary adenomas.

Materials and methods

Study design

This is a single-center retrospective cohort study designed to compare the outcomes of two surgical approaches for giant pituitary adenomas. The study was approved by the Ethics Committee of Wuxi No. 2 People's Hospital and adhered to the principles of the Declaration of Helsinki. Due to the retrospective nature of the study, which involved only the analysis of existing anonymized clinical data, the requirement for informed consent was waived.

Study population

A total of 300 patients diagnosed with giant pituitary adenomas who underwent surgical resection at Wuxi No. 2 People's Hospital between August 2019 and August 2025 were retrospectively reviewed (**Figure 1**). Inclusion criteria were: ① Diagnosis of pituitary adenoma confirmed by preoperative head computed tomography (CT) and magnetic resonance imaging (MRI) [15]; ② Tumor diameter ≥4 cm; ③ Age between 18 and 70 years; ④ Complete medical records. Exclusion criteria were: ① Comorbid psychiatric disorders; ② Comorbid dysfunction of vital organs such as heart, liver, or kidney, or hematopoietic system diseases; ③ Presence of nasal or sinus infections; ④ Tumors extending into the middle cranial fossa, posterior cranial fossa, or recurrent prolactin adenomas; ⑤ Previous treatments received; ⑥ Pregnant or lactating women; ⑦ Comorbid other intracranial tumors, cerebrovascular malformations, or other central nervous system diseases.

According to the surgical approach, the 300 patients who met the inclusion and exclusion criteria were defined into the transcranial

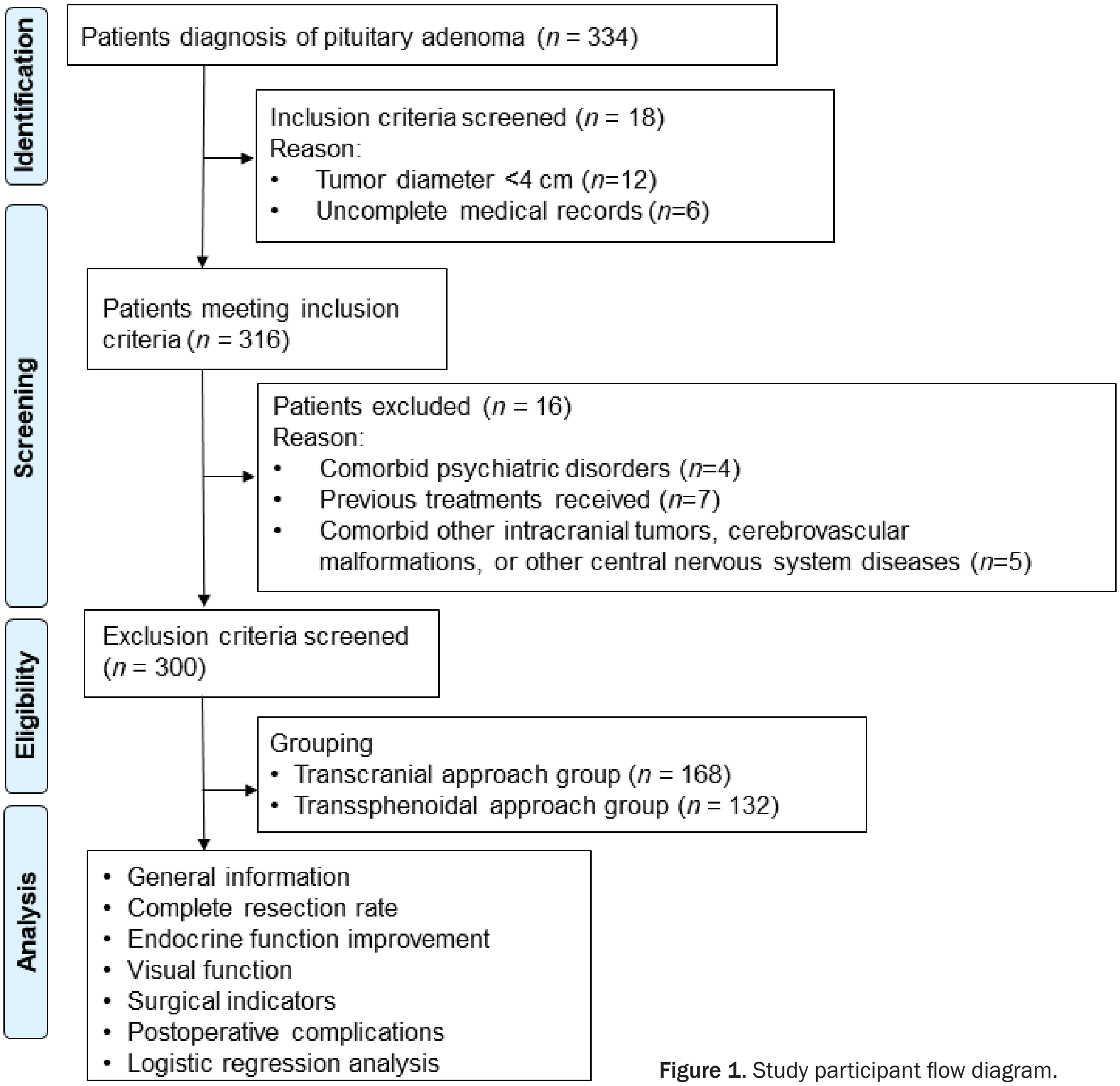

Figure 1. Study participant flow diagram.

approach group (n=168) and the transsphenoidal approach group (n=132). Patients in the transcranial approach group underwent microscopic subfrontal-transtemporal combined approach pituitary adenoma resection, while patients in the transsphenoidal approach group received neuronavigation-assisted neuroendoscopic transnasal transsphenoidal pituitary adenoma resection.

The selection of surgical approach for each patient was made by a multidisciplinary team (MDT) involving neurosurgeons, endocrinologists, and radiologists, based on a comprehensive assessment of the following factors: (1) tumor anatomical characteristics: primary considerations included the pattern and degree of suprasellar extension, cavernous sinus invasion (assessed by Knosp grade), and the relationship to critical neurovascular structures (e.g., optic chiasm, internal carotid arteries). Tumors with predominant suprasellar growth and minimal lateral extension were more likely to be considered for the transsphenoidal approach. (2) clinical presentation: patient symptoms, particularly the severity of visual impairment and the type of endocrine dysfunction, were evaluated; (3) surgeon's expertise and assessment: the final decision incorporated the operating surgeon's experience and intraoperative judgment regarding the feasibility of achieving safe and maximal resection via each route; (4) patient-specific factors: General health status, nasal anatomy, and patient preference (when applicable) after detailed consultation were also considered.

Data extraction and outcome measures

Data were extracted from the hospital's electronic medical record system. The primary outcome measures were the gross total resection rate and improvement in endocrine function. Secondary outcomes included visual function, surgical parameters, and postoperative complications. All postoperative outcome assessments (MRI evaluation, hormone level analysis, and visual field testing) were performed by independent assessors who were blinded to the patients' surgical group allocation.

(1) Complete resection rate: Within 48 hours after surgery, an MRI (MAGNETOM Prisma, Siemens, Germany) was performed to determine the extent of tumor resection. Complete resection was defined as no residual tumor visible on MRI, subtotal resection was defined as residual tumor volume <10%, and partial resection was defined as residual tumor volume between 10% and 20% [16].

(2) Endocrine function improvement: Hormone levels were measured preoperatively and two weeks postoperatively using an electrochemiluminescence immunoassay analyzer (Cobas e801, Roche Diagnostics, Switzerland), including prolactin (PRL), adrenocorticotropic hormone (ACTH), and growth hormone (GH).

(3) Visual function: Visual field assessments were conducted preoperatively and two weeks postoperatively using an automated perimeter (HFA3, Carl Zeiss Meditec AG, Germany). The main assessment indicators included the visual field index (VFI), pattern standard deviation (PSD), and mean deviation (MD). Higher VFI values and lower PSD and MD (absolute values) indicated better visual function.

(4) Surgical indicators: The patient's operation time, intraoperative blood loss, and postoperative stay were recorded.

(5) Postoperative complications: Within one week postoperatively, the occurrence of complications such as cerebrospinal fluid leakage (defined as persistent clear rhinorrhea after surgery, confirmed by positive beta-2 transferrin testing), diabetes insipidus (defined as excessive urine output (>4 mL/kg/h for consecutive 2 hours, or >300 mL/h in adults) with low urine specific gravity [<1.005] or hypernatremia, requiring desmopressin administration), hypopituitarism (defined as new-onset or worsened insufficiency of one or more pituitary axes (adrenal, thyroid, or gonadal) in the immediate postoperative period, requiring initiation or adjustment of hormone replacement therapy), and optic nerve injury (defined as new-onset or significant worsening of visual acuity (a decrease of >2 lines on the Snellen chart) or visual field defect attributable to surgical manipulation, as evaluated by an ophthalmologist.) were observed and recorded.

Surgical approach

Microscopic transcranial approach: General anesthesia with intravenous combined anesthesia was administered, and the patient was placed in a supine position with the head tilted 10° to the left and extended 15°. A coronal skin incision was made within the hairline of the forehead, followed by the creation of a right frontal-temporal bone flap near the cranial base of the frontal bone. The sphenoid ridge was ground down until it approached the superior orbital fissure, after which the dura mater was incised. Cerebrospinal fluid from the suprasellar cistern and lateral fissure was slowly released to reduce intracranial pressure. An automatic brain retractor was then gently used to elevate the frontal lobe. The pre-chiasmatic region was exposed via the subfrontal approach, identifying the boundaries of the tumor's suprasellar portion. Initially, a 22 G syringe was used to puncture the tumor lesion to rule out the possibility of an aneurysm. Bipolar coagulation was then applied to the vessels on the surface of the diaphragma sellae, followed by a cruciate incision of the diaphragma sellae. The tumor tissue was removed piecemeal using a pituitary curette combined with an aspirator. After complete removal, thorough hemostasis was achieved, and the wound was closed layer by layer. A subdural drain was placed for 48 hours.

Neuronavigation-assisted neuroendoscopic transnasal transsphenoidal approach: One day prior to surgery, a cranial MRI scan was performed, and the imaging data were uploaded to the navigation workstation iPlan 3.0 (Brain-

Lab, Feldkirchen, Germany). General anesthesia with intravenous combined anesthesia was administered, and the patient was placed in a supine position with the head extended 15° and secured. At the start of the surgery, a navigation reference frame was fixed to the headframe, and navigation registration was completed using an infrared positioning system, with registration errors controlled to less than 2 mm. The accuracy of anatomical landmarks was verified using a navigation probe, after which the reference frame, probe, markers, and other temporary markings were removed. The patient's nasal cavity was disinfected, and the disinfected navigation reference frame and probe were reinserted into the nasal cavity. The nasal mucosa was then incised. Under the assistance of neuronavigation and neuroendoscopy, the anterior wall and opening of the sphenoid sinus were observed, and the sphenoid septum was removed to expose the sellar floor. The sellar floor was drilled open, and the size of the bone window was determined based on the tumor size while ensuring surgical safety. After fully exposing the dura mater of the sellar floor, bipolar coagulation was used to coagulate the surface vessels, followed by a cruciate incision of the dura mater. The tumor boundaries were clearly observed under neuroendoscopy. For softer tumors, an aspirator combined with a curette was used for piecemeal removal. For harder or encapsulated tumors, an ultrasonic aspirator was first used to fragment the tumor tissue before aspiration. During the procedure, the extent of tumor resection was confirmed in real-time using the navigation system to avoid damaging important structures around the sella, ensuring the safety of normal pituitary tissue and surrounding neurovascular structures. After tumor resection, the sellar floor was reconstructed, thorough hemostasis was achieved, and petroleum gauze strips were packed into the nasal cavity.

All surgeries were performed by the same fixed, experienced neurosurgical team. The core members of this team, including the senior surgeons, are proficient in both microscopic transcranial surgery and endoscopic transsphenoidal surgery. For the two surgical procedures involved in this study, the lead surgeons each have extensive experience, having independently completed over 200 surgeries of each type, thereby surpassing their respective learning curves.

Statistical analysis

This study used SPSS 29.0 statistical software (SPSS Inc., Chicago, IL, USA) for data processing and analysis. A two-tailed significance level of $\alpha=0.05$ was set, with $P<0.05$ considered statistically significant. Initially, all continuous variables were assessed for normality using the Shapiro-Wilk test, which confirmed that they followed a normal distribution and were expressed as mean ± standard deviation (M ± SD). Between-group comparisons for continuous variables were performed using independent samples t-tests. Categorical variables were expressed as frequencies and percentages [n (%)] and compared between groups using the χ^2 test. Univariate and multivariate logistic regression analyses were conducted with incomplete tumor resection as the dependent variable (incomplete resection [including subtotal and partial resection] = 1, complete resection = 0) to identify independent risk factors for incomplete tumor resection.

Given that this study adopted a retrospective design, a prospective sample size estimation was not conducted prior to the commencement of the study. To evaluate the statistical power of the final sample size, a post-hoc power analysis was performed after the completion of data analysis. Based on the observed rates of complete resection, with α set at 0.05 (two-tailed), the chi-square test for comparing two proportions was analyzed using G*Power software (version 3.1). The calculations revealed that the statistical power for the current sample size (total n=300) was 82.1%, which exceeds the conventional threshold of 80%, indicating that the present sample size is adequate to detect the observed differences between groups.

Results

General information

In the comparison of general information between the Transcranial approach group and the Transsphenoidal approach group (**Table 1**), no significant differences were observed for age, gender distribution, BMI, hypertension, diabetes mellitus, tumor diameter, tumor type, Knosp grade, vertical height, optic chiasm involvement, close relation to Willis circle vessels, 3rd ventricular floor compression/invasion, "Hourglass" configuration, or preoperative

Table 1. Comparison of general information between two groups

Parameter	Transcranial approach group (n=168)	Transsphenoidal approach group (n=132)	t/χ^2	P
Age (years)	45.66 ± 10.23	47.23 ± 10.01	1.331	0.184
Gender [n (%)]			0.081	0.776
Male	102 (60.71%)	78 (59.09%)		
Female	66 (39.29%)	54 (40.91%)		
BMI (kg/m^2)	23.56 ± 2.82	24.08 ± 2.25	1.758	0.080
Hypertension [n (%)]			0.010	0.919
Yes	50 (29.76%)	40 (30.30%)		
No	118 (70.24%)	92 (69.70%)		
Diabetes mellitus [n (%)]			0.001	0.981
Yes	32 (19.05%)	25 (18.94%)		
No	136 (80.95%)	107 (81.06%)		
Tumor diameter (cm)	8.02 ± 1.53	8.16 ± 1.47	0.828	0.408
Tumor type [n (%)]			0.018	0.893
Functional adenoma	38 (22.62%)	29 (21.97%)		
Non-functional adenoma	130 (77.38%)	103 (78.03%)		
Knosp grade [n (%)]			0.006	0.940
Grade 0-2	100 (59.52%)	78 (59.09%)		
Grade 3-4	68 (40.48%)	54 (40.91%)		
Vertical height (cm)	3.85 ± 0.91	3.78 ± 0.86	0.697	0.486
Optic chiasm involvement [n (%)]	145 (86.31%)	110 (83.33%)	0.514	0.474
Close relation to Willis circle vessels [n (%)]	141 (83.93%)	109 (82.58%)	0.097	0.755
3rd ventricular floor compression/invasion [n (%)]	107 (63.69%)	80 (60.61%)	0.300	0.584
"Hourglass" configuration [n (%)]	47 (27.98%)	34 (25.76%)	0.185	0.667
Preoperative hydrocephalus [n (%)]	25 (14.88%)	18 (13.64%)	0.093	0.760

BMI, body mass index.

Table 2. Comparison of the extent of tumor resection between two groups [n (%)]

Parameter	Transcranial approach group (n=168)	Transsphenoidal approach group (n=132)	χ^2	P
Complete resection	100 (59.52%)	94 (71.21%)	4.420	0.036
Subtotal resection	43 (25.60%)	25 (18.94%)	1.868	0.172
Partial resection	25 (14.88%)	13 (9.85%)	1.692	0.193

hydrocephalus (P>0.05 for all). These results indicate that the two groups were well-matched in terms of baseline characteristics, supporting their comparability for further analysis.

Complete resection rate

In the comparison of the extent of tumor resection between the Transcranial approach group and the Transsphenoidal approach group (**Table 2**), a significant difference was observed in the rate of complete resection, which was higher in the Transsphenoidal approach group (71.21% vs. 59.52%, χ^2=4.420, P=0.036). No significant differences were found for subtotal resection or partial resection between the two groups (P>0.05 for both). These findings suggest that the Transsphenoidal approach may be more effective for achieving complete tumor resection.

Endocrine function improvement

In the comparison of hormone levels between the Transcranial approach group and the Transsphenoidal approach group (**Figure 2**), preoperative levels of PRL, ACTH, and GH did not show significant differences (P>0.05 for

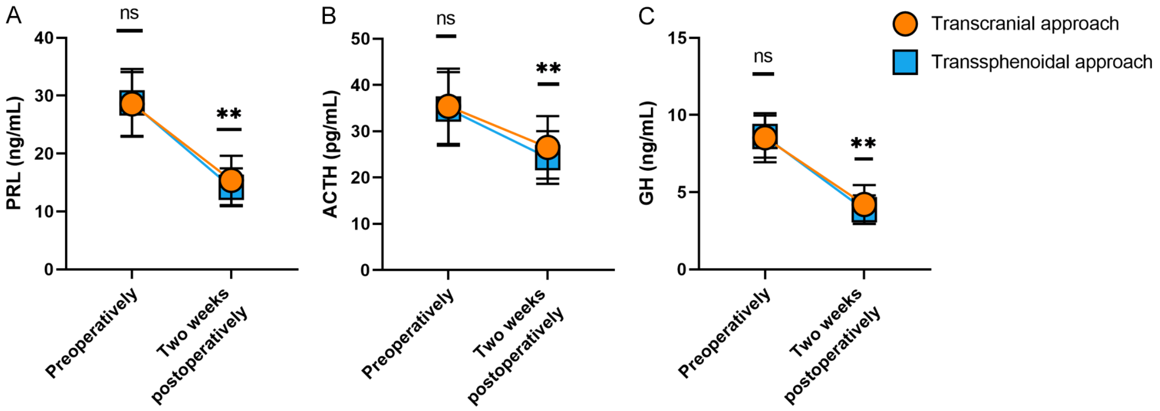

Figure 2. Comparison of hormone levels between two groups. A. PRL; B. ACTH; C. GH. The data are presented as M ± SD. The transcranial approach group (n=168) is shown in orange, and the transsphenoidal approach group (n=132) is shown in blue. ns indicates no significant difference between groups, **indicates a statistically significant difference between groups, P<0.01. PRL, prolactin; ACTH, adrenocorticotropic hormone; GH, growth hormone.

Table 3. Comparison of visual function between two groups

Parameter	Transcranial approach group (n=168)	Transsphenoidal approach group (n=132)	t	P
VFI (%)				
Preoperatively	65.52 ± 7.29	66.27 ± 6.98	0.899	0.369
Two weeks postoperatively	90.75 ± 7.53	92.83 ± 6.25	2.606	0.010
PSD (dB)				
Preoperatively	8.72 ± 1.64	8.61 ± 1.57	0.575	0.566
Two weeks postoperatively	3.08 ± 0.98	2.86 ± 0.79	2.142	0.033
MD (dB)				
Preoperatively	-12.82 ± 2.71	-12.48 ± 2.62	1.072	0.285
Two weeks postoperatively	-3.84 ± 1.22	-3.55 ± 0.94	2.348	0.020

VFI, visual field index; PSD, pattern standard deviation; MD, mean deviation.

all). Two weeks postoperatively, significant differences were observed in PRL (Transcranial: 15.38 ng/mL vs. Transsphenoidal: 14.19 ng/mL, t=2.736, P=0.007), ACTH (Transcranial: 26.51 pg/mL vs. Transsphenoidal: 24.32 pg/mL, t=3.042, P=0.003), and GH (Transcranial: 4.21 ng/mL vs. Transsphenoidal: 3.87 ng/mL, t=2.675, P=0.008). These results indicate that while both groups had similar preoperative hormone levels, the Transsphenoidal approach was associated with significantly lower hormone levels two weeks after surgery.

Visual function

In the comparison of visual function between the Transcranial approach group and the Transsphenoidal approach group (**Table 3**), preoperative values for VFI, PSD, and MD did not show significant differences (P>0.05 for all). Two weeks postoperatively, significant improvements were observed in VFI (Transcranial: 90.75% vs. Transsphenoidal: 92.83%, t= 2.606, P=0.010), PSD (Transcranial: 3.08 dB vs. Transsphenoidal: 2.8 6dB, t=2.142, P= 0.033), and MD (Transcranial: -3.84 dB vs. Transsphenoidal: -3.55 dB, t=2.348, P=0.020). These findings indicate that while both groups had similar preoperative visual function parameters, the Transsphenoidal approach resulted in significantly better visual outcomes two weeks after surgery.

Surgical indicators

In the comparison of surgical indicators between the Transcranial approach group and the Transsphenoidal approach group (**Figure 3**), significant differences were observed in operation time (Transcranial: 146.57 min vs. Trans-

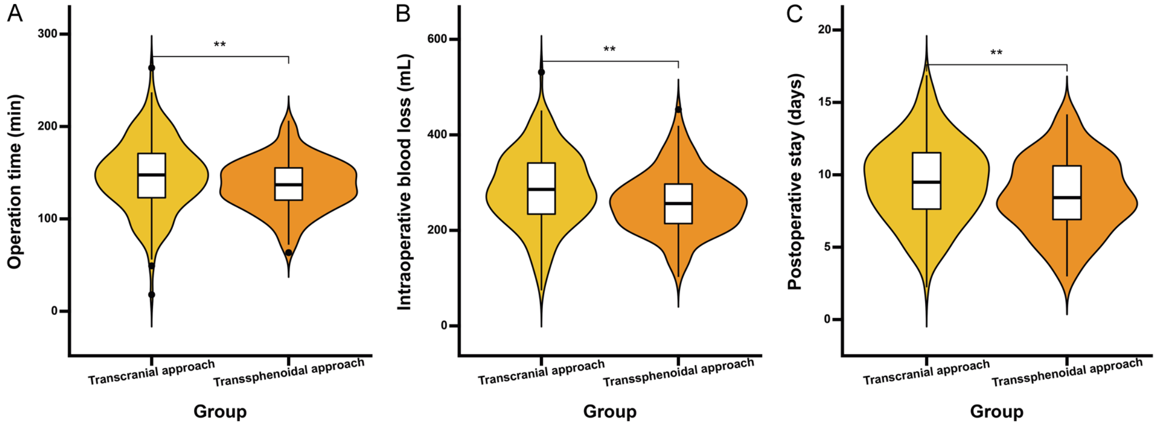

Figure 3. Comparison of surgical indicators between two groups. A. Operation time; B. Intraoperative blood loss; C. Postoperative stay. The data are presented as M ± SD. The transcranial approach group (n=168) is shown in yellow, and the transsphenoidal approach group (n=132) is shown in orange. **indicates a statistically significant difference between groups, P<0.01.

Table 4. Comparison of postoperative complications between two groups [n (%)]

Parameter	Transcranial approach group (n=168)	Transsphenoidal approach group (n=132)	χ^2	P
Incidence of complications	39 (23.21%)	18 (13.64%)	4.406	0.036
Cerebrospinal fluid leakage	3 (1.79%)	9 (6.82%)		
Diabetes insipidus	12 (7.14%)	8 (6.06%)		
Hypopituitarism	23 (13.69%)	5 (3.79%)		
Optic nerve injury	16 (9.52%)	2 (1.52%)		

Table 5. Univariate logistic regression analysis of risk factors for incomplete tumor resection

Parameter	Coefficient	Std Error	Wald	P	OR	95% CI
Surgical approach (Transsphenoidal approach)	-0.867	0.215	16.254	0.012	0.607	0.410-0.898
Tumor diameter	0.318	0.065	23.916	0.045	1.128	1.002-1.268
Tumor type (Functional adenoma)	0.105	0.228	0.212	0.617	1.051	0.864-1.279
Knosp grade (Grade 0~2)	-1.435	0.221	42.228	<0.001	0.522	0.381-0.714

OR, odds ratio; CI, confidence interval.

sphenoidal: 136.39 min, t=2.654, P=0.008), intraoperative blood loss (Transcranial: 285.62 mL vs. Transsphenoidal: 259.84 mL, t=3.128, P=0.002), and postoperative stay (Transcranial: 9.54 days vs. Transsphenoidal: 8.56 days, t=3.121, P=0.002). These results indicate that the Transsphenoidal approach was associated with shorter operation times, less intraoperative blood loss, and shorter postoperative stays compared to the Transcranial approach.

Postoperative complications

In the comparison of postoperative complications between the Transcranial approach group and the Transsphenoidal approach group (**Table 4**), the overall incidence of complications was significantly higher in the Transcranial approach group (23.21% vs. 13.64%, χ^2=4.406, P=0.036).

Logistic regression analysis

In the univariate logistic regression analysis of risk factors for incomplete tumor resection (**Table 5**), the Transsphenoidal surgical approach (OR=0.607, 95% CI=0.410-0.898, P=0.012) and lower Knosp grade (Grade 0~2) (OR=0.522, 95% CI=0.381-0.714, P<0.001) were associated with reduced odds of incom-

Table 6. Multivariate logistic regression analysis of risk factors for incomplete tumor resection

Parameter	Coefficient	Std Error	Wald Stat	P	OR	OR CI Lower	OR CI Upper
Surgical approach (Transsphenoidal approach)	-0.755	0.238	10.063	0.029	0.619	0.402	0.952
Tumor diameter	0.215	0.078	7.599	0.045	1.105	1.002	1.219
Tumor type (Functional adenoma)	0.085	0.241	0.124	0.739	1.041	0.823	1.317
Knosp grade (Grade 0~2)	-1.223	0.256	22.820	<0.001	0.549	0.409	0.736

OR, odds ratio; CI, confidence interval.

plete resection. Larger tumor diameter was also associated with increased odds of incomplete resection (OR=1.128, 95% CI=1.002-1.268, P=0.045). Tumor type (Functional adenoma) did not show a significant association (P>0.05).

In the multivariate logistic regression analysis of risk factors for incomplete tumor resection (**Table 6**), the Transsphenoidal surgical approach (OR=0.619, 95% CI=0.402-0.952, P=0.029) and lower Knosp grade (Grade 0~2) (OR=0.549, 95% CI=0.409-0.736, P<0.001) were identified as protective factors against incomplete resection. Larger tumor diameter was associated with increased odds of incomplete resection (OR=1.105, 95% CI=1.002-1.219, P=0.045). Tumor type (Functional adenoma) did not show a significant association (P>0.05). These results indicate that the surgical approach, tumor diameter, and Knosp grade are independently associated with the likelihood of incomplete tumor resection.

Discussion

The present study aimed to compare the complete resection rate and endocrine function improvement between neuronavigation-assisted neuroendoscopic transnasal transsphenoidal approach and microscopic transcranial approach for the surgical treatment of giant pituitary adenomas. Our findings suggest that the transsphenoidal approach may offer several advantages over the transcranial approach in terms of tumor resection completeness, postoperative endocrine function, visual outcomes, and surgical indicators. These differences can be attributed to various mechanisms related to the anatomical and technical aspects of each surgical method.

The higher rate of complete tumor resection observed in the transsphenoidal group could be due to the direct access to the sellar region provided by this approach. The transsphenoidal route allows surgeons to operate closer to the tumor site with less manipulation of surrounding structures, potentially leading to more precise and thorough resection [17, 18]. In contrast, the transcranial approach involves navigating through multiple layers of brain tissue, which may limit visibility and accessibility, particularly for tumors extending into the suprasellar region. This increased precision in the transsphenoidal approach could explain its superior performance in achieving complete resection [19]. The use of neuronavigation technology enhances the surgeon's ability to localize and remove the tumor accurately, further contributing to improved resection rates.

Our results indicate better postoperative endocrine function in patients undergoing the transsphenoidal approach. Beyond the general concept of reduced surgical trauma, several specific anatomical and physiological mechanisms may explain this advantage. The transsphenoidal route provides direct midline access to the sellar region without requiring manipulation of the frontal lobes or dissection of the Sylvian fissure, thereby minimizing traction on the hypothalamus-pituitary stalk complex [20]. This preservation of the stalk's structural integrity is critical for maintaining portal blood flow and antegrade delivery of hypothalamic releasing hormones to the anterior pituitary [21]. In contrast, the transcranial approach, particularly when employing subfrontal or pterional corridors, often necessitates some degree of brain retraction and manipulation of the suprasellar cisterns, which can lead to traction injury, vasospasm of the small perforating arteries supplying the stalk and gland, or direct contusion of the hypothalamic floor [22]. These iatrogenic insults may precipitate or exacerbate postoperative pituitary dysfunction. Furthermore, the enhanced visualization and angled optics of the neuroendoscope allow for superior discrimination between adenoma tissue and the compressed but otherwise normal pituitary gland, facilitating selective tumor removal while preserving functional gland parenchyma [23]. This precise dissection is more challenging under the limited direct line-of-sight of the operating microscope in the deep and narrow corridor of a transcranial approach. Collectively, the combination of atraumatic access, preservation of critical vascular supply, and superior visualization underpins the better endocrine outcomes observed with the neuronavigation-assisted endoscopic transsphenoidal approach.

Visual function also showed improvement favoring the transsphenoidal approach. Anatomically, the optic chiasm and nerves are most frequently displaced superiorly and anteriorly by the upward-growing tumor. The transsphenoidal corridor approaches the tumor from below, allowing the surgeon to decompress the optic apparatus from its inferior surface first, which is often the site of maximal compression [24]. This approach facilitates the gentle dissection of the tumor capsule away from the chiasm under direct vision, within the natural anatomical planes, thereby minimizing additional traction or manipulation of the already compromised nerve fibers [25]. The mechanism of visual recovery is primarily the relief of mechanical compression, which alleviates conduction block and restores axoplasmic flow. However, the surgical approach can influence the efficiency and safety of this decompression. The transcranial route may approach the optic nerves from a lateral or superior perspective, potentially requiring some manipulation of the nerves themselves to access the tumor within the sella, thereby carrying a higher risk of direct iatrogenic injury [7]. Additionally, the risk of ischemic damage to the optic apparatus may differ. The transsphenoidal approach, by avoiding extensive dissection around the supraclinoid internal carotid arteries and the superior hypophyseal arteries that supply the undersurface of the chiasm, may better preserve the microvascular supply to the anterior visual pathways [26, 27]. The lower rate of postoperative optic nerve injury in our transsphenoidal cohort provides strong clinical support for this protective effect. Thus, the anatomical trajectory of the transsphenoidal route, combined with the enhanced visualization of the endoscope, enables a safer, more direct, and more complete decompression of the optic apparatus, translating into the superior early visual outcomes observed in this study.

It is noteworthy that while the differences in VFI and MD between groups at two weeks were statistically significant, their absolute magnitudes were modest. We acknowledge that these intergroup differences fall below the conventionally cited thresholds for the Minimal Clinically Important Difference (MCID) in chronic optic neuropathies, which often are set at a ≥5% change in VFI or a ≥2.0 dB change in MD [28]. This presents a critical point for discussion: the phenomenon of statistical significance in the absence of a clear, established clinical significance threshold for this specific postoperative context. However, several contextual factors warrant consideration before dismissing these differences as clinically irrelevant. First, the baseline severity of visual dysfunction in our cohort of giant adenoma patients was profound. In such severe compression, the trajectory and completeness of early recovery may be as important as the final absolute value. The significant improvement from baseline is itself a major clinical achievement. The small but consistent between-group advantage in the transsphenoidal cohort might represent a more efficient or complete early decompression of the optic apparatus, potentially translating into a more favorable long-term recovery plateau. Second, the convergence of evidence across multiple, independent visual field indices (VFI, PSD, and MD all showing statistically significant and directionally consistent advantages for the transsphenoidal approach) substantially reduces the likelihood that this finding is a statistical artifact. This multi-parameter validation strengthens the inference of a real, albeit numerically small, biological effect attributable to the surgical approach. Third, the clinical implication of this finding must be integrated with the overall risk-benefit profile. The transsphenoidal approach in our study was also associated with a significantly lower rate of optic nerve injury. Therefore, the slightly better visual field outcomes, when combined with a substantially lower risk of causing new visual deficits, reinforce the safety profile and potential functional superiority of the endoscopic approach for selected cases. Ultimately, the determination of a true MCID for visual field recovery after pituitary surgery requires prospective studies incorporating patient-reported outcome measures (PROMs) and longer-term follow-up. Our data suggest a consistent, statistically significant early advantage for the neuronavigation-assisted endoscopic approach. Whether this incremental advantage translates into a perceptible difference in patients' quality of life or long-term visual stability requires further investigation. Nevertheless, within the context of a procedure that also offers higher gross total resection rates, better endocrine outcomes, and reduced surgical trauma, even a marginal gain in visual function recovery contributes to a compelling cumulative benefit.

Surgical indicators such as operation time, intraoperative blood loss, and postoperative stay were also more favorable in the transsphenoidal group. The shorter operation times and reduced blood loss observed in the transsphenoidal approach are likely due to the minimally invasive nature of this technique. By avoiding extensive craniotomy and brain retraction, the transsphenoidal approach reduces operative complexity and trauma, leading to faster recovery and shorter hospital stays [29, 30]. The use of neuronavigation technology facilitates quicker and more accurate tumor localization, further shortening the duration of the procedure.

Postoperative complications were lower in the transsphenoidal group, as reflected by the significantly lower overall incidence. This reduction was primarily driven by notably lower rates of hypopituitarism and optic nerve injury. However, consistent with the inherent challenges of the transnasal route, the incidence of cerebrospinal fluid (CSF) leakage was observed to be higher in the transsphenoidal group. This contrasts with the transcranial approach, which had a lower CSF leakage rate but carried a higher burden of other complications such as hypopituitarism and optic nerve injury. The incidence of diabetes insipidus was comparable between the two groups. These findings suggest that the transsphenoidal approach offers a favorable overall complication profile for selected giant adenomas, albeit with a specific trade-off regarding CSF leakage risk that requires meticulous skull base reconstruction [31].

The logistic regression analysis provides further statistical support for the superiority of the transsphenoidal approach in achieving complete resection. After adjusting for potential confounders, the transsphenoidal approach itself emerged as a significant independent protective factor against incomplete tumor resection. This reinforces the conclusion that the surgical approach is a key determinant of resection success, beyond inherent tumor characteristics. The analysis also corroborates established clinical knowledge, identifying larger tumor diameter as a risk factor for incomplete resection, while lower Knosp grades, indicative of less cavernous sinus invasion, served as another independent protective factor. These findings collectively underscore that in addition to selecting an optimal surgical approach, careful preoperative assessment of tumor size and invasion remains crucial for predicting resectability and planning surgical strategy for giant pituitary adenomas.

An interesting finding from our multivariate analysis was that tumor type (functional versus non-functional) was not an independent predictor of the extent of resection. This may seem counterintuitive, as functional adenomas (e.g., those secreting GH or ACTH) often present a compelling surgical imperative for complete removal to achieve biochemical cure. Several interrelated factors may explain this result. First, the study specifically enrolled giant adenomas (≥4 cm). At this enormous size, the primary challenge for gross total resection shifts from the tumor's secretory phenotype to its mass effect and invasive anatomical behavior. Features such as cavernous sinus invasion (reflected by Knosp grade) and suprasellar extension become the dominant technical obstacles, potentially overshadowing the influence of secretory status on resectability. Second, the surgical goal in this cohort, while always aiming for maximal safe resection, may have been pragmatically adjusted based on intraoperative findings. For some giant functional adenomas with extensive invasion, the priority may have shifted to effective debulking for mass effect relief and creating a favorable anatomy for adjuvant therapy (e.g., radiotherapy or medical treatment for residual functional tissue), rather than pursuing a risky radical resection. This could reduce the observed difference in complete resection rates between functional and non-functional types. Third, the high level of expertise of the surgical team in managing both types of adenomas may have minimized performance bias. Finally, it is possible that the biological behavior influencing resectability is more closely captured by the anatomical variables already in the model (size, Knosp grade), rather than by the simple functional/non-functional dichotomy. This finding underscores that for giant pituitary adenomas, anatomical complexity rather than endocrine activity is the principal determinant of surgical resectability.

In comparing our findings to previous literature, one notable study conducted by Gao et al. [32], reported the use of a combined endoscopic endonasal transsphenoidal and microscopic transcranial approach for the primary resection of giant pituitary adenomas. Their results demonstrated a high rate of gross total resection, aligning with our observation that the transsphenoidal component contributes significantly to achieving complete tumor removal. Both studies underscore the importance of direct sellar access and advanced visualization in managing these complex tumors.

Despite these promising results, there are several limitations to our study that warrant consideration. First and foremost, the relatively short-term follow-up period (assessment of primary outcomes at two weeks postoperatively) represents a significant constraint. While this timeframe is adequate for evaluating initial surgical outcomes such as gross resection extent, early hormonal changes, and acute postoperative complications, it is insufficient to assess several critical long-term endpoints. These include tumor recurrence or progression rates, which require serial MRI surveillance over years; the durability of endocrine function improvement or the potential delayed onset of hypopituitarism; and the long-term stability of visual field recovery. Consequently, our findings regarding the superiority of one approach over the other are primarily indicative of early efficacy and safety profiles. The long-term oncological control and functional outcomes remain to be determined through extended follow-up studies. Additionally, the retrospective design inherently limits the ability to control for all potential confounding variables, despite our efforts to match baseline characteristics. The selection of the surgical approach for each patient was not randomized but was determined by a multidisciplinary team based on a comprehensive assessment of tumor anatomy, clinical presentation, surgeon expertise, and patient-specific factors. While this reflects real-world clinical decision-making and the two groups were well-matched in key baseline characteristics, this non-randomized assignment inevitably introduces the potential for selection bias. For instance, tumors with more favorable anatomy for a transsphenoidal resection (e.g., less lateral extension) might have been systematically assigned to that group, which could influence the observed outcomes in favor of the transsphenoidal approach. Future prospective studies with standardized, long-term follow-up protocols are essential to validate these preliminary findings and to establish the sustained benefits and risks associated with each surgical approach for giant pituitary adenomas.

Conclusion

This study suggests that the neuronavigation-assisted neuroendoscopic transnasal transsphenoidal approach may offer potential advantages over the microscopic transcranial approach in the management of giant pituitary adenomas. These potential benefits include a higher likelihood of complete tumor resection, better preservation of endocrine function, improved visual outcomes, and reduced surgical trauma, as indicated by shorter operation times, less intraoperative blood loss, and shorter postoperative stays. The transsphenoidal approach appears to be associated with a lower incidence of certain postoperative complications. The transsphenoidal approach shows promise as a valuable option for the treatment of giant pituitary adenomas but requires additional investigation to fully understand its long-term efficacy and safety.

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Disclosure of conflict of interest

None.

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