Neurosurgical Review (2026) 49:227
https://doi.org/10.1007/s10143-025-04101-z

REVIEW

Surgically treated giant pituitary neuroendocrine tumors: systematic review and meta-analysis with institutional cohort

Sara Antonietti[1] · Pier Paolo Panciani[1] · Alessandro Fiorindi[1] · Vittorio Rampinelli[2] · Francesco Doglietto[3,4] · Marco Maria Fontanella[1] · Edoardo Agosti[1]

Received: 7 August 2025 / Revised: 21 December 2025 / Accepted: 25 December 2025

Abstract

Introduction This study aims to compare endoscopic endonasal approaches (EEAs) and transcranial approaches (TCAs) for the surgical treatment of giant pituitary neuroendocrine tumors (GPitNETs).

Methods A systematic literature review was conducted using PubMed, Ovid MEDLINE, and Web of Science for studies on GPitNETs treated with EEA or TCA up to April 2025, following PRISMA guidelines. Meta-analysis was performed using random effects to estimate pooled event rates and heterogeneity. Risk of bias was assessed with the ROBINS-I tool. Additionally, a retrospective cohort of 20 patients was included, for a total of 1,052 patients across 21 studies. Seven studies were comparative.

Results A total of 21 studies (2010–2024) met inclusion criteria, with 1,032 patients undergoing EEAs or TCAs for GPitNETs. Additionally, we included a retrospective cohort of 20 patients from our institution, for a total sample of 1,052. Meta-analysis was conducted on 7 comparative studies with a total of 273 patients. Visual improvement was significantly higher with EEA (OR 3.73; 95% CI: 1.44–9.64; $p<0.01$). Gross total resection (GTR), progression rates and most postoperative complications, including cerebrospinal fluid (CSF) leak, infection, diabetes insipidus, and hypopituitarism (HP), showed no significant differences. However, intracranial hemorrhage (ICH) was more frequent with TCAs (OR 0.09; 95% CI: 0.02–0.45; $p<0.01$). Study heterogeneity ranged from low to moderate depending on the endpoint.

Conclusions Endoscopic endonasal approaches provide better visual outcomes and lower ICH risk in GPitNETs. No statistically significant differences were observed between EEAs and TCAs in terms of GTR, progressive rates, or postoperative complications, including CSF leak, infection, diabetes insipidus, and HP.

Keywords Giant pituitary neuroendocrine tumors · Transcranial approach · Endoscopic endonasal · Systematic reviews · Meta-analysis · Outcomes

Introduction

Giant pituitary neuroendocrine tumors (GPitNETs) are PitNETs measuring ≥4 cm in maximum diameter, according to the most recent WHO classification of pituitary tumors (2022) and Pituitary Society consensus definitions [1] They represent a significant neurosurgical challenge due to their size, invasive behavior, and proximity to critical neurovascular structures [1]. Giant pituitary adenomas are estimated to represent 5% to 15% of all pituitary adenomas [1].

Two primary surgical approaches are employed in their treatment: endoscopic endonasal approaches (EEAs) and transcranial approaches (TCAs). While EEAs offers a direct ventral route with enhanced visualization and direct access

✉ Edoardo Agosti
edoardo_agosti@libero.it

1 Division of Neurosurgery, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Piazza Spedali Civili 1, 25123 Brescia, Italy

2 Unit of Otorhinolaryngology, Head and Neck Surgery, Department of Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy

3 Neurosurgery, Fondazione Policlinico Universitario A. Gemelli IRCSS, Rome, Italy

4 Neurosurgery, Università Cattolica del Sacro Cuore, Rome, Italy

Published online: 17 February 2026

to the sellar and suprasellar regions, TCAs provide superior exposure for laterally or superiorly extending tumors [2–9].

Despite EEAs having increased in recent years, the comparative efficacy and safety of these approaches in the context of GPitNETs remains under debate [1–3].

Unlike previous meta-analyses, this study provides updated pooled estimates including a recent institutional cohort, with a specific focus on visual outcomes and ICH, which are not detailed in Tang et al. [4]. Furthermore, our work stratifies complications and radiological features in greater detail.

This systematic review and meta-analysis aim to compare EEAs and TCAs in terms of extent of resection (EoR), recurrence, visual improvement and postoperative complications.

Materials and methods

Systematic review and meta-analysis

Search strategy

This systematic review and meta-analysis were conducted in accordance with PRISMA guidelines [10]. A comprehensive literature search was performed in PubMed, Ovid MEDLINE, and Web of Science. The last search was updated on April 22, 2025. The full search strategy is provided in Supplementary Material (Fig. S1).

Study selection

Studies were considered eligible if they met the following criteria: (1) published in English; (2) reported clinical outcomes or postoperative complications related to GPitNETs; (3) included direct comparisons between TCAs and EEAs; and (4) reported at least one clinical or surgical outcome per surgical strategy. Exclusion criteria included: (1) editorials, reviews, conference abstracts or previously published meta-analyses; (2) studies without stratified surgical data; and (3) studies involving combined surgical techniques (comprising hybrid cases).

Data extraction

Two reviewers independently extracted data using a predefined template. The extracted data included: authorship, year of publication, sample size, patient demographics (age, sex), tumor characteristics (functioning/non-functioning, size, Knosp grade, cavernous sinus invasion), surgical technique, EoR (gross total, subtotal, partial), visual outcomes, postoperative complications (e.g., cerebrospinal fluid (CSF) leak, infections, cranial nerve deficits), use of adjuvant radiotherapy, and follow-up duration.

Outcomes of interest

The primary outcomes were the EoR and visual outcome. Gross total resection (GTR) was defined as no residual tumor on postoperative imaging. Visual improvement was defined as postoperative enhancement in visual acuity or field, as assessed by ophthalmologic examination. Cavernous sinus invasion was defined in the Results section as Knosp grade III-IV. Secondary outcomes included postoperative complications and tumor progression referred to the combined incidence of recurrence and regrowth. Recurrence was defined as the reappearance or progression of tumour tissue following GTR, whereas regrowth referred to an increase in the size of residual tumour after subtotal (STR) or partial resection (PR).

Risk of bias assessment

The methodological quality of the included studies was assessed using the ROBINS-I tool (Risk of Bias in Non-Randomized Studies of Interventions). The risk of bias was independently assessed by two reviewers, and discrepancies were resolved by discussion and consensus. Each study was evaluated across multiple domains including confounding, selection bias, deviations from intended interventions, and measurement of outcomes. The overall risk of bias was rated as low, moderate, or high (Fig. S2). Small-study effects or publication bias were not formally assessed due to the limited number of studies per outcome.

Statistical analysis

Statistics were performed using R statistical software (v. 4.3.2). Descriptive statistics of the systematic review were also performed to summarize baseline characteristics, radiological data, surgical data, surgical outcomes and postoperative complications of the included studies.

For the meta-analysis, the Mantel–Haenszel method with a random-effects model was used to estimate pooled odds ratios (ORs) for dichotomous outcomes. Heterogeneity was quantified using the I^2 statistic; I^2 values > 50% were considered indicative of substantial heterogeneity. A p-value < 0.1 for Cochran's Q test was deemed statistically significant. Zero-event studies were handled by applying a standard continuity correction of 0.5 in the Mantel–Haenszel random-effects model.

Retrospective institutional registry

Data collection

A single-center retrospective analysis was conducted and collected patients added to meta-analysis registry. Patients who underwent surgery for GPitNETs between January 2015 and December 2024 were included. Inclusion criteria mirrored those of the systematic review: adult patients (>or=18 years old) with histologically confirmed GPitNETs (>4 cm), treated with EEAs or TCAs.

This retrospective study was conducted in accordance with the principles outlined in the 1964 Declaration of Helsinki and its subsequent amendments. [11] The study protocol received approval from the Institutional Review Board (approval code: IRB-5924). Given the retrospective design of the study, the requirement for patient consent was waived by the Institutional Review Board, as all data were anonymized to protect patient privacy.

Statistical analysis

Data from the retrospective institutional registry were analyzed using R statistical software (v. 4.3.2). Descriptive statistics were computed to summarize patient demographics, clinical characteristics, and treatment outcomes. Categorical variables were presented as percentages, while continuous variables were reported as means with standard deviations.

Results

Systematic review

PRISMA data

A total of 567 publications were identified (150 from Pubmed, 592 from Ovid Medline, 123 from Web of Science). After removal of duplicates, 256 records underwent full-text screening. Among these, 21 studies met inclusion criteria the systematic review. Of these, 7 studies provided direct comparative data between EEA and TCA and were therefore included in the quantitative meta-analysis. Reasons for exclusion included irrelevant topic (n=195), lack of outcome data (n=15), absence of methodology (n=4), and not English (n=5), literature review and meta-analysis (n=16). The included studies encompassed clinical and surgical outcomes stratified by surgical approach.

The PRISMA statement's flow chart is seen in Fig. 1.

The PRISMA Extension for Scoping Reviews (PRISMA-ScR) checklist is available as supplementary material (Fig. S3).

Characteristics of the included studies

Data from published retrospective studies included 1032 patients with GPitNETs, of which 919 underwent EEAs and 113 TCAs. The mean age was similar in both groups (EEAs: 50.5 years; TCAs: 50.3 years), though male predominance was higher in the EEAs group (EEAs: 51.9%; TCAs: 30.9%). Functioning GPitNETs were observed in 15% of EEAs cases and 16.8% of TCAs cases.

Visual disturbances were common: combined visual field and acuity impairment affected59% and 51.3% of the EEAs and TCAs. Headache (EEAs: 10.5%; TCAs: 23.9%) and hydrocephalus (EEAs: 0.9%; TCAs: 9.7%) were more frequent in TCAs, while apoplexy was slightly more common in EEAs (EEAs: 4.5%; TCAs: 1.8%).

Tumors were slightly larger in the TCAs group (EEAs: 4.6 cm; TCAs:4.9 cm). Cavernous sinus invasion (Knosp grade III–IV) was present in 52.9% of EEAs and 59% of TCAs cases. Third ventricular invasion was also more common in TCAs (EEAs: 3.6%; TCAs: 5.3%).

Gross total resection was achieved in 38.1% of EEAs and 36.2% of TCAs. Partial resections were more frequent in TCAs (EEAs: 25.2%; TCAs: 35.4%). Progression rate was lower in the EEAs group (EEAs: 14.2%; TCAs: 28.8%). Adjuvant radiotherapy was reported in 8.5% of EEA and 15.6% of TCA cases.

Visual improvement was significantly higher in EEAs (72.2%) compared to TCAs (52.2%). Field improvement occurred in 80.9% of EEAs and 80.7% of TCAs cases; acuity improvement in 62.5% of EEAs. Hormonal remission in functioning tumors was rare (EEAs: 11.6%; TCAs: 10%).

Postoperative complications included CSF leaks (7.8%) exclusively in the EEAs group. Diabetes insipidus (EEAs: 21.2%; TCAs: 37.2%) and HP (EEAs: 14.7%; TCAs: 32.7%) were more frequent in TCAs patients. Persistent cranial nerve deficits occurred in 1.1% of EEAs and 5.2% of TCAs. The mean follow-up was 31.4 months.

A summary of baseline characteristics, radiological and surgical data, surgical outcomes, and post-operative complications of the included studies reporting on EEAs and TCAs for the surgical treatment of GPitNETs is presented in Tables 1, 2, 3.

Meta-analysis

A summary of the studies included in meta-analysis is presented in Fig. S4. Detailed baseline characteristics of the included studies, along with clinical and surgical outcome data used for the meta-analysis, are available in the Supplementary Material (Fig. S5-Fig. S6).

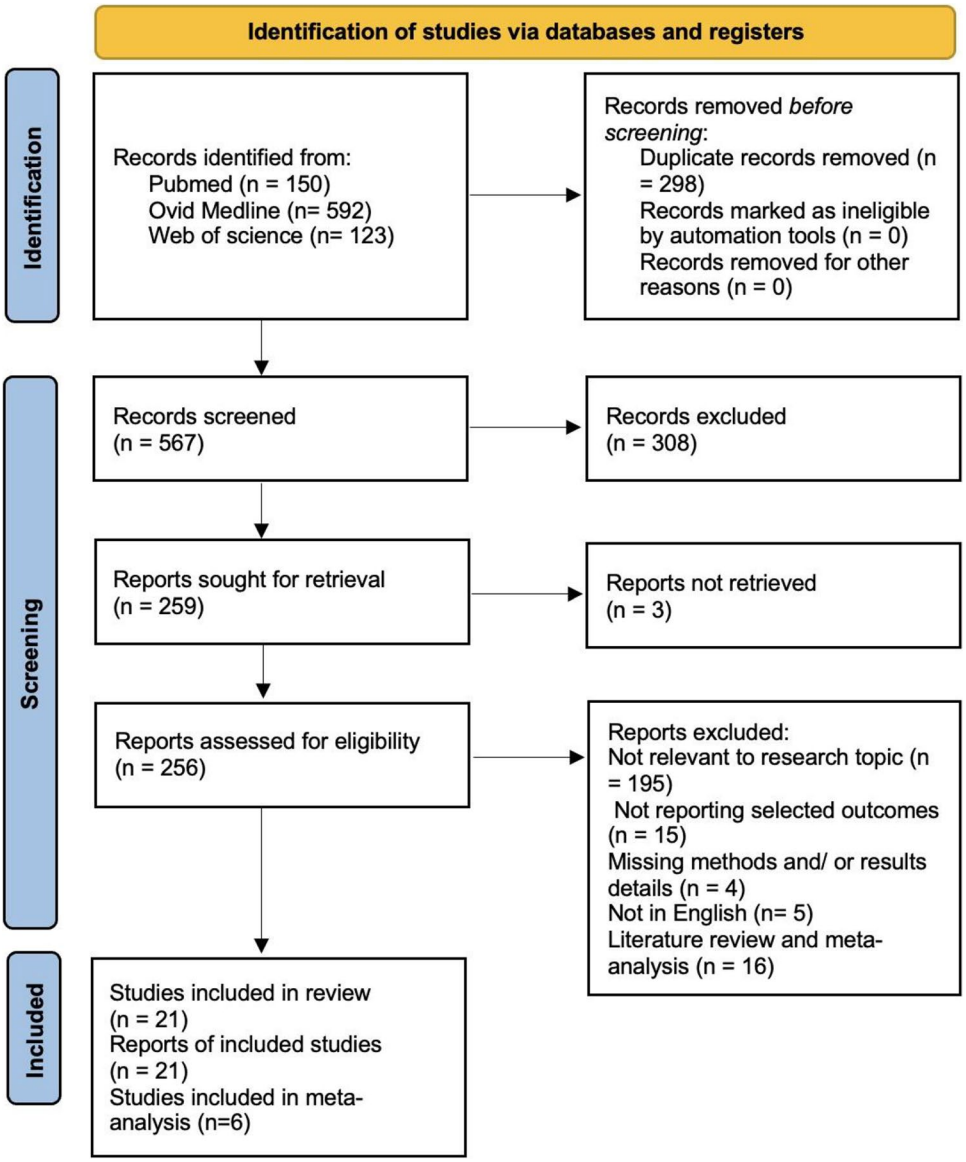

Fig. 1 PRISMA statement's flow chart

Surgical outcomes

Gross total resection

A total number of 7 studies comprising 273 patients have been included for the random effects meta-analysis. The rate of GTR in the EEAs group was 100/210 (47.6%), and it was 10/63 (15.9%) in the TCAs group. The meta-analysis of pooled data showed a trend toward benefit from EEAs in the rate of GTR (OR 2.65; 95% CI: 0.74–9.5; Fig. 2); however, the result did not reach statistical significance ($p = 0.14$). The I^2 statistic of 51.9% indicated a significant heterogeneity among included studies ($p = 0.05$).

Visual outcomes

A total number of 5 studies comprising 208 patients have been included for the random effects meta-analysis. The rate of visual improvement in the EEAs group was 133/156 (85.3%), and it was 34/52 (65.4%) in TCAs group. The meta-analysis of pooled data showed a significant benefit from the EEAs in terms of improved visual function (OR 3.73; 95% CI: 1.44–9.64; $p < 0.01$; Fig. 3). The I^2 statistic of 0% indicated no significant heterogeneity among included studies ($p = 0.91$).

Progression rate

A total number of 4 studies comprising 171 patients have been included for the random effects meta-analysis. The

Table 1 Baseline characteristics

Author and year	Patients (N)	Anamnestic data		Endocrinological data		Clinical features				Follow up (mean in months)
		Age (mean, range)	Male (N, %)	Functioning (F)/non functioning (NF)	Type of hormon (N)	Clinical presentation	Visual disturbance		Cranial nerve deficit	
							Acuity	field		
de Paivia Neto et al., [3]	51	48	32, 63%	NF (39, 76%) F (12, 23.6%)	ACTH (1, 8.3%) PRL (8, 66.7%) GH (3, 25%)	Hypopituitarism (41, 80.4%) Hyperprolactinemia (18, 43%) Apoplexy (13, 25.4%) Visual disturbance (38, 74.5%)	N/A	N/A	N/A	12
Guo et al., [8]	15	49.5 (24–63)	8, 53.3%	NF (10, 66.7%) F (5, 33.3%)	FSH (3, 6%) PRL (1, 2%) GH (1, 2%)	Headache (5, 33.3%) Gait disturbance (2, 13.3%) Visual disturbance (11, 73.3%)	N/A	N/A	N/A	N/A
Cusimano et al., [18]	58	EEA: 50.3 TCA: 53.5	EEA: 16, 55% TCA: 8, 27.6%	NF (EEA: 25, 86.2% TCA: 27, 93.1%) F (EEA: 4, 13.8% TCA: 2, 6.9%)	N/A	Headache EEA: 14, 48.2% TCA: 11, 37.9% Apoplexy: EEA: 2, 6.9% TCA: 2, 6.9%	N/A	68, 94.4%	11, 15.3%	73.9
Gondim et al., [21]	50	N/A	N/A	NF (42, 84%) F (8, 16%)	PRL (3, 37.5%) GH (5, 62.5%)	Headache (18, 36%) Gait disturbance and cognitive dysfunction (3. 6%), hydrocephalus (3, 6%) Visual disturbance (48, 96%)	N/A	N/A	16, 32%	60
Juraschka et al., [13]	73	54.5 (22–48)	50, 68.5%	NF (65, 89%) F (6, 8.2%)	N/A	Hypopituitarism (47, 64.4%) Apoplexy (6, 8.2%)	63, 86.3%	55, 75.4%	7, 9.6%	8
Chabot et al., [14]	6	56.3 (23–80)	N/A	N/A	N/A	N/A	6, 100%	5, 83.3%	N/A	12
Costantino et al., [29]	28	46 (15–62)	17, 60.7%	NF (23, 82,1%) F (5, 17.8%)	PRL (1, 20%) GH (2, 40%) GH/PRL (1, 20%) TSH (1, 20%)	Endocrinopaty (16, 57%) Headache (10, 35%) Hypogonadism (5, 17.8%), Hypothyroidism (4, 14.3%) Acromegaly (1, 3.6%) Galactorrhea (1, 3.6%) obstructive hydrocephalus (2, 7.1%), apoplexy (2, 7.1%)	12, 48%	N/A	N/A	30
Han et al., [36]	47	47.5	N/A	NF (EEA: 38, 88.7% TCA 4, 100%) F (7, 16.3%)	N/A	N/A	N/A	N/A	2, 3.2%	46.9
Elshazly et al., [26]	55	55.5 (22–88)	35, 64%	NF (51, 93%) F (4, 7.2%)	PRL (1, 25%) ACTH (1, 25%) GH (2, 50%)	Endocrinopaty (29, 52%) Visual impairment (49, 89.1%)	N/A	N/A	3, 5.5%	41
Peto et al., [16]	10	58.2	8,80%	NF (8, 80%) F (2, 20%)	PRL (2, 100%)	Headache (2, 20%) Hypothyroidism (2, 20%) Hypocortisolism (1, 10%) Panhypopituitarism (1, 10%)	N/A	7, 70%	2,20%	5.9

Table 1 (continued)

Author and year	Patients (N)	Anamnestic data		Endocrinological data		Clinical features				Follow up (mean in months)
		Age (mean, range)	Male (N, %)	Functioning (F)/non functioning (NF)	Type of hormon (N)	Clinical presentation	Visual disturbance		Cranial nerve deficit	
							Acuity	field		
Shen et al., [9]	37	43.6	12, 32.4%	NF (27, 72.9%) F (10, 27.0%)	GH (8, 80%) TSH (2, 20%)	Hydrocephalus (10, 27.0%) Visual impairment (37, 100%)	N/A	N/A	N/A	12
Ismail et al., [12]	21	EEA: 43.75 TCA: 47.11	EEA: 8, 66.7% TCA: 5, 55.6%	NF (EEA: 9, 75% TCA: 7, 77.8%) F (EEA: 3, 25% TCA: 2, 22.2%)	PRL (3, 60%) GH (2, 40%)	Headache EEA: 8, 66.7% TCA: 7, 77.8%	N/A	N/A	N/A	3
Ceylan et al., [33]	205	46.9 (16–80)	143, 69.7%	NF (153, 74.6%) F (52, 25.4%)	N/A	headache (77, 37.6%) pituitary dysfunction (165, 80.5%) Visual impairment (167, 81.5%)	N/A	N/A	5, 2.43%	50.2
Chibarro et al., [17]	96	52.2 (26–81)	55, 57.3%	NF (96, 100%)	N/A	Anterior pituitary insufficiency (53, 55.2%) Headache (12 12.5%) Drowsiness (3, 3.1%)	9, 9.4%	78, 81.3%	N/A	52.4
Jamaluddin et al., [19]	8	38.5 (17–52)	5, 62.5%	NF (6, 75%) F (2, 25%)	PRL (1, 50%) GH (1, 50%)	Headache (4, 50%) Ataxia (2, 25%) Seizures (1, 12.5%), Polyuria (2, 25%) Amenorrhea (1, 12.5%) Fatigue (2, 25%) Altered sensorium (1, 12.5%) memory disturbance (1, 12.5%)	N/A	6, 75%	N/A	24.6
Rahimli et al., [34]	44	46.9, (13–64)	31, 70.4%	NF (24, 54.5%) F (20, 45.5%)	PRL (11, 55%) GH (9, 45%)	Headache (14, 31.8%) Hypopituitarism (18, 40.9%) Apoplexy (12, 27.3%) Hydrocephalus (2, 4.5%) Visual impairment (33, 75%)	N/A	N/A	9, 20.5%	38.5
Micko et al., [35]	64	51 (22–84)	31, 48%	NF (57, 89%) F (7, 11%)	GH (4, 57.1%) PRL (2, 28.6%) ACTH (1, 14.3%)	Headache (36, 56%) Hypopituitarism (26, 41%) Visual impairment (55, 86%)	N/A	N/A	7, 11%	36
Ke et al., [37]	84	52.6	50, 53.2%	N/A	N/A	N/A	N/A	N/A	12, 10.7%	N/A
Saad et al., [38]	14	46.5 (25–47)	N/A	N/A	N/A	Headache (11, 78.6%) Hydrocephalus (6, 42.8%) hypopituitarism (9, 64.3%)	N/A	N/A	4, 28.6%	N/A
Krishna et al., 2024	29	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Table 1 (continued)

Author and year	Patients (N)	Anamnestic data		Endocrinological data		Clinical features				Follow up (mean in months)
		Age (mean, range)	Male (N, %)	Functioning (F)/non functioning (NF)	Type of hormon (N)	Clinical presentation	Visual disturbance		Cranial nerve deficit	
							Acuity	field		
Eguiluz-Melendezet al., [15]	37	48.1	23, 62.2%	NF: 32, 86.5% F: 5, 13.5%	GH (2, 40%) PRL (3, 60%)	Headache 22(59.5%)	36, 97.3%	35, 94.6%	7, 18.9%	23.8
Our institute	20	54.4, (22–79)	13, 65.0%	EEA: F (8, 44.4%) NF (10, 55.6%) TCA: NF (1, 50%) F (1, 50%)	PRL (2, 22.2%) FSH+LH (3, 33.3%) FSH (1, 11.1%) LH (1, 11.1%) TSH (1, 11.1%) GH (1, 11.1%)	Headache (5, 25.0%) Hypopituitarism (3, 15.0%) Diplopia (2, 10.0%) gait deficit (2, 10.0%) hydrocephalus (2, 10.0%)	EEA: 6/18 33.3% TCA:2/2 100%	EEA:13/18 72.2% TCA:2/2 100%	EEA: 3/18 16.7% TCA 0/2 0%	N/A

EEA = endoscopic endonasal approach, F = functioning, FSH = follicle- stimulating hormone, GH = growth hormone, N/A = not applicable, NF = non functioning, PRL = prolactin, TCA = transcranial approach

progression rate in the EEAs group was 24/126 (19.1%) and it was 18/45 (40%) in the TCAs group. No significant difference was detected in the progression rate between the two groups (OR 0.33, 95% CI: 0.11–1.03; p = 0.06; Fig. 4). The I^2 statistics of 22.9% indicated no significant heterogeneity among included studies (p = 0.27).

Postoperative complications

Cerebrospinal fluid leak

A total number of 7 studies comprising 273 patients have been included for the random effects meta-analysis. The rate of CSF leak in the EEAs group was 15/210 (7.1%), and it was 0/63 (0%) in the TCAs group. No significant difference was detected in the rate of CSF leak between the two groups (OR 1.51; 95% CI: 0.45–5.06; p = 0.5; Fig. 5). The I^2 statistic of 0% indicated no significant heterogeneity among included studies (p = 0.94).

Infections

A total number of 3 studies comprising 151 patients were included for random-effects meta-analysis. The rate of infection in the EEAs group was 8/133 (6%), and it was 3/18 (16.7%) in the TCAs group. No significant difference was detected in the rate of infections between the two groups (OR 0.27; 95% CI: 0.07–1.13; p = 0.07; Fig. 6). The I^2 statistics of 0% indicated no significant heterogeneity among included studies (p = 0.97).

Intracranial hemorrhage

A total number of 4 studies comprising 128 patients were included for the random-effects meta-analysis. The rate of ICH in the EEAs group was 2/84 (2.4%), and it was 8/44 (18.2%) in the TCAs group. The meta-analysis of pooled data showed a significantly higher risk from the TCA with respect to the rate of ICH (OR 0.09; 95% CI: 0.02–0.45; p < 0.01; Fig. 7). The I^2 statistic of 0 indicated no significant heterogeneity among included studies (p = 0.97).

Diabetes insipidus

A total number of 6 studies comprising 236 patients were included for the random-effects meta-analysis. The rate of DI in the EEAs group was 16/177 (9%), and it was 10/59 (16.9%) in the TCAs group. No significant difference was detected in the rate of DI between the two groups (OR 0.47; 95% CI: 0.18–1.23; p = 0.13; Fig. 8). The I^2 statistic of 19.6% indicated no significant heterogeneity among included studies (p = 0.32).

Hypopituitarism

A total number of 6 studies comprising 194 patients have been included for the random effects of meta-analysis. The rate of HP in the EEAs group was 28/137 (20.4%), and it was 17/57 (29.8%) in the TCAs group. No significant difference was detected in the rate of DI between the two groups (OR 0.77; 95% CI: 0.35–1.69; p = 0.52; Fig. 9). The

Table 2 Radiological and surgical data

Author and year	Radiological data				Surgical data					Second surgery	Post operative RT
					Reconstruction						
	Tumor size	Cavernous sinus invasion		Third ventricle invasion	Surgical approaches	Pedicle flap	Fascia lata	Fat graft	Gasket seal		
		Knosp grade (N, %)	Hardy grade (N,%)								
de Pavia Neto et al., [3]	4.5 cm	3 (14, 27.5%) 4 (17, 33%)	N/A		EEA (51, 100%)	N/A	N/A	N/A	N/A	N/A	12, 23.6%
Guo et al., [8]	5 cm	N/A	N/A	6, 40%	TCA (15, 100%)	N/A	N/A	N/A	N/A	N/A	5, 33.3%
Cusimano et al., [18]	EEA=4 cm, TCA=4.03 cm	N/A	N/A	N/A	EEA (29, 40.2%) TCA (29, 40.2%)	Mucosal flap (29, 100%)	6, 13.8%	N/A	N/A	EEA: 2,28.5% TCA: 6, 66.7%	N/A
Godim et al., [21]	5.4 cm	3 (8, 16%) 4 (8, 16%)	N/A	3, 6%	EEA (50, 100%)	N/A	N/A	N/A	N/A	10, 100%	RT (3, 6%)
Juraschka et al., [13]	4.1 cm	3 (23, 31.5%) 4 (11, 15.1%)	N/A	N/A	EEA (73, 100%)	Nasoseptal flap (62, 85%)	(11, 15%	N/A	N/A	7, 100%	RT (6, 8.2%)
Chabot et al., [14]	3–4 cm (33, 84.6%) >4 cm (6, 15.4%)	3 (5, 12.8%) 4 (10, 25.6%)	N/A	N/A	EEA (6, 100%)	N/A	N/A	N/A	N/A	N/A	N/A
Costantino et al., [29]	4.6 cm	N/A	N/A	N/A	EEA (28, 100%)	Nasoseptal flap (28, 100%)	N/A	N/A	N/A	9, 100%	N/A
Han et al., [36]	4.7 cm	N/A	N/A	N/A	EEA (43, 69.4%) TCA (4, 6.5%)	Nasoseptal flap (43, 72.6%)	N/A	N/A	N/A	N/A	N/A
Elshazly et al., [26]	5.1 cm	3A (13, 23%) 3B (8,15%) 4 (17, 31%)	N/A	18, 33%	EEA (55, 100%)	Nasoseptal flap (15, 28%)	15, 28%	N/A	N/A	1, 1.8%	10, 18.2%
Peto et al., [16]	N/A	N/A	N/A	N/A	EEA (10, 100%)	Nasoseptal flap (10, 100%)	N/A	N/A	N/A	N/A	N/A
Shen et al., [9]	4.8 cm	3 (9, 24.3%) 4 (13, 35.1%)	E (22, 59.5)	N/A	TCA (37, 100%)	Nasoseptal flap (14, 37.8%)	N/A	14, 37.8%	N/A	N/A	N/A
Ismail et al., [12]	N/A	N/A	N/A	N/A	TCA (9, 42.8%) EEA (12, 57.2%)	N/A	N/A	N/A	N/A	N/A	N/A
Ceylan et al., [33]	4.7 cm	N/A	N/A	N/A	EEA (205, 100%)	N/A	N/A	N/A	N/A	N/A	N/A
Chibarro et al., [17]	4.7 cm	3 (9, 9.4%) 4 (14, 14.6%)	N/A	N/A	EEA (96, 100%)	N/A	N/A	N/A	96, 100%	3, 3.1%	13, 13.5%
Jamaluddin et al., [19]	N/A	3 (3, 37.5%) 4 (3, 37.5%)	N/A	8, 100%	EEA (8, 100%)	Nasoseptal flap (8, 100%)	N/A	8, 100%	N/A	N/A	1, 12.5%
Rahimli et al., [34]	N/A	3A (16, 36.4%) 3B (1, 2.3%) 4 (16, 36.4%)	N/A	9, 20.4%	EEA (44, 100%)	Nasoseptal flap (44, 100%)	N/A	N/A	N/A	2, 4.5%	10, 22.7%
Micko et al., [35]	4.7 cm	N/A	N/A	N/A	EEA (64, 100%)	N/A	N/A	N/A	N/A	N/A	16, 25%

Table 2 (continued)

Author and year	Radiological data				Surgical data					Second surgery	Post operative RT
					Reconstruction						
	Tumor size	Cavernous sinus invasion		Third ventricle invasion	Surgical approaches	Pedicle flap	Fascia lata	Fat graft	Gasket seal		
		Knosp grade (N, %)	Hardy grade (N,%)								
Ke et al., [37]	4.5 cm	3 (29, 30.8%) 4 (10, 10.6%)	E (14, 14.9%)	N/A	EEA (72, 76.6%) TCA (12, 12.7%)	N/A	N/A	N/A	N/A	N/A	EEA: 9, 12.5% TCA: 6, 50%
Saad et al., [38]	5.1 cm	N/A	N/A	N/A	EEA (11, 35.5%) TCA (3, 9,7%)	N/A	N/A	N/A	N/A	N/A	N/A
Krishna et al., 2024	N/A	N/A	N/A	N/A	EEA (25, 86.2%) TCA (4, 13.8%)	N/A	N/A	N/A	N/A	N/A	N/A
Eguiluz-Melendezet al., [15]	N/A	3A (14, 37.8%) 3B (4, 10.8%) 4 (9, 24.3%)	N/A	N/A	EEA (37, 100%)	22, 59.5%	4, 10.8%	N/A	4, 10.8%	1, 100%	6, 16.2%
Our institute	EEA: 4.4 cm TCA: 5.9 cm	3A (EEA: 2, 11.1% TCA: 0, 0%) 4 (EEA: 3, 16.7% TCA: 1, 50%)	N/A	EEA: 4, 22.2% TCA: 2,100%	EEA (18, 90.0%) TCA (2, 10.0%)	N/A	N/A	N/A	N/A	2, 11.1%	N/A

EEA = endoscopic endonasal approach, TCA = transcranial approach, RT = radiotherapy

Table 3 Surgical outcomes and postoperative complications

Author and year	Surgical Outcomes					Postoperative Complications		
	Extent of Resection	Progression rate	Visual improvement	Disease remission if functioning	CN deficit improvement	CSF leak	CN deficit	Endocrine disorders
De Pavia Neto et al., [3]	GTR (21, 41%) STR (30, 59%)	7, 13.7%	31, 82%	N/A	N/A	1, 2%	N/A	N/A
Guo et al., [8]	GTR (10, 67%) STR (5, 33%)	0,0%	9, 82%	1, 6.7%	N/A	N/A	1, 6.7%	HP (3, 20%) DI (12, 80%)
Cusimano et al., [18]	EEA: GTR (6, 21%) STR (23, 79%) TCA=GTR (0, 0%) PR (29, 100%)	EEA: 7, 24% TCA: 9, 31.0%	EEA: 25, 86.2% MT: 12, 85.7% TCA: 21, 72.4%	N/A	EEA: 4, 100% MT: 4, 100% TCA: 2, 100%	1, 3.5%	N/A	HP: EEA (9, 31%) MT (5, 35.7%) TCA (12, 41.4%) DI: EEA (2, 7%) MT (2, 16.7%) TCA (3,10.3%)
Gondim et al., [21]	GTR (19, 38%) STR (9, 18%) PR (22, 44%)	10, 20%	38, 76%	1,2%	N/A	4, 8%	N/A	HP (18, 36%) DI (23, 46%)
Juraschka et al., [13]	GTR (16, 24%) STR (35, 53%) PR (15, 23%)	7, 9.6%	Acuity: 46, 73.0% Field: 34, 61.8%	N/A	5, 71.4%	7, 9.6%	N/A	SIADH (3, 4.1%)
Chabot et al., [14]	GTR (3, 50%) STR (3, 50%)	0, 0%	Acuity: 1, 16.7% Field: 3, 60%	N/A	N/A	N/A	N/A	N/A
Costantino et al., [29]	GTR (4, 14.3%) STR (14, 50%) PR (10, 35.7%)	9, 32%	9, 75%	4, 80%	N/A	5, 17.8%	1, 3.6%	DI (16, 57%) HP (10, 35.7%)
Han et al., [36]	EEA: GTR (11, 25.6%) STR (22, 51.2%) PR (10, 23.3%) TCA: GTR (3, 75%) STR (0, 0%) PR (1, 25%)	N/A	EEA: (35, 81.4%) TCA: (2,50%)	EEA: (3, 60%)	N/A	EEA: (2, 4.7%)	N/A	HP: EEA (1, 2.8%), TCA (0, 0%) DI: EEA (1, 2.4%%), TCA (2, 50%)
Elshazly et al., [26]	GTR (24, 44%) STR (31, 56.4%)	6, 11%	32, 67%	6, 20.1%	3, 100%	1, 2%	N/A	HP (8, 15%) DI (13, 24%) Apoplexy (1, 2%)
Peto et al., [16]	GTR (4, 40%) STR (5, 50%) PR (1, 10%)	N/A	5, 71.4%	N/A	N/A	7, 70%	N/A	HP (5, 50%) DI (5, 50%)
Shen et al., [9]	GTR (21, 57%) STR (15, 40.5%) PR (1, 2.7%)	N/A	16, 43%	N/A	N/A	N/A	3, 8%	HP (18, 49%) DI (20, 54%)
Ismail et al., [12]	TCA: GTR (1, 11.1%) STR (5, 55.6%) PR (3, 33.3%) EEA: GTR (5, 41.7%) STR (3, 25%) PR (4, 33.3%)	N/A	TCA: 2, 28.6% EEA: 5, 55.6%	EEA: 3, 100% TCA: 1, 50%	N/A	2, 16.7%	1, 8.3%	HP: TCA (2, 22.2%) EEA (4, 33%) DI: TCA (4, 44.4%) EEA (3, 25%)
Ceylan et al., [33]	GTR (72, 35.1%) STR (133, 64.9%)	N/A	109/167, 65.3%	N/A	N/A	8, 3.9%	N/A	HP: (46, 22.4%) DI: (16, 7.8%)
Chibbaro et al., [17]	GTR (34, 35.4%) STR (62 64.6%)	16, 17%	77, 99%	N/A	N/A	7, 7.3%	N/A	DI (37, 38%) Apoplexy (2, 2.1%)

Table 3 (continued)

Author and year	Surgical Outcomes					Postoperative Complications		
	Extent of Resection	Progression rate	Visual improvement	Disease remission if functioning	CN deficit improvement	CSF leak	CN deficit	Endocrine disorders
Jamaluddin et al., [19]	GTR (4, 50%) STR (4, 50%)	0, 0%	6, 100%	N/A	N/A	0, 0%	N/A	DI (2, 25%)
Rahmli et al., [34]	GTR (28, 64%) STR (10, 23%) PR (6, 14%)	4, 9%	27, 82%	N/A	6, 66.7%	5, 11%	N/A	DI (20, 46%)
Micko et al., [35]	GTR (18, 28%) STR (34, 53%) PR (12, 19%)	4, 9%	41/55, 74.5%	N/A	N/A	9, 14%	2, 3%	HP (11, 17%) DI (14, 21.9%)
Ke et al., [37]	EEA: GTR (49, 68.1%) STR (15, 20.1%) PR (8, 11.1%) TCA: GTR (3, 25%) STR (3, 25%) PR (6, 50%)	EEA: 9, 39.1% TCA: 6, 66.7%	EEA: 58, 87.7% TCA: 8, 11.1%	N/A	EEA: 7, 87.5% TCA: 2, 66.7%	EEA (4, 5.6%) TCA (0, 0%)	N/A	HP: EEA (3, 9.1%) TCA (1, 10%) DI: EEA (4, 6%) TCA (1,8.3%)
Saad et al., [38]	EEA: GTR (7, 63.6%) STR (3, 27.3%) TCA: GTR (1, 33.3%) STR (1, 33.3%) PR (1, 33.3%)	EEA: 5, 45.5% TCA: 3, 100%	N/A	N/A	N/A	EEA: 3, 27.7% TCA: 0, 0%	EEA: 2, 18.2% TCA: 1, 33.3%	HP: EEA (2, 18.2%) TCA (1, 33.3%) DI: EEA (2, 18.2%), TCA (0, 0%)
Krishna et al., 2023	EEA: GTR (10, 40%) STR (15, 60%) TCA: GTR (2, 50%) STR (2, 50%)	N/A	N/A	N/A	N/A	EEA: 2, 8% TCA: 0, 0%	N/A	N/A
Eguiluz-Melendez et al., [15]	GTR (15, 40.5%) STR (9, 24.3%) PR (13, 35.1%)	1, 2.7%	Acuity: 20/36, 55.6% Field: 19/35, 54.3%	N/A	5, 71.4%	4/37, 10.8%	5/28, 17.9%	HP: (28, 75.6%) DI: (26, 70.2%)
Our institute	EEA: GTR (12, 66.7%) STR (3, 16.7%) PR (3, 16.6%) TCA: GTR (1, 50%) STR (1, 50.0%)	EEA: 3, 21.4% TCA: 0, 0%	Acuity: EEA: 5, 83.3% TCA: 1, 50% Field: EEA: 10, 76.9% TCA: 1, 50%	N/A	N/A	EEA: 1, 5.9% TCA: 0, 0%	N/A	HP: EEA (9, 69.2%) TCA (1, 50%); DI: EEA (5, 31.3%) TCA (0, 0%)

EEA = endoscopic endonasal approach, GTR = gross total approach, HP = hypopituitarism, PR = partial resection, STR = subtotal resection, SIADH = syndrome of inappropriate antidiuretic hormone secretion, TCA = transcranial approach

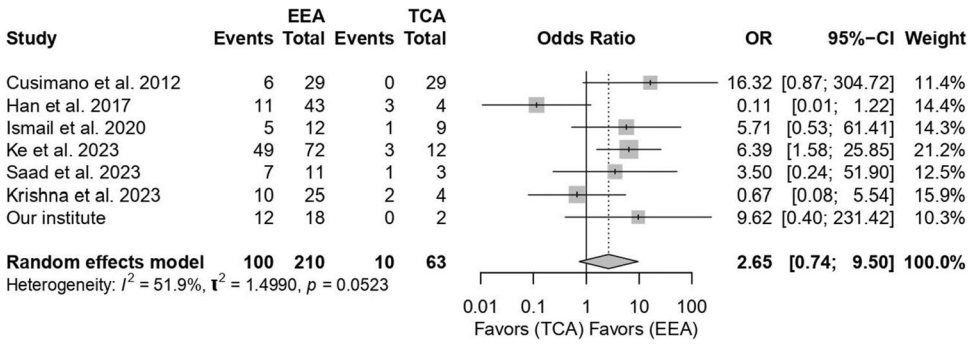

Fig. 2 Forest plot of GTR comparing EEAs and TCAs for GPitNETs

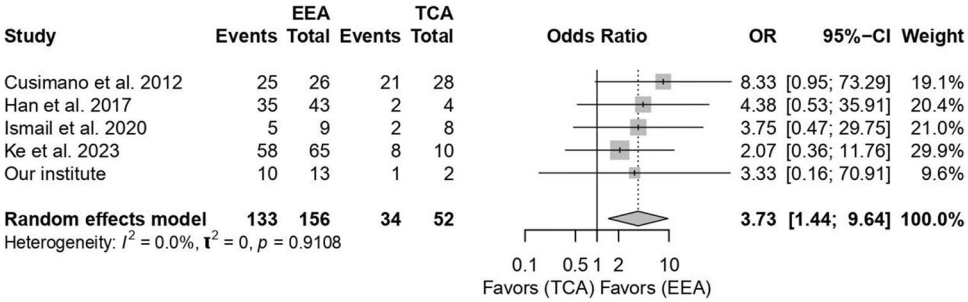

Fig. 3 Forest plot of visual improvement comparing EEAs and TCAs for GPitNETs

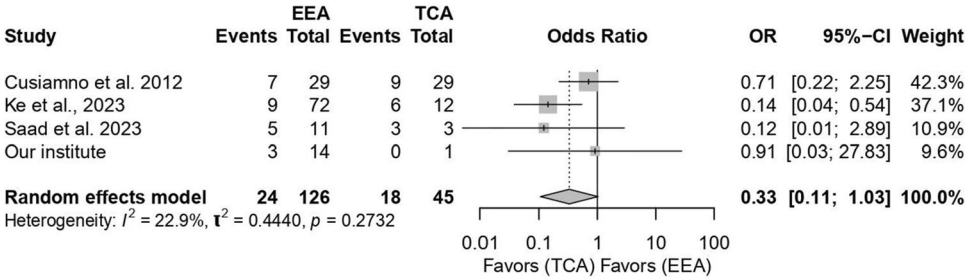

Fig. 4 Forest plot of progression rate comparing EEAs and TCAs for GPitNETs

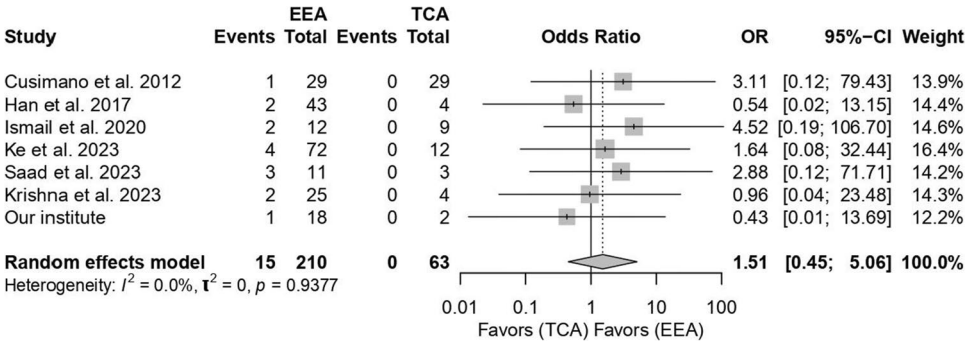

Fig. 5 Forest plot of CSF leak comparing EEAs and TCAs for GPitNETs

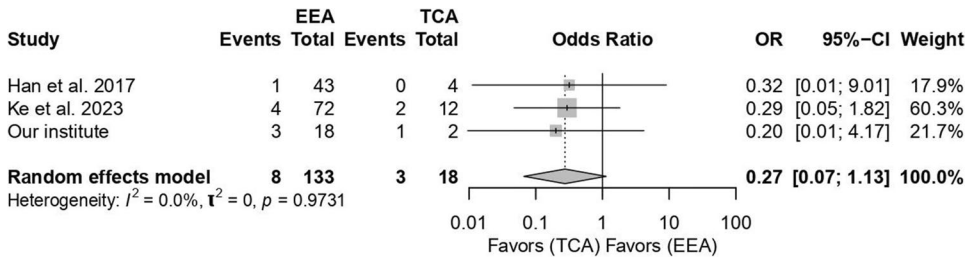

Fig. 6 Forest plot of postoperative infection comparing EEAs and TCAs for GPitNETs

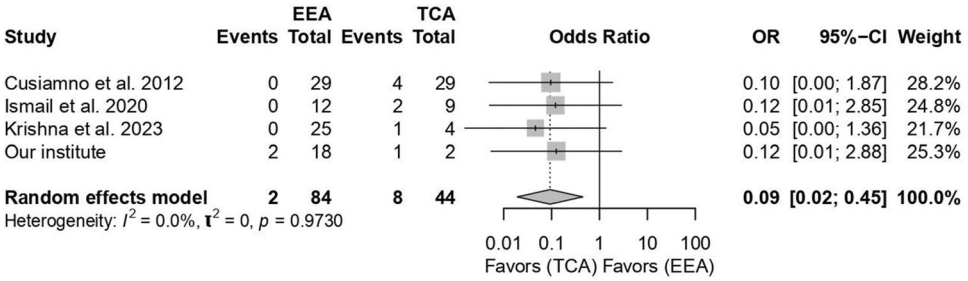

Fig. 7 Forest plot of postoperative ICH comparing EEAs and TCAs for GPitNETs

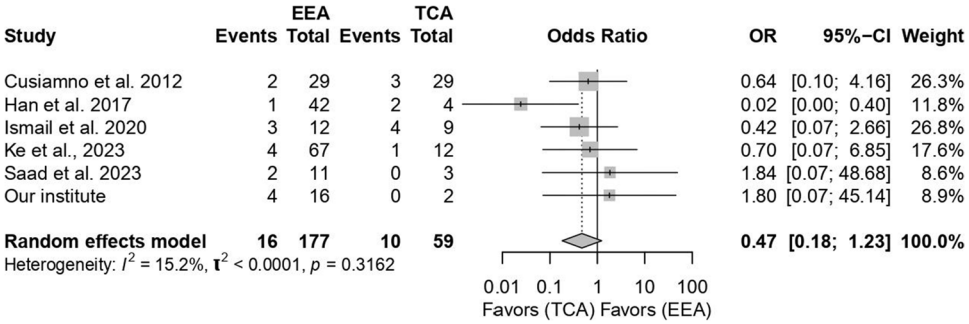

Fig. 8 Forest plot of postoperative DI comparing EEAs and TCAs for GPitNETs

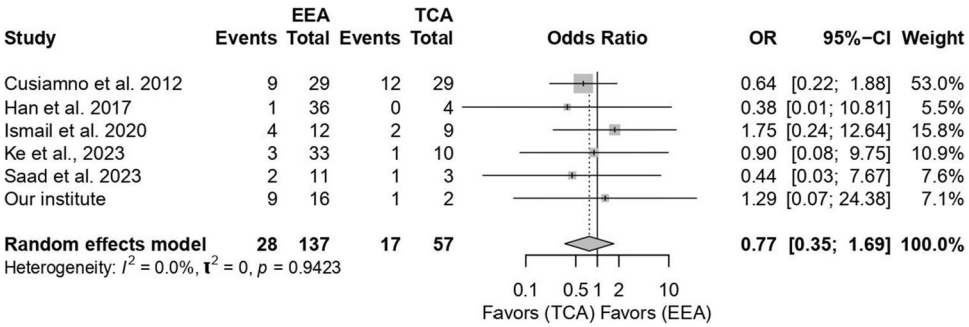

Fig. 9 Forest plot of postoperative HP comparing EEAs and TCAs for GPitNETs

I^2 statistics of 0% indicated no significant heterogeneity among included studies (p = 0.94).

Retrospective institutional cohort

Characteristics of the included studies

Between 2015 and 2024, 20 patients with GPitNETs were treated. Of these, 18 (90%) underwent EEAs, and 2 (10%) underwent TCAs. The mean age was lower in the EEAs group (53.6 ± 17.8 years) compared to the TCA group (65.5 ± 14.8 years). Most EEAs patients were male (72.2%), while both TCAs patients were female.

Functioning PitNETs were observed in 44.4% of patients in the EEAs group (8 of 18) and 50% in the TCAs group (1 of 2). Visual acuity deficits and visual field defects were more frequent in the TCAs group (100% for both visual acuity and visual field deficit) compared to the EEAs group (33.3% for visual acuity and 72.2% for visual field deficit). Headache (33.3%), apoplexy (22.2%), and hydrocephalus (5.6%) occurred only in the EEAs group, except for 1 TCAs patient with hydrocephalus (50%). Cavernous sinus invasion was detected in 27.8% of EEAs cases and in one TCAs patient (Knosp 4). Third ventricular invasion was present in 27.8% of EEAs patients and both TCAs cases.

Gross total resection was achieved in 66.7% of EEAs patients, while none of the TCAs patients underwent GTR. Subtotal and partial resections were performed in 16.7% of cases treated via the EEAs, respectively. Among cases managed with the TCAs, the resection rate was equally distributed, with 50% being subtotal and 50% partial. Progression occurred in 21.4% of EEA patients and in none of the TCA cases. All patients with recurrence underwent a second surgery, one underwent adjuvant RT. Among patients with preoperative visual impairment, improvement in visual acuity and visual fields was observed in 66.7% and 76.9% of EEAs patients, respectively. In the TCAs group, 1 patient (50%) improved and 1 (50%) remained stable. Postoperative complications in the EEAs group included CSF leak (5.6%), DI (16.7%), HP (56.3%), ICH (5.6%), and infection (5.6%). In the TCA group, HP, ICH, and infection each occurred in 50% of patients. The mean follow-up was 57 months.

Discussion

This systematic review and meta-analysis compared EEAs and TCAs for GPitNETs. Endoscopic endonasal approaches were associated with a higher rate of visual improvement. No significant difference was found in GTR or progression rates. An increased risk of ICH for TCAs was detected, while no significant differences were observed in CSF leak, infection, DI, and HP between the two approaches.

As reported by Ismail et al. [12], several anatomical and tumor-related factors including cavernous sinus invasion, anterior or lateral extension, suprasellar growth into the third ventricle, and firm tumor consistency can limit the possibility of achieving gross total resection. Endoscopic endonasal approaches are favored in midline, soft tumors, whereas TCA are often reserved for more complex or laterally extending lesions, or when prior transsphenoidal surgery has altered anatomical landmarks [13–21]. Variants

such as a poorly pneumatized sphenoid sinus or encasement of vascular structures may also restrict EEAs [22]. As a result, despite the advantages of the EEA, GTR and progression rates may remain comparable to TCA in practice, especially in anatomically complex cases [23–25]. In these cases, adjuvant radiotherapy (RT) plays a critical role in achieving long-term tumor control. Elshazly et al.[26] report that although GTR was accomplished in most of patients via EEAs, 10 out of 55 patients still required postoperative RT to manage residual disease. As emphasized by Gondim et al. [21], a strategy combining STR followed by RT (3 patients out of 9 with STR, 33.3%) offers a balanced approach that avoids surgical morbidity while maintaining disease control. Although statistical significance was not achieved, the lower progression rate observed after EEA compared with TCA may have clinical relevance, as it could reflect improved resection of midline and suprasellar lesions through enhanced visualization and direct tumor access.

The superior visual outcomes observed with the EEAs can be explained by tumor-induced displacement of the optic chiasm. As described by Agosti et al. [27], a prechiasmatic lesion such as a pituitary adenoma can mimic a postfixed chiasm configuration by pushing the optic chiasm posteriorly. This displacement enlarges the infrachiasmatic surgical corridor, making it more accessible via an endonasal trajectory. Endoscopic endonasal approaches offer a direct line of sight to this corridor from below, facilitating safer tumor manipulation and reducing the need for brain retraction. In contrast, TCAs are limited by the interposed optic apparatus, particularly when the chiasm is displaced posteriorly, thus restricting visibility and access to the tumor base [27–29]. The superior visual outcomes observed with EEAs likely reflect a combination of anatomical and surgical factors rather than solely a tumour-induced ‘post-fixed’ chiasm configuration. Variables such as tumour extension pattern, consistency, cisternal expansion, and vascular relationships (particularly with the superior hypophyseal arteries and ICA) play a crucial role in determining approach feasibility and visual recovery.

Biochemical remission rates were low (11.6% for EEA and 10% for TCA), reflecting the difficulty of achieving hormonal control in large, invasive functioning adenomas and the frequent need for adjuvant therapy.

Transcranial approaches have been associated with a higher risk of ICH compared to EEA. This increased risk is likely due to the need for brain retraction, longer operative times, and greater manipulation of vascular structures. EEAs minimize cerebral handling and provide direct access to the tumor, reducing vascular injury [16, 18, 25, 30].

While CSF leak is traditionally a concern with EEAs, no significant difference (OR 1.51; 95% CI: 0.45–5.06) in CSF leak rates was found in our meta-analysis. Improvements in reconstruction techniques, including the use of vascularized flaps and multilayer closures, have likely reduced CSF leak rates in EEAs to levels comparable to TCAs [31–34].

Additionally, no significant differences were found between EEAs and TCAs regarding the incidence of postoperative infection, DI, or HP [16, 35]. These outcomes are likely influenced more by tumor characteristics such as size, invasiveness, and proximity to the pituitary stalk than by the surgical approach itself [18, 36–38].

Outcomes may also be influenced by the surgical learning curve and institutional experience, as previously reported in the literature. A staged or combined strategy (initial EEA followed by a TCA) can optimize resection of giant PitNETs by leveraging the strengths of each corridor, minimizing brain retraction and midline access during EEA then addressing lateral or superior extensions with TCA. For example, Endoscopic transcranial transdiaphragmatic approach in a single-stage surgery for giant pituitary adenomas reported that a combined approach enabled safe maximal excision of GPitNETs with extensive suprasellar extension [39].

Limitations

Although our search strategy included PubMed, Ovid MEDLINE, and Web of Science, the exclusion of other major databases such as Embase and the Cochrane Library may have resulted in the omission of relevant studies, potentially limiting the completeness of the evidence base. Only 7 comparative studies met the criteria for quantitative synthesis. This limited sample size reduces the statistical power of our findings. There is also a marked imbalance in sample size between the EEA and TCA groups, which represents a potential limitation and may have affected the meta-analytical estimates. Moreover, the observed heterogeneity ($I^2 = 51.9\%$) indicates moderate statistical variability in the GTR outcomes across studies. This may reflect differences in study design, reporting, or baseline characteristics, although not necessarily clinical heterogeneity. Further, none of the included studies were randomized, and most had a moderate risk of bias as assessed using the ROBINS-I V2 tool, particularly in the domain of confounding, where surgical strategy was often determined by tumor anatomy and surgeon preference without statistical adjustment. In addition, relevant variables such as tumor consistency, degree of vascular encasement, and intraoperative factors were not consistently reported across studies, precluding a more detailed analysis of their influence on surgical outcomes. Furthermore, no meta-regression or subgroup analyses could be performed due to insufficient stratified data, which limits the ability to explore potential effect modifiers such as tumor size, invasion grade, or

surgical approach selection. Histopathological, and biological heterogeneity among GPitNETs was not accounted for, as information on tumor subtype, proliferative markers, and hormonal activity was inconsistently reported across studies. Additional limitations include variability in reporting of baseline data, such as tumor consistency or cavernous sinus invasion, and the lack of long-term follow-up data in several studies. Due to the limited number of comparative studies, we could not formally assess small-study effects or publication bias, which may influence the robustness of pooled estimates. The small number of comparative studies per outcome precluded reliable sensitivity analyses (e.g., leave-one-out analysis or Baujat plots) to further explore sources of heterogeneity. Moreover, the inclusion of our institutional cohort as one of the comparative datasets in the meta-analysis may represent a further source of selection bias and confounding by indication, which should be considered when interpreting the pooled results. Finally, outcome definitions (EoR, progression, or visual improvement) were not always standardized, which has introduced further inconsistency in pooled estimates.

Conclusions

This meta-analysis suggests that EEAs are associated with superior visual outcomes and a lower risk of ICH compared to TCAs in the treatment of GPitNETs. However, no significant differences were observed between the two techniques in terms of GTR, recurrence, or other postoperative complications. From a surgical perspective, the EEAs are preferrable for GPitNETs associated with a postfixed optic chiasm configuration, whereas TCAs remain indicated for tumors with significant lateral or superior extension beyond the endonasal corridor.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10143-025-04101-z.

Authors' contribution S.A. and E.A. designed the study and performed the literature search, data extraction, and meta-analysis. P.P.P., A.F., V.R., F.D., and M.M.F. supervised each stage of the systematic review and meta-analysis process, including study selection, methodological choices, and interpretation of data. E.A. drafted the manuscript. All authors critically revised the manuscript for intellectual content and approved the final version.

Funding No funding has been received.

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethical approval We received approval by the Institutional Review Board (approval code: IRB-5924).

Informed consent Not applicable.

Clinical trial number Not applicable.
This systematic review was not registered in PROSPERO.

Conflict of interest The authors declare no competing interests.

References

1. Tang OYY, Hsueh WDD, Liu JKK, Eloy J (2022) Giant pituitary adenoma - special considerations. Otolaryngol Clin North Am 55(2):351–379
2. Louis RG, Eisenberg A, Barkhoudarian G, Griffiths C, Kelly DF (2014) Evolution of minimally invasive approaches to the sella and parasellar region. Int Arch Otorhinolaryngol 18(2):S136-148
3. de Paiva Neto MA, Vandergrift A, Fatemi N, Gorgulho AA, Desalles AA, Cohan P et al (2010) Endonasal transsphenoidal surgery and multimodality treatment for giant pituitary adenomas. Clin Endocrinol (Oxf) 72(4):512–519
4. Tang OY, Chen JS, Monje S, Kumarapuram S, Eloy JA, Liu JK (2025) Comparison of surgical modalities for giant pituitary adenoma: a systematic review and meta-analysis of 1413 patients. Oper Neurosurg 28(1):1–18. https://doi.org/10.1227/ons.0000000000001238
5. Fatemi N, Dusick J, de Paiva Neto M, Kelly D (2008) The endonasal microscopic approach for pituitary adenomas and other parasellar tumors: a 10-year experience. Oper Neurosurg (Hagerstown) 63(4):244–56
6. Hall WA, Das JM. Transsphenoidal Hypophysectomy. In: StatPearls. Treasure Island (FL): StatPearls http://www.ncbi.nlm.nih.gov/books/NBK556142/
7. Salama MM, Rady MR (2021) Transcranial approaches for pituitary adenomas: current indications and clinical and radiological outcomes. Egypt J Neurosurg 36(1):21. https://doi.org/10.1186/s41984-021-00117-x
8. Guo F, Song L, Bai J, Zhao P, Sun H, Liu X et al (2012) Successful treatment for giant pituitary adenomas through diverse transcranial approaches in a series of 15 consecutive patients. Clin Neurol Neurosurg 114(7):885–890
9. Shen M, Chen Z, Shou X, Ma Z, Ye Z, He W et al (2020) Surgical Outcomes and Predictors of Visual Function Alterations After Transcranial Surgery for Large-to-Giant Pituitary Adenomas. World Neurosurg 141:e60-9
10. Page M, Moher D, Bossuyt P, Boutron I, Hoffmann T, Mulrow C, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. OSF; https://osf.io/gwdhk_v1
11. Resneck JS Jr (2025) Revisions to the declaration of Helsinki on its 60th anniversary: a modernized set of ethical principles to promote and ensure respect for participants in a rapidly innovating medical research ecosystem. JAMA 333(1):15–17
12. Ismail M, Ragab OAAAM, Salama MM, Ayoub BM, Elmahdy W (2020) Transcranial versus endoscopic transsphenoidal approaches in management of recurrent giant pituitary adenomas. Open Access Maced J Med Sci 8:273–80
13. Juraschka K, Khan OH, Godoy BL, Monsalves E, Kilian A, Krischek B et al (2014) Endoscopic endonasal transsphenoidal approach to large and giant pituitary adenomas: institutional

experience and predictors of extent of resection. J Neurosurg 121(1):75–83
14. Chabot JD, Chakraborty S, Imbarrato G, Dehdashti AR (2015) Evaluation of outcomes after endoscopic endonasal surgery for large and giant pituitary macroadenoma: a retrospective review of 39 consecutive patients. World Neurosurg 84(4):978–988
15. Eguiluz-Melendez A, Sangrador-Deitos MV, Calderón-Yrigoyen PJ, Rodríguez-Hernández AL, Guinto-Nishimura YG, Alcazar-Felix JR et al (2024) Clinical and Surgical Outcomes of Endoscopic Endonasal Approach for Giant Pituitary Adenomas: Analysis of Predictive Factors. World Neurosurg 184:e659-73
16. Peto I, Abou-Al-Shaar H, White T, Abunimer A, Kwan K, Zavadskiy G et al (2020) Sources of residuals after endoscopic transsphenoidal surgery for large and giant pituitary adenomas. Acta Neurochir 162(10):2341–2351
17. Chibbaro S, Signorelli F, Milani D, Cebula H, Scibilia A, Bozzi M et al (2021) Primary endoscopic endonasal management of giant pituitary adenomas: outcome and pitfalls from a large prospective multicenter experience. Cancers. https://doi.org/10.3390/cancers13143603
18. Cusimano M, Kan P, Nassiri F, Anderson J, Goguen J, Vanek I et al (2012) Outcomes of surgically treated giant pituitary tumours. Can J Neurol Sci J Can Sci Neurol 39(4):446–457
19. Jamaluddin MA, Patel BK, George T, Gohil JA, Biradar HP, Kandregula S et al (2021) Endoscopic Endonasal Approach for Giant Pituitary Adenoma Occupying the Entire Third Ventricle: Surgical Results and a Review of the Literature. World Neurosurg 154:e254-63
20. Yano S, Hide T, Shinojima N (2017) Efficacy and complications of endoscopic skull base surgery for giant pituitary adenomas. World Neurosurg 99:533–542
21. Gondim JA, Almeida JPC, Albuquerque LAF, Gomes EF, Schops M (2014) Giant pituitary adenomas: surgical outcomes of 50 cases operated on by the endonasal endoscopic approach. World Neurosurg 82(1–2):e281-290
22. Emengen A, Yilmaz E, Gokbel A, Uzuner A, Balci S, Tavukcu Ozkan S et al (2025) Refining endoscopic and combined surgical strategies for giant pituitary adenomas: a tertiary-center evaluation of 49 cases over the past year. Cancers (Basel) 17(7):1107
23. Famurewa OC, Ibitoye BO, Ameye SA, Asaleye CM, Ayoola OO, Onigbinde OS (2018) Sphenoid sinus pneumatization, septation, and the internal carotid artery: a computed tomography study. Niger Med J 59(1):7–13
24. Elwy R, Younes AR, Elsamman AK (2024) Effect of the extent of posterior septectomy on surgical access during the endoscopic endonasal approach to the sella: a technical note. Brain Spine 4:102831
25. Kasemsiri P, Prevedello DMS, Otto BA, Old M, Filho LD, Kassam AB et al (2013) Endoscopic endonasal technique: treatment of paranasal and anterior skull base malignancies. Braz J Otorhinolaryngol 79(6):760–779
26. Elshazly K, Kshettry VR, Farrell CJ, Nyquist G, Rosen M, Evans JJ (2018) Clinical outcomes after endoscopic endonasal resection of giant pituitary adenomas. World Neurosurg 114:e447-56
27. Agosti E, Alexander AY, Leonel LCPC, Pinheiro-Neto CD, Peris-Celda M (2022) Endoscopic endonasal surgical anatomy through the prechiasmatic sulcus: the key window to suprachiasmatic and infrachiasmatic corridors. Acta Neurochir (Wien) 164(7):1929–1938
28. Norris JH, Norris JS, Akinwunmi J, Malhotra R (2011) Optic canal decompression with dural sheath release; a combined orbito-cranial approach to preserving sight from tumours invading the optic canal. Orbit 31(1):34–43. https://doi.org/10.3109/01676830.2011.605500
29. Constantino ER, Leal R, Ferreira CC, Acioly MA, Landeiro JA (2016) Surgical outcomes of the endoscopic endonasal transsphenoidal approach for large and giant pituitary adenomas: institutional experience with special attention to approach-related complications. Arq Neuropsiquiatr 74(5):388–395
30. Karki M, Sun J, Yadav CP, Zhao B (2017) Large and giant pituitary adenoma resection by microscopic trans-sphenoidal surgery: surgical outcomes and complications in 123 consecutive patients. J Clin Neurosci 44:310–314
31. Joshi K, Kolb B, Khalili B, Munich S, Byrne R (2024) Surgical strategies in the treatment of giant pituitary adenomas. Oper Neurosurg 26(1):4–15
32. Laing B, Best B, Aaronson D, Harrison G, Zwagerman N (2024) Predictors and complications of cerebrospinal fluid leak after endoscopic endonasal surgery: a single institution retrospective review. J Neurol Surg B Skull Base 85(1):9–14
33. Ceylan S, Sen HE, Ozsoy B, Ceylan EC, Ergen A, Selek A et al (2022) Endoscopic approach for giant pituitary adenoma: clinical outcomes of 205 patients and comparison of two proposed classification systems for preoperative prediction of extent of resection. J Neurosurg 136(3):786–800
34. Rahimli T, Hidayetov T, Yusifli Z, Memmedzade H, Rajabov T, Aghayev K (2021) Endoscopic endonasal approach to giant pituitary adenomas: surgical outcomes and review of the literature. World Neurosurg 149:e1043-55
35. Micko A, Agam MS, Brunswick A, Strickland BA, Rutkowski MJ, Carmichael JD et al (2022) Treatment strategies for giant pituitary adenomas in the era of endoscopic transsphenoidal surgery: a multicenter series. J Neurosurg 136(3):776–785
36. Han S, Gao W, Jing Z, Wang Y, Wu A (2017) How to deal with giant pituitary adenomas: transsphenoidal or transcranial, simultaneous or two-staged? J Neurooncol 132(2):313–321
37. Ke D, Xu L, Wu D, Yang S, Liu S, Xie M et al (2023) Surgical management of giant pituitary adenomas: institutional experience and clinical outcomes of 94 patients. Front Oncol 13:1255768
38. Saad M, Taha A, Serag S, Shata H, Zakaria W (2023) Giant invasive pituitary adenomas: surgical approach selection paradigm and its influence on the outcome-case series. Egypt J Neurosurg. https://doi.org/10.1186/s41984-023-00214-z
39. Wu X, Bao Z, Tian W, Wang J, Miao Z, Wang Q, Lu X (2023) Endoscopic transcranial transdiaphragmatic approach in a single-stage surgery for giant pituitary adenomas. Front Oncol 13:1133861. https://doi.org/10.3389/fonc.2023.1133861