



Two- and three-dimensional endoscopic endonasal surgery of large and giant pituitary adenomas—outcome analysis of a series of 62 patients from a single pituitary center

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Abstract

To analyze the perioperative course and clinical outcome of patients with large (IPA) and giant (gPA) pituitary adenoma who underwent endoscopic endonasal transsphenoidal surgery (EETS) using either two-dimensional (2D-E) or three-dimensional (3D-E) endoscopic systems. Single-center retrospective study of consecutive patients with IPA and gPA who underwent EETS between November 2008 and January 2023. LPA were defined as ≥ 3 cm and < 4 cm in diameter in at least one dimension and a volume of ≥ 10 ccm; gPA were defined as larger than 4 cm in diameter and with a greater volume than 10ccm. Patient data (age, sex, endocrinological and ophthalmological status) and tumor data (histology, tumor volume, size, shape, cavernous sinus invasion according to the Knosp classification) were analyzed. 62 patients underwent EETS. 43 patients were treated for IPA (69.4%) and 19 patients for gPA (30.6%). 46 patients (74.2%) underwent surgical resection using 3D-E and 16 patients 2D endoscopy (25.8%). Statistical results are referred to the comparison between 3D-E and 2D-E. Patients' age ranged from 23–88 years (median 57), 16 patients were female (25.8%), 46 male (74.2%). Complete tumor resection was possible in 43.5% (27/62), partial resection in 56.5% (35/62). Resection rates did not differ between 3D-E (27 patients [43.5%]) and 2D-E (7 patients [43.8%], ($p = 0.985$)). Visual acuity improved in 30 of 46 patients with preoperative deficit (65.2%). In the 3D-E group 21 of 32 patients (65.7%) improved, compared to 9 of 14 patients in the 2D-E group (64.3%). Improvement of visual field was achieved in 31 of 50 patients (62.0%; 22 of 37 patients in the 3D-E group [59.4%] and 9 of 13 patients in the 2D-E group [69.2%]). CSF leak was the most frequent complication and occurred in 9 patients (14.5%, [8 patients 17.4% 3D-E]) without statistical significance. Other surgical complications like postoperative bleeding, infection (meningitis) and deterioration of visual acuity and field were detected without statistical difference. New pituitary anterior lobe dysfunction was observed in 30 of 62 patients (48.4%, 8 patients [50.0%] in the 2D-E group and 22 patients [47.8%] in the 3D-E group). A transient deficit of posterior lobe was detected in 22.6% (14/62). No patient died within 30 days of surgery. Although 3D-E may improve surgical dexterity, in this series of IPA and gPA it was not associated with higher resection rates compared to 2D-E. However, 3D-E visualization during resection of large and giant PA is safe and feasible and patient's clinical outcome is not different compared to 2D-E.

Keywords 2D endoscopy · 3D endoscopy · Pituitary adenoma · Giant pituitary adenoma (gPA) · Large pituitary adenoma (IPA) · Endoscopic endonasal transsphenoidal surgery (EETS)

Introduction

Pituitary Adenomas (PA) account for 10–25% of intracranial tumors [11, 21]. Large and giant PA are less common and surgical treatment of these tumors may be challenging. Definitions of large pituitary adenoma (IPA) are lacking

consistency [9], but in most recently series they were classified as IPA with a maximum diameter in any plane greater than 3 cm and a tumor volume larger than 10ccm [26, 38]. Giant pituitary adenoma (gPA) are commonly defined as larger than 4 cm in diameter [7, 24, 37] and having a volume greater than 10ccm [35]. Transcranial and transsphenoidal microsurgical approaches, simultaneously or consecutively have been advocated while endoscopic transsphenoidal surgery has become the standard treatment in the majority of

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large and giant PA in recent years [7, 24, 26, 33–35, 38, 46]. Endoscopic endonasal transsphenoidal surgery (EETS) has been reported to result in higher tumor resection rates, improved visual outcome, a higher percentage of pituitary function preservation, less postoperative complications and decreased hospital stay [16, 34, 49]. However, surgery of IPA and gPAs remains challenging [24] and treatment often requires multiple approaches not only because of their particular size, invasiveness and extrasellar extension but also because of encasement of neurovascular structures and multi-compartment growth. The disadvantage of endoscopic surgery is the lack of binocular stereoscopic vision, reduced depth perception, image distortion, reduced hand eye coordination and difficulties in estimating the correct size of objects. Three-dimensional (3D) endoscopy (3D-E) may have, at least from a technical point of view, the potential to overcome the disadvantages of two-dimensional (2D) endoscopy (2D-E). A few series show, that three-dimensional endoscopic pituitary surgery has similar results compared to 2D endoscopy [3, 22, 25, 51]. However, no data are published comparing the use of 3D-E and 2D-E for surgery of large and giant pituitary adenomas. Therefore, we aimed to analyze the results of our consecutive series of patients with IPA and gPA with regard to tumor resection, perioperative complications, mortality and morbidity as well as ophthalmological and endocrine outcome.

Material and methods

Study design

This is a retrospective, single center observational surgical case series, performed in a tertiary referral center including a consecutive series of patients with endoscopic endonasal transsphenoidal surgery for treatment of PA. The study was approved by the local ethics committee (Reference number 22748/2016/32). Data of all patients who underwent EETS were retrieved from a prospectively maintained database of sellar and parasellar tumors at the authors' institution. Between November 2008 and January 2023, 480 patients with lesions of the anterior and central skull base underwent EETS. Patients with large and giant PA were included, while patients with other pathologies (craniopharyngiomas, chordomas, meningiomas, cysts etc.) were excluded from further analysis.

Patient's characteristics (age, gender, endocrinological and ophthalmologic status) were continuously entered into the database. In addition, tumor variables were added (histology, tumor size, tumor volume, tumor extension, shape and growth direction, hemorrhagic apoplexy). The extension of the tumor into the intra-, para- and suprasellar space was assessed separately. For definition of parasellar growth, the

Knosp criteria were applied [29]. The maximum diameter on preoperative MRI (either T1- or T2-weighted imaging; coronal, sagittal, or axial slices) was determined for each case. Preoperative tumor volume was analyzed using the Brainlab Elements software (Brainlab AG, Munich, Germany) based on thin sliced preoperative MRI data sets using the manual segmentation tool function by 2 authors (RG and DL).

Large pituitary adenomas (IPA) were defined as ≥ 3 cm and < 4 cm in at least one dimension and ≥ 10 ccm in volumetric analysis. Giant pituitary adenomas (gPA) were classified as larger than 4 cm in diameter and more than 10ccm in volume. The median follow-up was 4 years.

Perioperative complications, such as postoperative hemorrhage (intracranial, nasal), cerebrospinal fluid (CSF) leak with the necessity for lumbar drainage, revision surgery or ventriculoperitoneal shunt as well as meningeal infection or pneumocephalus were analyzed.

Extent of resection was evaluated by comparing pre- vs. postoperative (8 to 12 weeks) contrast-enhanced MR-imaging. Complete resection was defined as no residual tumor visible on postoperative MRI. If remaining tumor was detected on postoperative MRI, it was defined as partial resection without further subdivision.

Endocrinologic assessment

All patients had standardized preoperative endocrinological testing and re-testing 8 to 12 weeks after surgery. Any new deficit of any element of the pituitary axis compared to preoperative tests was considered as new deficit. Endocrinological remission was defined in accordance with the most recent consensus criteria [4, 18].

Ophthalmologic assessment

All patients underwent pre- and postoperative ophthalmologic investigation and change in visual acuity and visual fields was assessed.

Surgical treatment

All patients were operated by an interdisciplinary team of a neurosurgeon (R.G.) and otorhinolaryngologist (G.K.). The patients were operated using one of the 3 different endoscopy systems, 2D-HD, 3D-SD or 3D-HD. The visualization systems used during the EETS have been used in accordance with their availability, but not randomly selected. During the first years, the 2D-HD endoscopy system (Karl Storz, Germany) was used. Subsequently, 3D-SD (VisionSense vsii) and 3D-HD (VisionSense vsiii) (VisionSense, New York) became available, which were successively utilized. EETS was performed without procedural modifications over the entire time period. Surgery was performed using image

guidance (Brainlab AG, Munich, Germany). All patients were observed in the ICU overnight and referred to the peripheral ward 1 day after surgery, in the absence of postoperative complications.

Statistical analysis

Statistical analysis was performed using SPSS software version 25.0 (Chicago, USA). Non-parametric statistical tests (Kolmogorov–Smirnov test and Kruskal–Wallis) were used to compare the two categories and their variables. Chi-square (X^2) test and Wilcoxon test were applied to compare continuous variables between the different EETS-visualization technique groups. For the conducted analysis, *p* values less than 0.05 were considered to be statistically significant ($\alpha=0.05$).

Results

62 patients underwent endoscopic EETS for treatment of IPA or gPA. No patient died within 30 days of surgery. The patients' age ranged from 23 to 88 years (median 57), 16 patients were female (25.8%) and 46 male (74.2%). In general, patient and tumor characteristics were found to be normally distributed (age, sex and tumor volume, growth direction and recurrence rate) although a ratio of 2.88:1 was detected for the two different endoscopic visualization groups (3D-E:2D-E, Kolmogorov–Smirnov test). Altogether, there was no significant difference of the patient's preoperative characteristics such as age, sex, number of hormone secreting tumors and inactive adenomas, ophthalmologic and endocrine status. For tumor variables (largest diameter, volume, growth direction, tumor shape and hemorrhagic apoplexy) no significant differences were found (X^2 test; Table 1).

43 patients underwent EETS for treatment of an IPA (69.4%) and 19 patients (30.6%) for a gPA. The rate of patients with IPA and gPA was not statistically significant between groups. 46 patients (74.2%) underwent surgical resection using 3D-E and 16 patients (25.8%) using 2D-E. Of the 43 patients with IPA, 32 patients underwent EETS using 3D-E and 2D-E was used in 11 cases. Of the 19 patients, who suffered from a gPA, 14 were operated with 3D-E and 5 with 2D-E (Table 1).

Although neither the tumor volume nor the largest diameter was significantly different between the 3D-E and 2D-E group it is worth mentioning that in the 3D-E group less patients had a round-shaped PA and more patients had a multilobular tumor shape compared to the 2D-E group (Table 1). 5 patients underwent an extended approach during EETS for tumor resection in the 3D-E group (Table 2). However, extent of tumor resection did not significantly differ

between the 3D-E and 2D-E visualization technique. EETS using 3D-E resulted in complete resection in 20 patients (43.5%) and partial resection in 26 of 46 patients (56.5%) compared to 7 patients (43.8%) with complete resection and 9 patients (56.3%) with partial resection in the 2D-E group, respectively (X^2 test: $p=0.985$, Table 3).

The overall rate of preoperative ophthalmological deficits (visual acuity and visual field) was high in the whole cohort. In the 3D-E group, 32 of 46 patients (69.6%) had reduced visual acuity and 37 had deficits in visual field (80.4%). In the 2D-E group, the number of patients with ophthalmological deficits was even higher (visual acuity deficit was detected in 14 of 16 patients [87.5%] and deficit of visual field in 13 of 16 cases [81.3%]; Table 1). During follow-up, the postoperative ophthalmological assessment revealed that 30 of overall 46 patients (65.2%) had visual acuity improvement, 21 of 32 patients in the 3D-E group (65.7%) and nine of 14 patients in the 2D-E group (64.3%). Overall improvement of visual field was achieved in 31 of 50 cases (62.0%). 22 of 37 patients (accordingly 59.4%) presented with a better visual field in the 3D-E group compared to 9 of 13 patients (69.2%) in the 2D-E group (Tables 1 and 4). In 13 of all 62 patients (48.4%) postoperative visual acuity remained stable (9 [19.6%] in the 3D-E group and 4 [25.0%] in the 2D-E group), regardless of whether they had a visual deficit preoperatively or not. In 18 of all 62 patients (29.0%) the visual field remained stable postoperatively (15 [32.6%] in the 3D-E group and 3 [18.8%] in the 2D-E group), regardless of whether they had a preoperative deficit or not (Tables 1 and 4). Worsening of visual acuity occurred in 6 patients overall, all of which were in the 3D-E group (6/46 [13.0%]). 1 patient, who was also in the 3D-E group, suffered from postoperative deterioration of the visual field. However, there was no statistical significance for both complications compared to the 2D-E group ($p=0.376$ and $p=0.777$).

The overall number of perioperative complications was statistically significantly higher in the group of patients who underwent EETS using 3D-E (16 out of 46 patients) compared to one patient out of 16 in the 2D-E group ($p<0.05$, X^2 test). However, when all types of complications were assessed separately (postoperative hemorrhage, CSF leak, meningitis and deterioration of visual acuity and visual field) there was no statistically significant difference between both visualization groups (Table 4). The complication rate was not depended on tumor volume, tumor extension, intratumoral hemorrhage, endocrinological status or previous surgical treatment.

Intraoperative CSF leak occurred in 21 of 46 patients in 3D-E group (45.7%) and in 6 of 16 patients in 2D-E group (37.5%), without statistical difference ($p=0.571$, X^2 test). However, one of the most frequent complications was postoperative CSF leak, which was encountered in 8 (17.4%) and 1 (6.25%) patients in the 3D-E and 2D-E group, respectively.

Table 1 Patients and tumor baseline characteristics

	total	3D-E	2D-E	<i>p</i> -values
Number of patients with IPA or gPA	62 (100%)	46 (74.2%)	16 (25.8%)	
Recurrent Tumors	9/62 (14.5%)	7/46 (15.2%)	2/16 (12.5%)	<i>p</i> = 0.790
Age in years				
Mean	57.6	57.0	59.4	<i>p</i> = 0.688
Median	57.0	57.0	59.5	
Min	23	23	36	
Max	88	88	76	
Range	65	65	40	
Sex				
Female	16/62 (25.8%)	12/46 (26.0%)	4/16 (25.0%)	<i>p</i> = 0.931
Male	46/62 (74.2%)	34/46 (73.9%)	12/16 (75.0%)	
Tumor volume in cm ³				
Mean	18.48	18.31	18.96	
Median	15.45	15.45	15.95	
Min	10.30	10.30	10.30	<i>p</i> = 0.143
Max	60.50	60.50	38.50	<i>p</i> = 0.7415
Range	50.20	50.20	28.20	
Standard deviation (SD)	9.70	10.05	8.93	
Tumor volume (≥ 10 cm ³)	62/62 (100%)	46/46 (100%)	16/16 (100%)	
LPA (≥ 3 cm und < 4 cm in at least one dimension)	43/62 (69.4%)	32/46 (69.6%)	11/16 (68.8%)	<i>p</i> = 0.951
GPA (≥ 4 cm in at least one dimension)	19/62 (30.6%)	14/46 (30.4%)	5/16 (31.3%)	<i>p</i> = 0.951
Largest diameter in cm	6.4	6.3	6.4	<i>p</i> = 0.627
Tumor growth				
intrasellar	62/62 (100%)	46/46 (100%)	16/16 (100%)	<i>p</i> = 1.000
parasellar	39/62 (62.9%)	29/46 (63.0%)	10/16 (62.5%)	<i>p</i> = 0.970
suprasellar	61/62 (98.4%)	45/46 (97.8%)	16/16 (100%)	<i>p</i> = 0.156
CSI (Knosp classification ≥ 2)	55/62 (88.7%)	40/46 (87.0%)	15/16 (93.8%)	<i>p</i> = 0.460
Tumor Shape				<i>p</i> = 0.755
Round	19/62 (30.6%)	13/46 (28.3%)	6/16 (37.5%)	
Dumbbell-shaped	24/62 (38.7%)	18/46 (39.1%)	6/16 (37.5%)	
Multilobular	19/62 (30.6%)	15/46 (32.6%)	4/16 (25.0%)	
Intratumoral hemorrhage	11/62 (17.8%)	6/46 (13.0%)	5/16 (31.3%)	<i>p</i> = 0.101
Hormone inactive PA	51/62 (82.3%)	40/46 (87.0%)	11/16 (68.8%)	<i>p</i> = 0.101
Visual acuity deficit	46/62 (74.2%)	32/46 (69.6%)	14/16 (87.5%)	<i>p</i> = 0.158
Visual field deficit	50/62 (80.6%)	37/46 (80.4%)	13/16 (81.3%)	<i>p</i> = 0.943
Endocrinological deficit				<i>p</i> = 0.317
No	31/62 (50.0%)	23/46 (50.0%)	8/16 (50%)	
Partial	22/62 (35.5%)	18/46 (39.1%)	4/16 (25%)	
Complete	9/62 (14.5%)	5/46 (10.9%)	4/16 (25%)	
Anterior lobe	31/62 (50.0%)	23/46 (50.0%)	8/16 (50%)	<i>p</i> = 1.000
Posterior lobe	3/62 (4.8%)	2/46 (4.3%)	1/16 (6.3%)	<i>p</i> = 0.760

Preoperative data (absolute numbers and %) on patients, tumor size and volume, extension and growth direction, ophthalmological and endocrinological status etc. in the two different groups, who underwent ETTS. Volumetric analysis was performed using Brainlab software). No significant differences were found between techniques

Eight patients (12.9%) were treated with lumbar drainage and all 9 patients (14.5%) underwent revision surgery ($p = 0.276$ and $p = 0.357$; X^2 test). Postoperative epistaxis occurred in 5 out of 46 patients in the 3D-E group (10.9%). Meningeal

infection was suspected or proven after lumbar puncture and culturing CSF in 4 of 62 patients (6.45%, Table 4).

New pituitary anterior lobe dysfunction was observed in 30 of 62 patients (48.4%, 8 patients [50.0%] in the 2D-E

Table 2 Surgical specifications

	total	3D-E	2D-D	p-values
Extended endonasal approach	5/62 (8.1%)	5/46 (8.9%)	0/16 (0.0%)	<i>p</i> = 0.315
Duraplasty	54/62 (87.1%)	40/46 (87.0%)	14/16 (87.5%)	<i>p</i> = 0.955
Autologous	35/62 (56.5%)	24/46 (52.2%)	11/16 (68.8%)	
Xenogenic	19/62 (30.6%)	16/46 (34.8%)	3/16 (18.8%)	
Combined	18/62 (29.0%)	15/46 (32.6%)	3/16 (18.8%)	
Intraoperative CSF leak	27/62 (43.5%)	21/46 (45.7%)	6/16 (37.5%)	<i>p</i> = 0.571

Extension of endoscopic approach, intraoperative CSF leak and duroplasty (absolute numbers and %). No significant differences were found between the two groups

Table 3 Outcome

	total	3D-E	2D-D	p-values
Extent of resection				
Complete	27/62 (43.5%)	20/46 (43.5%)	7/16 (43.8%)	<i>p</i> = 0.985
Partial	35/62 (56.5%)	26/46 (56.5%)	9/16 (56.3%)	
Further treatment				
Second surgery	7/62 (11.3%)	6/46 (13.0%)	1/16 (6.25%)	<i>p</i> = 0.460
Endonasal	4/62 (6.5%)	3/46 (6.5%)	1/16 (6.25%)	
Transcranial	3/62 (4.8%)	3/46 (6.5%)	0/16 (0.0%)	
Radiotherapy	10/62 (16.1%)	7/46 (15.2%)	3/16 (18.8%)	
Conventional	1/62 (1.6%)	1/46 (2.2%)	0/16 (0.0%)	
Radiosurgery	9/62 (14.5%)	6/46 (13.0%)	3/16 (18.8%)	
Adjuvant medical therapy	4/62 (6.5%)	4/46 (8.7%)	0/16 (0.0%)	
New endocrine deficit				
Anterior lobe	30/62 (48.4%)	22/46 (47.8%)	8/16 (50.0%)	<i>p</i> = 0.881
Posterior lobe	14/62 (22.6%)	10/46 (21.7%)	4/16 (25.0%)	<i>p</i> = 0.788
Postoperative visual acuity				
Improved	30/62 (48.4%)	21/46 (45.7%)	9/16 (56.3%)	<i>p</i> = 0.465
Stable	13/62 (21.0%)	9/46 (19.6%)	4/16 (25.0%)	<i>p</i> = 0.645
Postoperative visual field				
Improved	31/62 (50.0%)	22/46 (47.8%)	9/16 (56.3%)	<i>p</i> = 0.562
Stable	18/62 (29.0%)	15/46 (32.6%)	3/16 (18.8%)	<i>p</i> = 0.293
30-day-mortality	0/62 (0.0%)	0/46 (0.0%)	0/16 (0.0%)	<i>p</i> = 1.000

Extent of resection, further treatment and endocrinological and ophthalmological outcome (absolute number and %) following EETS

Table 4 Postoperative complications

	total	3D-E	2D-D	p-values
Postoperative bleeding				
Intracranial	1/62 (1.6%)	1/46 (2.2%)	0/16 (0.0%)	<i>p</i> = 0.844
Nasal	5/62 (8.1%)	5/46 (10.9%)	0/16 (0.0%)	<i>p</i> = 0.991
CSF leak				
Revision surgery	9/62 (14.5%)	8/46 (17.4%)	1/16 (6.25%)	<i>p</i> = 0.276
Lumbar drainage	8/62 (12.9%)	7/46 (15.2%)	1/16 (6.25%)	<i>p</i> = 0.357
Meningitis	4/62 (6.45%)	4/46 (8.7%)	0/16 (0.0%)	<i>p</i> = 0.565
Postoperative deterioration of visual acuity	6/62 (9.7%)	6/46 (13.0%)	0/16 (0.0%)	<i>p</i> = 0.376
Postoperative deterioration of visual field	1/62 (1.6%)	1/46 (2.2%)	0/16 (0.0%)	<i>p</i> = 0.777
Overall complication rate (per patients)	17/62 (27.4%)	16/46 (34.8%)	1/16 (6.35%)	<i>p</i> = 0.028

Postoperative complications such as hemorrhage, CSF leak with revision surgery and visual deterioration (absolute number and %) in all patients, who underwent EETS with different visualization techniques

group and 22 patients [47.8%] in the 3D-E group). A new deficit of the posterior lobe was detected in 22.6% (14/62).

Discussion

Endonasal transsphenoidal endoscopic surgery is considered as state-of-the-art treatment for patients with pituitary adenomas [5, 43]. This holds especially true for large and giant PA with extrasellar extension and multilobular growth and/or encasement of critical neurovascular structures [12, 20, 26, 31, 33–35, 46, 56]. Improvement in visualization technique and image resolution with high definition (HD) or 4 K displays [10, 48], the understanding of tumor growth patterns [55] and the detailed anatomical knowledge of critical neurovascular structures with improved outcome of patients [15, 52, 53] fostered a broader application of endoscopy over the recent years in patients with large and giant PA.

However, the lack of stereoscopic vision remains a major disadvantage of 2D endoscopy. Thus, 3D endoscopy, which enables stereoscopic vision with improved depth perception during endoscopic surgery, may help to overcome the limitations of 2D endoscopy. 3D-E may allow for improved dexterity and safety during surgical resection of large and giant PA while working behind and around neurovascular structures and identifying tissue planes for dissection. This can aid in recognizing layers of dissection and understanding neurovascular relationships especially in the suprasellar space [41, 54]. The first application of a rigid 3D endoscope in EETS was described in 2009 [51]. Over the recent years, 3D-E underwent further refinement and the development of endoscopes with smaller diameters and improvement in image quality with HD resolution resulted in 3D-E implementation in a few pituitary centers, which has been described in a limited number of reports [1–3, 13, 22, 27, 39, 41, 44, 47]. A few authors compared surgical results of 3D-E to 2D-E for primary or recurrent PA. They found similar extent of resection and complication rates compared to 2D-E and no difference for perioperative (estimated blood loss, operative time) and postoperative factors (length of stay, complications, and readmission rate) [3, 22, 27]. Barkhoudarian et al. found a significantly shorter total operative time, which was needed for adenoma resection in the 3D-E group independently of the surgical experience (residents or fellows). In particular, residents, who were inexperienced with endoscopy, were quicker to learn how to manipulate the 3D endoscope, especially for maneuvers within the sphenoid sinus [3]. However, a broad acceptance of 3D-E in EETS is missing. This may be due to periprocedural strain and dizziness, general discomfort, the need to wear polarization glasses or reduced color fidelity, although the learning curve for implementation of 3D-E was rather flat [14].

Extend of resection

To the best of our knowledge, no data are published for patients with large and giant PA who underwent EETS using 3D-E so far. We therefore analyzed a consecutive series of patients with IPA and gPA, who underwent EETS. All operations were performed by the same interdisciplinary surgical team, which excludes a surgeon-related bias. A recent definition of IPA was applied [9, 23]. Latest studies suggest a volume of ≥ 10 ccm as a definition of giant pituitary adenomas, rather than the conventional definition of a tumor diameter larger than 4 cm. Thus, we analyzed large and giant PA together and the total mean tumor volume in this series was 18.1ccm, which therefore compares well with other studies, eg. Cusimano et al. (mean preoperative tumor volume was 19.95 ± 15.69 ccm) [9]. The maximum tumor diameter in our patients was 6.4 cm, which was also comparable to the other studies [40, 56]. Other authors, namely Cappabianca et al. pointed out, that “size does not matter”; instead, attention should mostly be paid to the pattern of intracranial growth [5]. Moreover, hemorrhagic component, posterior extension and sphenoid sinus invasion were found to be significant predictors for the extent of resection [26]. In this series of patients with large and giant PA who were treated with 3D-E and 2D-E, complete resection was achieved in almost half of the cases (43.5% complete resection and 56.5% partial resection in 3D-E group compared to 43.8% complete and 56.3% partial resection in the 2D-E group). Therefore, no statistically significant difference was found. Our resection rate compares well with other series [20, 35, 40, 56].

Juraschka et al. describe a complete resection in 24.2%, near-total ($\geq 90\%$) 16.7%, subtotal (70%–89.9%) in 36.4%, and partial ($< 70\%$) in 22.7% after EETS for large and giant PA [26]. Cusimano et al. reported a 20.7% GTR rate and 90.6% average resection rate using a binostiril EETS [9]. Gondim et al. recently published a series of patients with gPA (> 4 cm) with total removal of the tumor occurred in 38%, near-total removal in 18%, and partial removal in 44% [20]. In a larger series of 239 patients with gPA Chen et al. reported gross-total resection was achieved in 19.25%, near total in 23.43%, subtotal in 28.45%, and partial in 28.87% patients [7]. Yano et al. found a near-total resection of gPA in 16 of 34 (47.1%) cases. Near total resection was achieved significantly more often in anterior extension types and round tumor in superior extension types compared with multiple extension types [56]. Koutourousiou et al. achieved near-total resection ($> 90\%$) in 66.7% in 2013 [31]. In a series of large and giant PA Fallah et al. achieved gross total resection in 82.5%, near-total resection in 12.5%, and subtotal resection 5% [12]. Komotar et al. conducted a systematic review of endoscopic transsphenoidal surgery for giant (≥ 4 cm) pituitary adenomas, and described GTR of 47.5% [30]. Thus, there is a remarkable discrepancy in the reported

resection rates of large and giant pituitary adenomas depending on the postoperative definition of residual tumor.

Koutourousiou et al. found the “true limitations of endoscopic endonasal surgery” are tumors with a multilobular configuration and extensions beyond the lateral wall of the cavernous sinus [31]. Moreover, the lateral extension of PA into the middle fossa is also a limitation of the endoscopic approach and can be a reason for incomplete resection [34]. In this series, 63% of all patients were found to have a parasellar tumor extension and 93.8% (3D-E group) and 88.7% (2D-E group) had a cavernous sinus invasion greater than Knosp 2. Micko et al. published a series including gPA where overall gross-total resection rates were 64% in round gPAs, 46% in dumbbell-shaped gPAs, and 8% in multilobular gPA [35]. They concluded that EETS is “a primary treatment modality to relieve mass effect in GPAs and extent of resection are dependent on gPA morphology” [35]. In the 3D-E group, 30.6% of patients had a multilobular tumor extension compared to 25% in the 2D-E group. 38.7% had a dumbbell shape tumor in the 3D-E group and 37.5% 2D-E group, which may explain the relatively high number of residual tumor, as it was shown by Micko et al., that the neck-to-dome area ratio was of prognostic value for prediction of intraoperative tumor non-descent in dumbbell shaped adenoma [36].

Ophthalmological outcome

Our postoperative data showed that 30 of 46 patients (65.2%) had visual acuity improvement. In 31 of 50 cases (62.0%) visual field was improved after EETS, which is comparable to other series where improvements are reported to be between 60–90% [9, 12, 19, 20, 31, 42, 45, 56].

Perioperative complications

“Giant adenomas are not only difficult to resect but also have a greater risk of complications “ as constituted by Iglesias et al. [24]. In 2017, Nishioka et al. presented a surgical series of 128 giant nonfunctioning adenomas. Permanent surgical complications developed in 28 patients (22.0%) [40]. In our study the overall complication rate was 27.4% and therefore was comparable to the series from Nishioka et al. One of the most frequent complications was postoperative CSF leak, which was encountered in 8 (17.4%) and 1 (6.25%) patients for 3D-E and 2D-E, respectively (overall in 14.5%). They were treated with lumbar drainage and underwent revision surgery, but without statistically significant difference between the 3D-E and 2D-E groups (X^2 test: $p=0.276$ and $p=0.357$). The rate of postoperative CSF leaks in this cohort is in line with published reports, which postulated an incidence of 0–16% [6, 28, 32, 50, 57–59].

In previous studies, new anterior pituitary insufficiency following EETS of gPA was detected in 16–36% of cases [8, 12, 20, 31]. In our series, new pituitary anterior lobe dysfunction was observed in 30 of our 62 patients (48.4%). This relatively high number might be due to our relatively short follow-up period and the application of the latest diagnostic criteria.

Limitation of the study

A number of limitations have to be addressed. It is a retrospective single-center case series with a limited and an unbalanced number of patients per group ($n=16$ in the 2D-E and $n=46$ in the 3D-E group, respectively), with a ratio of 2.88:1. The majority of patients operated with 2D-E were treated at the beginning of the series and the application of the 3D-E and 2D-E systems varied later on according to their availability. We are well aware that each surgery increases the experience of the surgeon, especially in this long period of more than 14 years. However, the resection rate of the 3D and 2D endoscopy group are comparable. This may be due to the fact that even before starting to operate in an interdisciplinary team, both surgeons were trained over many years and had a large experience with regard to operative skills and also scientific evaluation of new technical developments during surgery [17]. In addition, we did not perform a side-by-side analysis during certain steps of surgery, which requires an increase of technical efforts during surgery and prolongs operation time.

Conclusion

In this series of patients with large and giant PA, the application of different 3D and 2D visualization systems during surgery did not show a significant difference for resection rate or for postoperative outcome. Our results show, that 3D-E is feasible for resection of large and giant PA.

Authors' contribution Denise Loeschner: data collection, statistical analysis, preparation of manuscript.

Andrei Enciu: data collection, literature research.

Gerald Kellner: surgery, data collection, approval.

Almuth Meyer: endocrinological diagnostic, data collection.

Henri Wallaschofski: endocrinological diagnostic, data collection.

Anna Cecilia Lawson McLean: statistical analysis, edition of the manuscript.

Ruediger Gerlach: study design, surgical treatment, data collection, statistical analysis, preparation of manuscript, final approval.

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Denise Loeschner, Anna Cecilia Lawson McLean and Ruediger Gerlach. The first draft of the manuscript was written by Denise Loeschner and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data availability The data set is stored in an SPSS file.

Declarations

Ethical approval The study was approved by the local ethics committee (Reference number 22748/2016/32, Landesärztekammer Thüringen). Patients gave informed consent for surgery, data collection and further analysis. The data were processed anonymously and therefore consent for publication was not required.

Informed consent Informed consent was not required.

Competing interests None.

References

- Altieri R, Tardivo V, Pacca P, Pennacchietti V, Penner F, Garbossa D, Ducati A, Garzaro M, Zenga F (2016) 3D HD endoscopy in skull base surgery: from darkness to light. *Surg Technol Int* 29:359–365
- Bae S, Korniski R, Shearn M, Manohara H, Shahinian H (2016) 4-mm-diameter three-dimensional imaging endoscope with steerable camera for minimally invasive surgery (3-D-MARVEL). *Neurophotonics* 4:011008
- Barkhoudarian G, Del Carmen Becerra Romero A, Laws ER (2013) Evaluation of the 3-dimensional endoscope in transsphenoidal surgery. *Neurosurgery* 73:ons74–78. <https://doi.org/10.1227/NEU.0b013e31828ba962>. discussion ons78–79
- Billor BM, Grossman AB, Stewart PM, Melmed S, Bertagna X, Bertherat J, Buchfelder M, Colao A, Hermus AR, Hofland LJ, Klibanski A, Lacroix A, Lindsay JR, Newell-Price J, Nieman LK, Petersenn S, Sonino N, Stalla GK, Swearingen B, Vance ML, Wass JA, Boscaro M (2008) Treatment of adrenocorticotropin-dependent Cushing's syndrome: a consensus statement. *J Clin Endocrinol Metab* 93:2454–2462. <https://doi.org/10.1210/jc.2007-2734>
- Cappabianca P, Cavallo LM, Solari D, de Divitiis O, Chiaramonte C, Esposito F (2014) Size does not matter. The intrigue of giant adenomas: a true surgical challenge. *Acta Neurochir (Wien)* 156:2217–2220. <https://doi.org/10.1007/s00701-014-2213-7>
- Cavallo LM, Solari D, Somma T, Di Somma A, Chiaramonte C, Cappabianca P (2013) Use of equine pericardium sheet (LYOMESH(R)) as dura mater substitute in endoscopic endonasal transsphenoidal surgery. *Transl Med @ UniSa* 7:23–28
- Chen Y, Xu X, Cao J, Jie Y, Wang L, Cai F, Chen S, Yan W, Hong Y, Zhang J, Wu Q (2022) Transsphenoidal surgery of giant pituitary adenoma: results and experience of 239 cases in a single center. *Front Endocrinol* 13:879702. <https://doi.org/10.3389/fendo.2022.879702>
- 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* 74:388–395. <https://doi.org/10.1590/0004-282x20160042>
- Cusimano MD, Kan P, Nassiri F, Anderson J, Goguen J, Vanek I, Smyth HS, Fenton R, Muller PJ, Kovacs K (2012) Outcomes of surgically treated giant pituitary tumours. *Can J Neurol Sci* 39:446–457. <https://doi.org/10.1017/s0317167100013950>
- D'Alessandris QG, Rigante M, Mattogno PP, La Rocca G, Romanello M, Auricchio AM, Bevacqua G, Fraschetti F, Giordano M, Di Bonaventura R, Pallini R, Anile C, Olivi A, Lauretti L (2020) Impact of 4K ultra-high definition endoscope in pituitary surgery: analysis of a comparative institutional case series. *J Neurosurg Sci*. <https://doi.org/10.23736/s0390-5616.20.04875-4>
- Ezzat S, Asa SL, Couldwell WT, Barr CE, Dodge WE, Vance ML, McCutcheon IE (2004) The prevalence of pituitary adenomas: a systematic review. *Cancer* 101:613–619. <https://doi.org/10.1002/cncr.20412>
- Fallah N, Taghvaei M, Sadaghiani S, Sadrhosseini SM, Esfahanian F, Zeinalizadeh M (2019) Surgical outcome of endoscopic endonasal surgery of large and giant pituitary adenomas: an institutional experience from the Middle East. *World Neurosurg* 132:e802–e811. <https://doi.org/10.1016/j.wneu.2019.08.004>
- Felisati G, Lenzi R, Pipolo C, Maccari A, Messina F, Revay M, Lania A, Cardia A, Lasio G (2013) Endoscopic expanded endonasal approach: preliminary experience with the new 3D endoscope. *Acta Otorhinolaryngol Ital* 33:102–106
- Felisati G, Pipolo C, Maccari A, Cardia A, Revay M, Lasio GB (2013) Transnasal 3D endoscopic skull base surgery: questionnaire-based analysis of the learning curve in 52 procedures. *Eur Arch Otorhinolaryngol* 270:2249–2253. <https://doi.org/10.1007/s00405-012-2328-5>
- Ferrareze Nunes C, Lieber S, Truong HQ, Zenonos G, Wang EW, Snyderman CH, Gardner PA, Fernandez-Miranda JC (2018) Endoscopic endonasal transoculomotor triangle approach for adenomas invading the parapeduncular space: surgical anatomy, technical nuances, and case series. *J Neurosurg* 1–11. <https://doi.org/10.3171/2017.10.Jns17779>
- Gao Y, Zhong C, Wang Y, Xu S, Guo Y, Dai C, Zheng Y, Wang Y, Luo Q, Jiang J (2014) Endoscopic versus microscopic transsphenoidal pituitary adenoma surgery: a meta-analysis. *World J Surg Oncol* 12:94. <https://doi.org/10.1186/1477-7819-12-94>
- Gerlach R, de Du Mesnil RR, Gasser T, Marquardt G, Reusch J, Imoehl L, Seifert V (2008) Feasibility of Polestar N20, an ultra-low-field intraoperative magnetic resonance imaging system in resection control of pituitary macroadenomas: lessons learned from the first 40 cases. *Neurosurgery* 63:272–284
- Giustina A, Chanson P, Kleinberg D, Bronstein MD, Clemmons DR, Klibanski A, van der Lely AJ, Strasburger CJ, Lamberts SW, Ho KK, Casanueva FF, Melmed S (2014) Expert consensus document: A consensus on the medical treatment of acromegaly. *Nat Rev Endocrinol* 10:243–248. <https://doi.org/10.1038/nrendo.2014.21>
- Gnanalingham KK, Bhattacharjee S, Pennington R, Ng J, Mendoza N (2005) The time course of visual field recovery following transphenoidal surgery for pituitary adenomas: predictive factors for a good outcome. *J Neurol Neurosurg Psychiatry* 76:415–419. <https://doi.org/10.1136/jnnp.2004.035576>
- Gondim JA, Almeida JP, Albuquerque LA, Gomes EF, Schops M (2014) Giant pituitary adenomas: surgical outcomes of 50 cases operated on by the endonasal endoscopic approach. *World Neurosurg* 82:e281–290. <https://doi.org/10.1016/j.wneu.2013.08.028>
- Goya RG, Sarkar DK, Brown OA, Herenu CB (2004) Potential of gene therapy for the treatment of pituitary tumors. *Curr Gene Ther* 4:79–87
- Hajdari S, Kellner G, Meyer A, Rosahl S, Gerlach R (2018) Endoscopic endonasal surgery for removal of pituitary adenomas - a surgical case series of treatment results using different two- and three-dimensional visualization systems. *World Neurosurg*. <https://doi.org/10.1016/j.wneu.2018.07.018>
- Hofstetter CP, Nanaszko MJ, Mubita LL, Tsiouris J, Anand VK, Schwartz TH (2012) Volumetric classification of pituitary macroadenomas predicts outcome and morbidity following endoscopic endonasal transsphenoidal surgery. *Pituitary* 15:450–463. <https://doi.org/10.1007/s11102-011-0350-z>
- Iglesias P, Rodríguez Berrocal V, Díez JJ (2018) Giant pituitary adenoma: histological types, clinical features and therapeutic

- approaches. *Endocrine* 61:407–421. <https://doi.org/10.1007/s12020-018-1645-x>
25. Inoue D, Yoshimoto K, Uemura M, Yoshida M, Ohuchida K, Kenmotsu H, Tomikawa M, Sasaki T, Hashizume M (2013) Three-dimensional high-definition neuroendoscopic surgery: a controlled comparative laboratory study with two-dimensional endoscopy and clinical application. *J Neurol Surg A Cent Eur Neurosurg* 74:357–365. <https://doi.org/10.1055/s-0033-1345100>
 26. Juraschka K, Khan OH, Godoy BL, Monsalves E, Kilian A, Krischek B, Ghare A, Vescan A, Gentili F, Zadeh G (2014) Endoscopic endonasal transsphenoidal approach to large and giant pituitary adenomas: institutional experience and predictors of extent of resection. *J Neurosurg* 121:75–83. <https://doi.org/10.3171/2014.3.Jns131679>
 27. Kari E, Oyesiku NM, Dadashev V, Wise SK (2012) Comparison of traditional 2-dimensional endoscopic pituitary surgery with new 3-dimensional endoscopic technology: intraoperative and early postoperative factors. *Int Forum Allergy Rhinol* 2:2–8. <https://doi.org/10.1002/alar.20036>
 28. Karnezis TT, Baker AG, Soler ZM, Wise SK, Rereddy SK, Patel ZM, Oyesiku NM, DelGaudio JM, Hadjipanayis CG, Woodworth BA, Riley KO, Lee J, Cusimano MD, Govindaraj S, Psaltis A, Wormald PJ, Santoreneos S, Sindwani R, Trosman S, Stokken JK, Woodard TD, Recinos PF, Vandergrift WA 3rd, Schlosser RJ (2016) Factors impacting cerebrospinal fluid leak rates in endoscopic sellar surgery. *Int Forum Allergy Rhinol* 6:1117–1125. <https://doi.org/10.1002/alar.21783>
 29. Knosp E, Steiner E, Kitz K, Matula C (1993) Pituitary adenomas with invasion of the cavernous sinus space: a magnetic resonance imaging classification compared with surgical findings. *Neurosurgery* 33:610–617 discussion 617–618
 30. Komotar RJ, Starke RM, Raper DM, Anand VK, Schwartz TH (2012) Endoscopic endonasal compared with microscopic transsphenoidal and open transcranial resection of giant pituitary adenomas. *Pituitary* 15:150–159. <https://doi.org/10.1007/s11102-011-0359-3>
 31. Koutourousiou M, Gardner PA, Fernandez-Miranda JC, Paluzzi A, Wang EW, Snyderman CH (2013) Endoscopic endonasal surgery for giant pituitary adenomas: advantages and limitations. *J Neurosurg* 118:621–631. <https://doi.org/10.3171/2012.11.Jns121190>
 32. Magro E, Graillon T, Lassave J, Castinetti F, Boissonneau S, Tabouret E, Fuentes S, Velly L, Gras R, Dufour H (2016) Complications related to the endoscopic endonasal transsphenoidal approach for nonfunctioning pituitary macroadenomas in 300 consecutive patients. *World Neurosurg* 89:442–453. <https://doi.org/10.1016/j.wneu.2016.02.059>
 33. Makarenko S, Alzahrani I, Karsy M, Deopujari C, Couldwell WT (2022) Outcomes and surgical nuances in management of giant pituitary adenomas: a review of 108 cases in the endoscopic era. *J Neurosurg* 1–12. <https://doi.org/10.3171/2021.10.Jns21659>
 34. Marigil Sanchez M, Karekezi C, Almeida JP, Kalyvas A, Castro V, Velasquez C, Gentili F (2019) Management of giant pituitary adenomas: role and outcome of the endoscopic endonasal surgical approach. *Neurosurg Clin N Am* 30:433–444. <https://doi.org/10.1016/j.nec.2019.05.004>
 35. Micko A, Agam MS, Brunswick A, Strickland BA, Rutkowski MJ, Carmichael JD, Shiroishi MS, Zada G, Knosp E, Wolfsberger S (2022) Treatment strategies for giant pituitary adenomas in the era of endoscopic transsphenoidal surgery: a multicenter series. *J Neurosurg* 136:776–785. <https://doi.org/10.3171/2021.1.Jns203982>
 36. Micko ASG, Keritam O, Marik W, Strickland BA, Briggs RG, Shahrestani S, Cardinal T, Knosp E, Zada G, Wolfsberger S (2021) Dumbbell-shaped pituitary adenomas: prognostic factors for prediction of tumor nondescent of the supradiaphragmal component from a multicenter series. *J Neurosurg* 1–9. <https://doi.org/10.3171/2021.9.Jns211689>
 37. Mohr G, Hardy J, Comtois R, Beauregard H (1990) Surgical management of giant pituitary adenomas. *Can J Neurol Sci* 17:62–66. <https://doi.org/10.1017/s0317167100030055>
 38. Müslüman AM, Cansever T, Yılmaz A, Kanat A, Oba E, Çavuşoğlu H, Sirinoğlu D, Aydın Y (2011) Surgical results of large and giant pituitary adenomas with special consideration of ophthalmologic outcomes. *World Neurosurg* 76:141–148. <https://doi.org/10.1016/j.wneu.2011.02.009>. discussion 163–146
 39. Nassimizadeh A, Lancer H, Hodson J, Ahmed S (2021) Three-dimensional endoscopic endonasal surgery: a systematic review. *Laryngoscope*. <https://doi.org/10.1002/lary.29939>
 40. Nishioka H, Hara T, Nagata Y, Fukuhara N, Yamaguchi-Okada M, Yamada S (2017) Inherent tumor characteristics that limit effective and safe resection of giant nonfunctioning pituitary adenomas. *World Neurosurg* 106:645–652. <https://doi.org/10.1016/j.wneu.2017.07.043>
 41. Ogino-Nishimura E, Nakagawa T, Sakamoto T, Ito J (2015) Efficacy of three-dimensional endoscopy in endonasal surgery. *Auris Nasus Larynx* 42:203–207. <https://doi.org/10.1016/j.anl.2014.10.004>
 42. Okamoto Y, Okamoto F, Yamada S, Honda M, Hiraoka T, Oshika T (2010) Vision-related quality of life after transsphenoidal surgery for pituitary adenoma. *Invest Ophthalmol Vis Sci* 51:3405–3410. <https://doi.org/10.1167/iovs.09-3763>
 43. Paluzzi A, Gardner P, Fernandez-Miranda JC, Snyderman C (2012) The expanding role of endoscopic skull base surgery. *Br J Neurosurg* 26:649
 44. Pennacchiotti V, Garzaro M, Grottole S, Pacca P, Garbossa D, Ducati A, Zenga F (2016) Three-dimensional endoscopic endonasal approach and outcomes in sellar lesions: a single-center experience of 104 cases. *World Neurosurg* 89:121–125. <https://doi.org/10.1016/j.wneu.2016.01.049>
 45. Peter M, De Tribolet N (1995) Visual outcome after transsphenoidal surgery for pituitary adenomas. *Br J Neurosurg* 9:151–157. <https://doi.org/10.1080/02688699550041485>
 46. Rahimli T, Hidayetov T, Rajabov T (2021) Endoscopic endonasal approach to multilobular giant pituitary adenoma with cavernous sinus invasion and petroclival extension. *World Neurosurg* 147:128–129. <https://doi.org/10.1016/j.wneu.2020.11.055>
 47. Rampinelli V, Doglietto F, Mattavelli D, Qiu J, Raffetti E, Schreiber A, Villaret AB, Kucharczyk W, Donato F, Fontanella MM, Nicolai P (2017) Two-dimensional high definition versus three-dimensional endoscopy in endonasal skull base surgery: a comparative preclinical study. *World Neurosurg* 105:223–231. <https://doi.org/10.1016/j.wneu.2017.05.130>
 48. Rigante M, La Rocca G, Lauretti L, D'Alessandris GQ, Mangiola A, Anile C, Olivi A, Paludetti G (2017) Preliminary experience with 4K ultra-high definition endoscope: analysis of pros and cons in skull base surgery. *Acta Otorhinolaryngol Ital* 37:237–241. <https://doi.org/10.14639/0392-100x-1684>
 49. Saeki N, Horiguchi K, Murai H, Hasegawa Y, Hanazawa T, Okamoto Y (2010) Endoscopic endonasal pituitary and skull base surgery. *Neurol Med Chir* 50:756–764. <https://doi.org/10.2176/nmc.50.756>
 50. Strickland BA, Lucas J, Harris B, Kulubya E, Bakhsheshian J, Liu C, Wrobel B, Carmichael JD, Weiss M, Zada G (2017) Identification and repair of intraoperative cerebrospinal fluid leaks in endonasal transsphenoidal pituitary surgery: surgical experience in a series of 1002 patients. *J Neurosurg* 1–5. <https://doi.org/10.3171/2017.4.Jns162451>
 51. Tabaei A, Anand VK, Fraser JF, Brown SM, Singh A, Schwartz TH (2009) Three-dimensional endoscopic pituitary surgery. *Neurosurgery* 64:288–293. <https://doi.org/10.1227/01.neu.0000338069.51023.3c>. discussion 294–285

52. Truong HQ, Lieber S, Najera E, Alves-Belo JT, Gardner PA, Fernandez-Miranda JC (2018) The medial wall of the cavernous sinus. Part 1: Surgical anatomy, ligaments, and surgical technique for its mobilization and/or resection. *J Neurosurg* 1–9. <https://doi.org/10.3171/2018.3.Jns18596>
53. Truong HQ, Najera E, Zanabria-Ortiz R, Celticki E, Sun X, Borghei-Razavi H, Gardner PA, Fernandez-Miranda JC (2018) Surgical anatomy of the superior hypophyseal artery and its relevance for endoscopic endonasal surgery. *J Neurosurg* 1–9. <https://doi.org/10.3171/2018.2.Jns172959>
54. Vasudevan K, Saad H, Oyesiku NM (2019) The role of three-dimensional endoscopy in pituitary adenoma surgery. *Neurosurg Clin N Am* 30:421–432. <https://doi.org/10.1016/j.nec.2019.05.012>
55. Xu Y, Mohyeldin A, Asmaro KP, Nunez MA, Doniz-Gonzalez A, Vigo V, Cohen-Gadol AA, Fernandez-Miranda JC (2022) Intracranial breakthrough through cavernous sinus compartments: anatomic study and implications for pituitary adenoma surgery. *Oper Neurosurg (Hagerstown, Md)* 23:115–124. <https://doi.org/10.1227/ons.0000000000000291>
56. Yano S, Hide T, Shinojima N (2017) Efficacy and complications of endoscopic skull base surgery for giant pituitary adenomas. *World Neurosurg* 99:533–542. <https://doi.org/10.1016/j.wneu.2016.12.068>
57. Zhan R, Chen S, Xu S, Liu JK, Li X (2015) postoperative low-flow cerebrospinal fluid leak of endoscopic endonasal transsphenoidal surgery for pituitary adenoma-wait and see, or lumbar drain? *J Craniofac Surg* 26:1261–1264. <https://doi.org/10.1097/scs.0000000000001691>
58. Zhang C, Ding X, Lu Y, Hu L, Hu G (2017) Cerebrospinal fluid rhinorrhoea following transsphenoidal surgery for pituitary adenoma: experience in a Chinese centre. *Acta Otorhinolaryngol Ital* 37:303–307. <https://doi.org/10.14639/0392-100x-1086>
59. Zhou Q, Yang Z, Wang X, Wang Z, Zhao C, Zhang S, Li P, Li S, Liu P (2017) Risk factors and management of intraoperative cerebrospinal fluid leaks in endoscopic treatment of pituitary adenoma: analysis of 492 patients. *World Neurosurg* 101:390–395. <https://doi.org/10.1016/j.wneu.2017.01.119>

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