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ARTICLE

Surgical outcomes of the endoscopic endonasal transsphenoidal approach for large and giant pituitary adenomas: institutional experience with special attention to approach-related complications

Resultados cirúrgicos do acesso endonasal endoscópico transesfenoidal para adenomas hipofisários grandes e gigantes: experiência institucional com ênfase às complicações relacionadas ao acesso cirúrgico

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ABSTRACT

Objective: In this study, we investigate our institutional experience of patients who underwent endoscopic endonasal transsphenoidal approach for treatment of large and giant pituitary adenomas emphasizing the surgical results and approach-related complications. **Method:** The authors reviewed 28 consecutive patients who underwent surgery between March, 2010 and March, 2014. **Results:** The mean preoperative tumor diameter was 4.6 cm. Gross-total resection was achieved in 14.3%, near-total in 10.7%, subtotal in 39.3%, and partial in 35.7%. Nine patients experienced improvement in visual acuity, while one patient worsened. The most common complications were transient diabetes insipidus (53%), new pituitary deficit (35.7%), endonasal adhesions (21.4%), and cerebrospinal fluid leak (17.8%). Surgical mortality was 7.1%. **Conclusions:** Endoscopic endonasal transsphenoidal surgery is a valuable treatment option for large or giant pituitary adenomas, which results in high rates of surgical decompression of cerebrovascular structures.

Keywords: endoscopic endonasal approach; giant pituitary adenomas; large pituitary adenomas; complication rates.

RESUMO

Objetivo: Neste manuscrito investigamos a experiência institucional com o acesso endonasal endoscópico transesfenoidal no tratamento de adenomas hipofisários grandes e gigantes com ênfase às complicações relacionadas ao acesso cirúrgico. **Método:** Foram incluídos neste estudo 28 pacientes consecutivos submetidos à cirurgia entre Março de 2010 e Março de 2014. **Resultados:** O diâmetro médio pré-operatório dos tumores era 4,6 cm. Uma ressecção total foi obtida em 14,3%; quase total, em 10,7%; subtotal, em 39,3% e parcial, em 35,7%. Nove pacientes evoluíram com melhora na acuidade visual, enquanto um paciente apresentou piora da função visual. As complicações mais comuns foram diabetes insipidus transitório (53%), novo défice hipofisário (35,7%), sinéquias endonasais (21,4%) e fistula liquórica (17,8%). A mortalidade cirúrgica foi 7,1%. **Conclusões:** A cirurgia por via endonasal endoscópica transesfenoidal é uma opção terapêutica extremamente útil para adenomas hipofisários grandes e gigantes, a resultar numa significativa descompressão das estruturas cerebrovasculares.

Palavras-chave: acesso endoscópico endonasal; adenoma hipofisário gigante; adenoma hipofisário grande; índices de complicação.

Introduced initially in the 1960s by Guiot et al.[1] as an additional visualization tool to the microscope for sellar tumors, the endoscope has revolutionized the treatment of pituitary disorders because of improved visualization allowing ultimately the expansion of the surgical view[2]. At present, the purely endoscopic endonasal approach is widely used worldwide for the treatment of pituitary adenomas and other sellar tumors due to its similar safety, resection and complication rates, as well as surgical outcome in comparison to the traditional microscopic approach[3,4]. Large and giant pituitary adenomas comprise a different issue, which pose a significant surgical challenge[5]. The definition is based on a

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purely morphological criterion in the way that when the tumor achieves a diameter greater than 4 cm in any plane, it is considered giant[5,6,7]. There is no consensus, however, on the definition of large pituitary adenomas[8,9]. Juraschka et al.[10] have considered large tumors as those having > 3 cm in the maximal diameter, while Cusimano et al.[11] have introduced a new volumetric assessment (≥ 10 cm^3) on the assumption of a better estimation of the tumor size and also for a better quantification of the extent of resection.

Traditionally, these tumors have been handled by the transcranial route, alone or in combination with the transsphenoidal resection[7,9,11,12]. Some recent reports have described the usefulness of the endoscopic endonasal route in the their management, even though its safety and effectiveness of treating large and giant pituitary adenomas is yet to be established in the literature[6,8,10,11,13,14,15,16]. Herein, we sought to investigate our institutional experience of patients who underwent endoscopic endonasal transsphenoidal approach for treatment of large and giant pituitary adenomas emphasizing the surgical results and approach-related complications.

METHOD

This study consists in a retrospective review of 28 consecutive patients who underwent endoscopic endonasal transsphenoidal surgery for treatment of large and giant pituitary adenomas between March, 2010 and March, 2014. Clinical presentation, endocrine status, neuroimaging, histopathological evaluation, extent of resection, clinical outcomes, and complication rates were analyzed. The institutional review board approved the terms and conditions of the present study.

Inclusion criteria

All patients undergoing endoscopic endonasal transsphenoidal resection for histologically proven pituitary macroadenomas with a maximal diameter > 3–4 cm (large) or > 4 cm (giant) were included in this analysis. Patients harboring smaller tumors, distinct histological diagnosis, or those who have been submitted to a previous transcranial resection were excluded.

Patient characteristics

The medical charts were reviewed to collect clinical data. The clinical characteristics included were gender, age, visual acuity (Humphrey visual field [HVF] testing), ophthalmoplegia, pituitary dysfunction (hypo- or hyperfunction syndromes), diabetes insipidus (DI), and prior surgery. All patients underwent preoperative magnetic resonance imaging (MRI) and computed tomography (CT) with navigation protocol. Neuroimaging were evaluated to measure the maximal tumoral diameter in any plane, and to assess suprasellar and parasellar extension based on the classification of Hardy[17] and Mohr et al.[18], as well as the occurrence of optic nerve compression, hydrocephalus, or haemorrhagic component. All patients were seen by an experienced endocrinological team being tested for serum growth hormone (GH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), adrenocorticotrophic hormone (ACTH), cortisol, insulin-like growth factor-I (IGF-1), prolactin, thyroid-stimulating hormone (TSH), T4, testosterone and estrogen levels.

Postoperatively, all patients performed cranial CT within 48 hours and cranial MRI at 2-, 12-months, and yearly thereafter. Gross-total resection (GTR) was assigned when the MRI scan showed no residual tumor, while near total resection (NTR) was attributed to the removal of ≥ 90%, subtotal resection (STR) with a tumor reduction from 70% to 89.9% and partial resection (PR) in the case of ≤ 70% of tumor resection. Follow-up imaging also addressed regrowth of a residual tumor or tumor recurrence in the case of GTR. The occurrence of postoperative complications, including DI (transient/permanent), new hypopituitarism, cerebrospinal fluid (CSF) leak, meningitis, ophthalmoplegia, endonasal synechiae, acute sinusitis, epistaxis, internal carotid artery injury, subarachnoid haemorrhage (SAH) and ischemic stroke were considered.

For hormone-secreting tumors, chemical remission was based on the following criteria: for prolactinomas, a prolactin level < 15ng/mL in men and < 20ng/mL in women; and for GH-secreting tumors, normalization of serum levels of IGF-1 matched for age and gender, random serum GH level of < 1ng/mL or a serum GH nadir of < 0.4 ng/mL following oral glucose tolerance test[19,20].

Surgical approach

The operative technique used was the endoscopic endonasal transsphenoidal approach. All surgeries were performed primarily by the senior neurosurgeon (J.A.L.) during this time period. The primary objective was maximum decompression of the optic apparatus, the pituitary gland and surrounding brain structures[12]. Patients were positioned with their heads secured by a Mayfield head holder. Then, the patients were registered to a frameless stereotactic navigation system (Stealth; Medtronic, Jacksonville, Florida, USA) for intraoperative guidance and anatomical verification. Lumbar drains were not used routinely.

The nasal cavity was prepared with adrenalin (1:1000) soaked cottonoids for at least 5 minutes in order to decrease bleeding. The surgical procedure started with the inventory of nasal cavity with a 0-degree 4-mm endoscope (Karl Storz GmbH & Co.KG, Tuttlingen, Germany). A right middle turbinate luxation or middle turbinectomy was developed before harvesting mucoperiosteal nasoseptal vascularized flap for skull base reconstruction after tumor resection. A posterior septectomy was undertaken for a two

nostril bimanual technique. An anterior sphenoidotomy was then carried out. Inside the sphenoid sinus, the sellae borders were demarcated by the aid of image guidance. Its front wall was opened with a fine chisel and expanded with a Kerrison forceps or drilling. Dural exposure was limited by the tuberculum sellae superiorly, clival recess inferiorly, and laterally by the medial walls of the cavernous sinus. Tumor was debulked by piecemeal resection and suction and ultimately the tumor border was defined for bimanual preparation of the neurovascular structures (Figure 1). The reconstruction of the skull base was performed with autologous fat patch, which was placed in the resection cavity with a special care not to overpack, followed by placement of the nasoseptal mucous flap. Tissue glue (Beriplast™, Behring) was applied to the flap edges and covered with Surgicel (Ethicon). A nasal Foley catheter was introduced for packing of the sphenoidal cavity in order to prevent flap migration only in the case of intraoperative CSF leakage.

RESULTS

Preoperative characteristics

Patients included 17 men (60%) and 11 women (40%). The mean age was 46 years (range, 15–62 years). The average tumor size was 4.6 cm (range, 3.9–9.7 cm). The most common presenting symptoms were endocrinopathy (57%), visual acuity deficits (42%), and headache (35%). There were 5 patients (17.8%) with preoperative hypogonadism, 4 patients (14.3%) had hypothyroidism, one patient (3.6%) had acromegaly and one patient (3.6%) was affected by galactorrhea. Gait apraxia and cognitive impairment were found in 7.1% of patients (2 patients) due to obstructive hydrocephalus (grade D of Hardy).

In 2 patients (7.1%), there was acute worsening of visual impairment and headache, which together with the imaging findings confirmed the diagnosis of tumor apoplexy. Prior to surgery, the imaging morphological characteristics of tumors are illustrated on Table 1. The majority of tumors were nonfunctioning pituitary adenomas (82%) (Figure 2).

Extent of resection and Clinical outcomes

The tumor resection rates were estimated by analysis of postoperative MRI exams, which were performed two months after surgery. Gross-total resection (GTR) was achieved in 14.3% (4 patients), near-total (NTR) in 10.7% (3 patients), subtotal (STR) in 39.3% (11 patients), and partial (PR) in 35.7% (10 patients). Nine (32.1%) patients experienced improvement in visual acuity, while only one patient (3.6%) worsened. Surgical resection alone achieved endocrinological remission in four of the five patients with hormone-secreting tumors (the remaining patient died after 30 days postoperatively).

Complications

The authors identified 11 different immediate/short-term and late complications related to the endoscopic transsphenoidal resection of giant pituitary adenomas

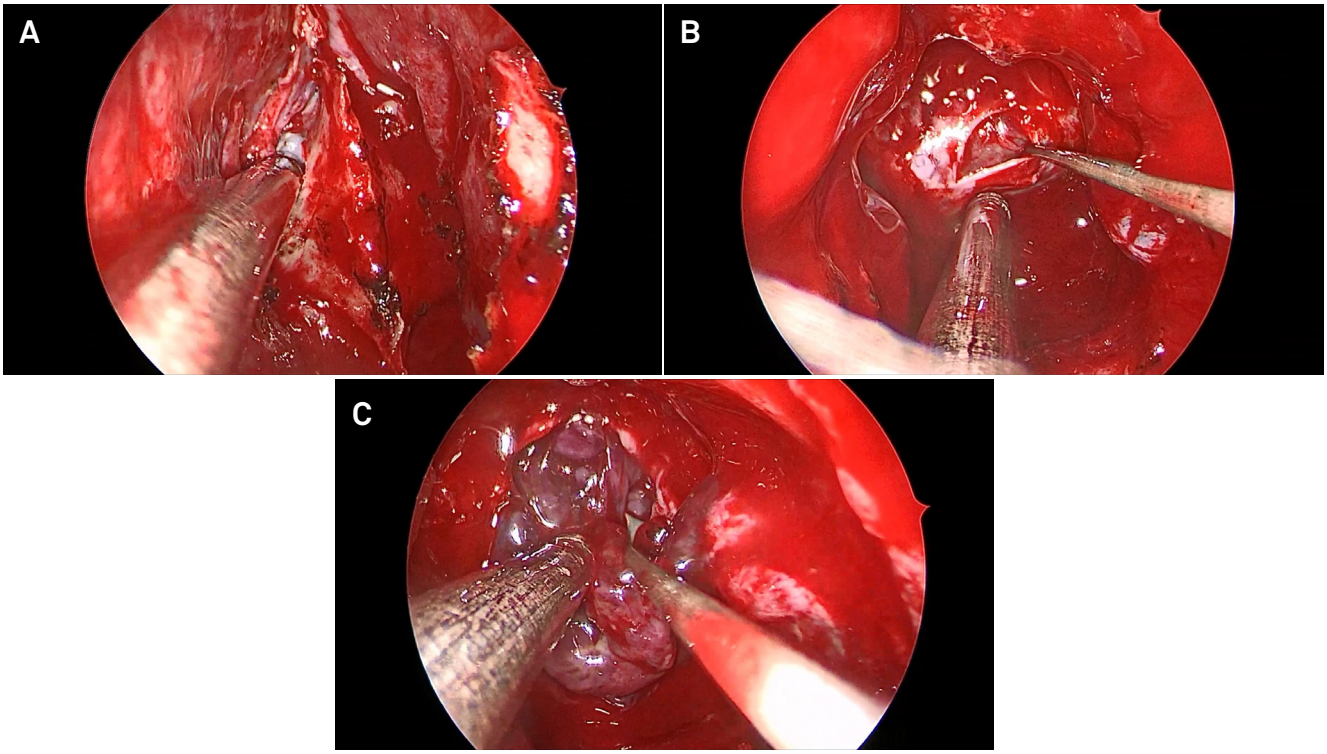

Figure 1. Intraoperative imaging demonstrating the surgical steps involved in the resection of a giant pituitary adenoma. (A) Anterior sphenoidotomy. (B) Dural opening and initial preparation of the tumor capsule. (C) Intracapsular resection.

Table 1. Imaging characteristics of large and giant pituitary adenomas.

Tumor characteristic	Nº of patients (%)
Optic nerve compression	22 (78.6)
Supra- and para-sellar extension	17 (60.7)
Hydrocephalus	2 (7.1)
Tumor apoplexy	2 (7.1)

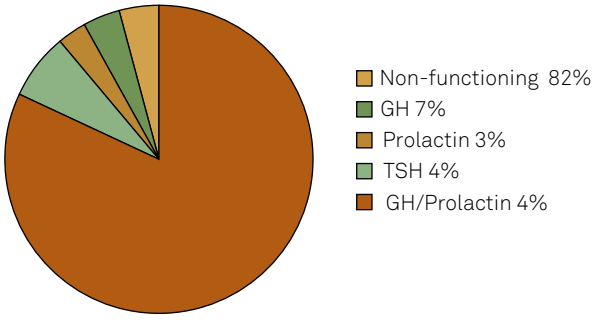

Figure 2. Tumor classification according to the immunohistochemical profile. (GH – growth hormone; TSH – thyroid-stimulating hormone).

(Table 2). The most common complications were transient diabetes insipidus (53%), new pituitary deficit (35.7%), endonasal adhesions (21.4%), and CSF leak (17.8%). From the immediate/short-term group, nasosinusal disorders, such as acute sinusitis and epistaxis occurred in 7.1%, each. Intraoperatively, CSF leak was detected in 21% and corrected at the end of tumor resection, even though 17.8% of the patients experienced postoperative CSF leak. All patients were placed on a conservative regimen of bed rest, acetazolamide and lumbar drain for 5 days with total symptom remission. Two patients developed postoperative meningitis after treatment for CSF leak.

Surgical mortality was 7.1% (2 patients). One patient had a severe subarachnoid/tetraventricular haemorrhage, which ultimately lead to diffuse cerebral vasospasm and brain death (Figure 3), while the second deceased from metabolic disorders as a result from DI. A third patient died more than 30 days postoperatively affected by nosocomial pneumonia and therefore was not considered surgical mortality. At the last follow-up, only one patient (3.6%) was affected by permanent DI. The ENT team monitored all endonasal adhesions in the outpatient clinic, but no surgery was necessary.

Recurrences and Follow-Up

During the mean follow-up time of 30 months (range, 12–36 months), 9 (32.1%) patients were reoperated on for tumor regrowth. In total, 28 patients underwent 32 endoscopic

Table 2. Perioperative and postoperative complications of the endoscopic endonasal transsphenoidal approach.

Complication	Nº of patients (%)
Diabetes insipidus	
transient	15 (53.6)
permanent	1 (3.6)
Adrenal insufficiency	10 (35.7)
Endonasal synechiae	6 (21.4)
CSF leak	5 (17.8)
Acute sinusitis	2 (7.1)
Meningitis	2 (7.1)
Epistaxis	2 (7.1)
SAH	1 (3.6)
Internal carotid artery injury	1 (3.6)
Stroke	1 (3.6)
Ophthalmoplegia	1 (3.6)

CSF: cerebrospinal fluid; SAH: subarachnoid haemorrhage.

endonasal transphenoidal procedures. Five of the 9 patients were given reoperation through open craniotomy. The mean time to regrowth was 2 years. All patients who underwent GTR (14.3%) remained free of tumor.

DISCUSSION

Giant pituitary adenomas are rare tumors with an estimated incidence between 5% and 16% of all pituitary tumors[1,21,22]. Complete resection is often a technical challenge, even for experienced neurosurgeons, considering that this subgroup of tumors may present with a high degree of invasion of neurovascular structures and large areas of supra- and parasellar extension[11,23]. In this way, the primary objective of surgery includes relief of mass effect by obtaining maximal tumor resection in order to decompress visual pathways, neurovascular structures and the pituitary gland[6,9,15].

The possible route to reach the sellar region in the management of giant pituitary adenomas can be divided into two main groups: the transcranial and the transsphenoidal approaches, either microscopic or endoscopic. A recent systematic review from the modern literature (1995–2010) was conducted to compare the benefits and limitations of the various surgical approaches[7]. Based on the collection of 478 patients affected of giant pituitary adenomas, Komotar et al.[7] found that the endoscopic cohort had higher rates of gross total resection (GTR) (47.2%) and improved visual outcome (91.1%) than the transcranial (9.6% and 40%) and the microscopic transsphenoidal cohorts (30.9% and 34.8%), respectively.

It is worth emphasizing that only one purely endoscopic surgical series was included in their analysis, since the manuscript by de Paiva Neto et al.[24] was mainly microscopic transphenoidal. Thereafter, few studies came out in the literature addressing the outcomes of patients undergoing resection for large and giant pituitary adenomas by the endoscopic approach[6,8,10,11,13,14,15,16]. Their main surgical outcomes and complications rates are detailed on Tables 3 and 4. Our group has recently analyzed the initial experience (2000–2010) in the management of 35 giant nonfunctioning pituitary adenomas operated on by the open and the endoscopic routes, but the main objective was to correlate Ki-67 expression with tumor recurrence[12].

Extent of resection of the endoscopic endonasal transsphenoidal approach

As aforementioned, GTR is not the goal for such large tumors because of neurovascular structures involvement and the recent success of adjuvant therapies[8]. Thus, the extent of resection is difficult to evaluate as an outcome for large and giant pituitary adenomas[8]. Moreover, there is no general consensus on the definition for near total (NTR), subtotal (STR), and partial resection (PR), as also noted by Chabot et al.[8]. Overall, the reported rate of GTR in the modern purely endoscopic series published after the systematic review by Komotar et al.[7] ranges from 14% in our series to 60% in the Naples series[13] (average of 36.7%) (Table 3).

Such higher rates of GTR are quite encouraging in comparison to the open and microscopic transsphenoidal groups (9.6% and 30.9%, respectively)[7]. It is worth discussing that cavernous sinus involvement is reported by most of the studies as the major limitation to GTR with the endoscopic approach[6,8,14,16], whereas for the microscopic transsphenoidal approach is the suprasellar extension[25]. Besides cavernous sinus involvement, tumor size greater than 10 cm[3,14]

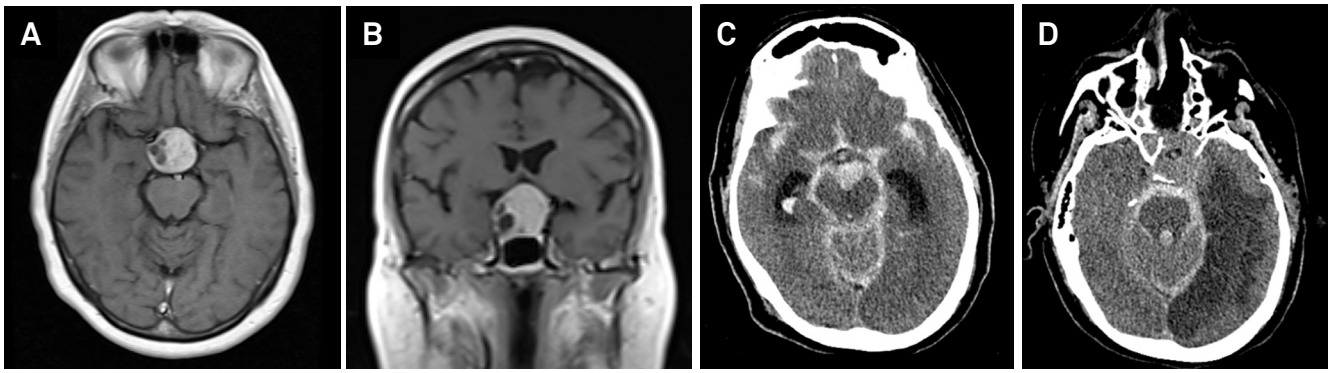

Figure 3. Preoperative axial (A) and coronal (B) T1-weighted gadolinium-enhanced MRI of a rounded giant pituitary tumor. (C, D) The patient underwent near-total resection of the adenoma, but experienced a severe subarachnoid/tetraventricular haemorrhage after cavernous sinus violation and internal carotid artery injury, which ultimately lead to diffuse cerebral vasospasm and brain death.

Table 3. Outcomes of main series of endoscopic endonasal transsphenoidal approach for large and giant pituitary adenomas.

Author, year	Nº of patients	Extent of resection (%)				Visual outcome			Surgical Mortality
		GTR	NTR	STR	PR	Improved	Unchanged	Worsened	
Nakao and Itakura, 2011[16]	43	47*	-	53	-	97.7	2.3	0	0
Di Maio et al., 2011[13]	20	60	20	15	5	85.7	7.1	7.1	0
Cusimano et al., 2012[11]	29[a]	20.7	-	79.3[a]	-	96.2	-	3.8[a]	0
Hofstetter et al., 2012[14]	43[b]	48.8	-	51.2[b]	-	85.7[b]	14.3	0	4.6
Koutourousiou et al., 2013[15]	54	20.4	66.7	-	12.9[c]	80	13.3	4.4	0
Gondim et al., 2014[6]	50	38	18	-	44**	76	22	0	4
Juraschka et al., 2014[10]	66***	24.2	16.7	36.4	22.7	73[d]	22.2	4.8	0
Chabot et al. 2015[8]	39	56.4	28.2	15.4[e]	-	53.6	46.4	0	0
Present Series	28	14.3	10.7	39.3	35.7	32.1	64.3	3.6	7.1

GTR: gross total resection; NTR: near total resection; PR: partial resection; STR: subtotal resection. *The extent of resection considered STR for any residual tumor; **The extent of resection considered PR for any residual tumor greater than 10%; ***Preoperative and postoperative MRI were available in 66 of the 72 patients reported; [a]Purely endoscopic transsphenoidal approach was done in 29 of the 72 patients reported. Residual tumor was not defined in NTR, STR or PR. One patient experienced no improvement on visual function, but it was not informed whether it was unchanged or worsened; [b]Purely endoscopic transsphenoidal approach for large (> 3 cm) and giant (> 10 cm^3) adenomas was done in 43 of the 71 patients reported. Residual tumor was not defined in NTR, STR or PR. Visual acuity was not included in the analysis. The reported rates of visual outcomes reflect visual field defect of the patients suffering from giant tumors only. [c]The extent of resection considered PR for any residual tumor greater than 10%. [d]Postoperative visual fields were available for 55 patients, of whom 61.8% experienced improvement. [e]The extent of resection considered STR for any residual tumor greater than 10%. Postoperative visual fields improved in 20 patients and remained unchanged in 6 patients.

multilobular configuration and extension to the middle fossa[15] are also reported to have a negative impact on surgical resection rates by the endoscopic technique.

Taking together the results of GTR, NTR and STR as an arbitrary threshold to provide satisfactory neurovascular structures decompression, the endoscopic cohort was able to achieve decompression rates of 78.9% (range 63–95%)[10,13,Present]. Even though a fair comparison cannot be performed, because of a different definition for STR (residual tumor > 10–20%)[7], the endoscopic rates of decompression are at least similar to open and microscopic transsphenoidal groups (78.8% and 81.2%, respectively)[7].

Finally, the surgical technique used by most of the endoscopic endonasal series is the standard approach, in which a wide exposure of the sellar floor is obtained from the medial walls of the cavernous sinus laterally, the tuberculum sellae cranially and the dural indentation of the clivus/inferior transcavernous sinus caudally[6,8,10,11,14,16]. Some studies have used the extended transplanum/transtuberculum endonasal approach to address some dumbbell-shaped or suprasellar adenomas or even fibrous tumors[6,8,10,13,14,15]. The role of the extended approach is yet to be defined, but the results are promising taken into consideration the higher rates of GTR in comparison to the standard endonasal approach (average of 41.3% vs. 27.3%, respectively; Table 3). Further studies are, however, necessary to clarify this issue.

Clinical outcomes of the endoscopic endonasal transsphenoidal approach

Nine patients in our series experienced visual acuity improvement and only one patient had visual deterioration. Similar results were described by recent endoscopic endonasal series, in which the rates of visual improvement achieved a mean of 75.5% (range 32.1%–97.7%; Table 3). Given that visual improvement is observed in up to 40% in the open and microscopic transsphenoidal cohorts[7], visual outcomes are by far the major advantage of the endoscopic endonasal approach over the remaining surgical techniques[8]. Chabot et al.[8] hypothesized that the endoscope provides a better visualization and therefore protection of the optic apparatus and its blood supply, which ultimately leads to such improved outcomes.

Conversely, the endocrine outcomes are generally not so encouraging as observed with visual outcomes. Our results indicate the occurrence of 35.7% of new postoperative pituitary insufficiency, which is similar to other endoscopic endonasal series (mean 17.2%; range 4.7%–36%; Table 4). The open and microscopic cohorts revealed better outcomes, however (9.1% and 9.5%, respectively)[7]. Even though Nakao and Itakura[16] and Juraschka et al.[10] reported lower rates of new postoperative hypopituitarism, the endocrine outcomes seems to correlate inversely with the greater extent of resection and therefore with the greater surgical manipulation provided by the endoscope.

Complications of the endoscopic endonasal transsphenoidal approach

The complications related to the endoscopic transsphenoidal surgery in our series show converging rates with published studies (Tables 3 and 4), suggesting the technical safety and efficacy compared to the open transcranial and microscopic transsphenoidal approaches. We have didactically divided postoperative complications into two major groups, namely the immediate/short-term and late complications. From the first group the occurrence of CSF leak, transient DI and nasosinusal disorders (sinusitis/epistaxis) are the most frequent.

CSF leak has been considered one of the major disadvantages of the endoscopic endonasal approach, especially in the

Table 4. Immediate, short- and late postoperative complications of main series of endoscopic endonasal transsphenoidal approach for large and giant pituitary adenomas.

Author, year	Nº of patients	Immediate & short-term (%)						Late (%)		
		Trans. DI	Sinusitis/ Epistaxis	CSF leak	Meningitis	SAH / Hematoma	Transient CN deficit	Permanent DI	Pituitary Insuf.	Nasal Synechiae
Nakao and Itakura, 2011[16]	43	25.6	- / -	0	-	0 / 4.7	-	0	4.7	2.3
Di Maio et al., 2011[13]	20	-	- / -	5	-	- / -	-	-	-	-
Cusimano et al., 2012[11]	29	-	- / -	27.6	-	- / 0	-	0.07	0.31	-
Hofstetter et al. 2012[14]	43	-	- / -	0	-	- / -	-	13.9	13.9	-
Koutourousiou et al., 2013[15]	54	24.1	- / -	16.7	5.5	- / 3.7	11.1	9.6	16.7	-
Gondim et al., 2014[6]	50	36	2 / 6	8	2	6 / -	-	0.1	0.36	-
Juraschka et al., 2014[10]	66	-	13.7 / 2.7	9.6	2.7	0 / 0	0	-	5.5	-
Chabot et al. 2015[8]	39	-	- / -	10.7	2.6	-	0	7.7	12.8	15.4*
Present Series	28	53.6	7.1 / 7.1	17.8	7.1	7.1 / 0	3.6	3.6	35.7	21.4

CN: cranial nerve; CSF: cerebrospinal fluid; DI: diabetes insipidus; Pituitary insuf.: new pituitary insufficiency of one or more axis; SAH: subarachnoid hemorrhage; Trans. DI: transient diabetes insipidus. *The authors described 15.4% of sinonasal symptoms, but they were not detailed.

case of extended approaches[8]. As the matter in fact, it should be noted that it is extremely difficult to resect such complex tumors without violating the arachnoid layer[8]. The advent of nasoseptal flaps has contributed enormously to decrease its incidence[10,15]. But, even after the routine use of nasoseptal flaps, 17.8% of our patients experienced a CSF leak postoperatively. The overall rates of postoperative CSF leaks among the endoscopic surgical series are 10.6% (range 0%–27.6%; Table 4). Several different reconstruction techniques were used by the endoscopic reports in the way that a direct comparison cannot be done. However, we did not use routinely any inlay besides abdominal fat, which could be a potential source for our increased rates of CSF leak. Further studies are necessary to address this issue definitely. Open and microscopic cohorts rendered CSF leak rates of 7.1% and 5.1%, respectively[7].

Transient DI is a common complication in the immediate postoperative period with a reported incidence of 24.1%–53.6% of the patients (Table 4). It is considered to occur as a result of direct surgical manipulation, especially associated to hypothalamic injury[6]. Still in the immediate/short-term complication group, we have faced a cavernous sinus violation and consequently internal carotid artery injury, which lead to subarachnoid/tetraventricular haemorrhage followed by severe cerebral vasospasm and death. This is a rare complication of the transsphenoidal surgery with an estimated incidence of 1.58%–4.6%[15,26].

From the late complication group, permanent DI and nasosinusal disorders are a common occurrence. Of note, however, is the frequent underreported description of nasosinusal complications. Only two previous studies addressed this complication[8,16], which has a significant negative impact on patient's quality of life[27]. Nakao and Itakura[16] reported an incidence of 2.3% of nasal synechiae without the development of a nasoseptal flap, while Chabot et al.[8] use the nasoseptal flap for skull base reconstruction rendering a rate of 15.4% of late nasosinusal symptoms, which is very similar to our results (Table 4).

Limitations

The retrospective data analysis and a reduced sample were the main limiting factors of this study.

In conclusion, endoscopic endonasal transsphenoidal surgery is a valuable treatment option for large or giant pituitary adenomas, which results in high rates of surgical decompression of cerebrovascular structures. Immediate, short-term and late complication rates are at least similar, if not less, to other surgical techniques, and well accepted in terms of disease complexity. Postoperative nasosinusal symptoms are frequently overlooked, but carry a significant negative impact on patient's quality of life.

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