Endoscopic Transsphenoidal Surgery of Pituitary Adenomas: Preliminary Results of the Neurosurgery Service of Hospital Cristo Redentor

Cirurgia endoscópica transesfenoidal de adenomas pituitários: resultados preliminares do Serviço de Neurocirurgia do Hospital Cristo Redentor

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Abstract

Objective   The transsphenoidal surgery is a safe and effective technique to manage different skull base pathologies, such as pituitary adenomas. The purpose of the present study is to describe the initial experience with endoscopic transsphenoidal surgery in the treatment of pituitary adenoma patients at a tertiary hospital that is a reference in neurosurgery in Southern Brazil.

Materials and Methods   We retrospectively analyzed data from 60 patients with pituitary adenoma who underwent endoscopic transsphenoidal surgery between 2012 and 2019. Demographic characteristics, type of tumor, baseline hormonal changes, and clinical presentation were reported, as well as postoperative outcomes, tumor resection rate, and complications.

Results   The male/female ratio was of 0.53:1, and the mean age of the sample was of 54 (range: 26 to 79) years. In total, 34 patients (57%) presented the non-functioning adenoma subtype, and 26 (43%), the functioning adenoma subtype. In the non-functioning and functioning subtype groups, the average tumor diameter was of 32 mm and 18 mm, and the mean follow-up was of 27 months and 32 months respectively. Regarding visual symptoms, 79% of the patients showed improvement after surgery. Hormonal remission was achieved in 71% of the patients with

prolactinoma, 85% of those with cushing, and 57% of patients with acromegaly. Overall, gross total resection (GTR) was achieved in 50% of patients but with a significantly lower rate among patients with tumors with parasellar growth (high grade on the Knosp classification). The most prevalent surgical complications observed were postoperative cerebrospinal fluid (CSF) leak and meningitis in 11% and 6% of the cases respectively.

Conclusion   We have shown that transsphenoidal endoscopic surgery can produce good results in the management of pituitary adenomas, with acceptable peri- and postoperative morbidity and mortality. Regardless of the technique used, the presence of large and giant pituitary adenomas with a high Knosp grade represents an enormous challenge for contemporary neurosurgery.

Resumo

Objetivo   A cirurgia transesfenoidal é uma técnica segura e eficaz para o tratamento de patologias da base do crânio, como os adenomas hipofisários. O objetivo deste estudo é demonstrar a experiência inicial com a cirurgia endoscópica transesfenoidal no tratamento de pacientes com adenoma hipofisário em hospital terciário, referência em neurocirurgia no Sul do Brasil.

Materiais e Métodos   Analisamos retrospectivamente os dados de 60 pacientes com adenoma hipofisário submetidos à cirurgia endoscópica transesfenoidal entre 2012 e 2019. Características demográficas, tipo de tumor, alterações hormonais basais e apresentação clínica foram relatadas, bem como evolução pós-operatória, grau de ressecção tumoral e complicações.

Resultados   A proporção homem/mulher foi de 0.53:1, e a idade média da amostra foi de 54 (variação: 26 a 79) anos. Ao todo, 34 pacientes (57%) tinham o subtipo funcional de adenoma, e 26 (43%), o subtipo não funcional de adenoma. Nos grupos não funcional e funcional, o diâmetro médio do tumor foi de 32 mm e 18 mm, e o tempo médio de acompanhamento foi de 27 meses e 32 meses, respectivamente. Em relação aos sintomas visuais, 79% dos pacientes apresentaram melhora após a cirurgia. A remissão hormonal foi alcançada em 71% dos pacientes com adenomas secretores de prolactina, em 85% daqueles com adenomas secretores de hormônio adrenocorticotrófico e em 57% dos pacientes com adenomas secretores de hormônio do crescimento. A ressecção total foi obtida em 50% dos pacientes, mas com taxa significativamente menor em pacientes com tumores com crescimento parasselar (grau elevado na classificação de Knosp). As complicações cirúrgicas mais prevalentes observadas foram fístula liquórica pós-operatória e meningite, em 11% e 6% dos casos, respectivamente.

Conclusão   Demonstramos que a cirurgia endoscópica transesfenoidal pode produzir bons resultados no manejo de adenomas hipofisários, com aceitável morbimortalidade peri e pós-operatória. Independentemente da técnica utilizada, a presença de adenomas hipofisários grandes e gigantes com grau de Knosp elevado representa um enorme desafio para a neurocirurgia contemporânea.

Palavras-chave
► cirurgia endoscópica
► glândula pituitária
► epidemiologia
► adenoma

Introduction

Transsphenoidal surgery dates back to the beginning of the twentieth century, when pioneering surgeons described the first access to the sella turcica region.[1–5] In 1910, Oskar Hirsch, a Viennese otolaryngologist, described his classic endonasal transseptal transsphenoidal approach;[6,7] in the same year, Albert Halstead described the sublabial access,[5]

popularized by Harvey Cushing, who performed more than 2 thousand operations between 1910 and 1925.[7,8]

In Brazil, in 1935, Dr. Correa Meyer and Dr. Eliseu Paglioli described the successful performance of the transsphenoidal access using Hirsch's technique to remove a pituitary tumor.[9] Since the historical technical contributions of Jules Hardy, published in the late 1960s and early 1970s, transsphenoidal surgery has been modernized and became popular as the

best option in the surgical management of intrasellar lesions.[5,10,11]

The advantages over the transcranial access are that it provides excellent visualization of the pituitary gland and neighboring structures, with lower rates of morbidity and mortality.[12] Gerard Guiot is recognized as the first neurosurgeon to use the endoscope in transsphenoidal surgery in 1963.[13]

The experience acquired by ear, nose and throat (ENT) physicians in sinus surgery, associated with that of neurosurgeons using the endoscope in an assisted manner, stimulated an interest in endoscopy that began in the end of the 1980s.[14]

As a result of this collaboration, the use of pure or isolated endoscopy started in the 1990s. In the last 25 years, there has been an exponential growth in its use, and it is currently considered a safe and effective technique to manage different skull base pathologies.[15–30]

Hospital Cristo Redentor (HCR), a public hospital part of Grupo Hospitalar Conceição (GHC), located in the City of Porto Alegre, Southern Brazil, is considered a national reference in neurosurgery. In its facilities, through the effort and integration of the neurosurgery and otorhinolaryngology specialties, endoscopy in transsphenoidal surgery began in 2012.

The objective of the present study is to describe the initial experience with endoscopic transsphenoidal surgery in the treatment of pituitary adenomas at HCR.

Materials and Methods

We conducted a retrospective study to evaluate the first 60 patients with pituitary adenomas submitted to endoscopic transsphenoidal surgery from 2012 to 2019 and treated by the same main team (GP and AM). The study was submitted and approved by the GHC Ethics in Research Committee.

All patients underwent a preoperative evaluation to confirm the diagnosis, which was based on history, clinical examination, laboratory tests, ophthalmological evaluation, and imaging tests.

All patients underwent an evaluation of the pituitary function by the endocrinologist (FA). Imaging studies, such as computed tomography (CT) of the sinuses and magnetic resonance imaging (MRI) of the sella with all sequences, were performed in all cases. The Hammer and Radberg classification[31] was used to assess the extent of pneumatization of the sphenoid sinus in all cases.

The patients were divided into two groups according to the adenoma subtype (non-functioning and functioning), and their respective data were analyzed individually. The sizes of the adenomas were described, and their extensions were classified using Hardy and Vezina[32] and Knosp classifications.[33]

Surgical Technique
The patients were in supine position under general anesthesia and orotracheal intubation, with the back elevated (10°) and the head slightly rotated to the right. Intrave-

nously, a single dose of cefazolin 1 g was administered as a prophylactic antibiotic during the initial phase of anesthesia.

The ENT physician and the neurosurgeon were positioned on the patient's right and left sides respectively. The video tower and rigid endoscopes of 4 mm at 0° and 30° were used, with the recording and storage of images performed routinely.

In the initial phase of the procedure, the nasoseptal flap was harvested. The flap was relocated to the original position at the end of the surgery using suture or biological.

The access to the sellar region was performed following the nasal, sphenoidal, and skull base phases. The use of the two nostrils enabled the surgical teams to work together with the optics and surgical instruments present in the operative field in an integrated manner.

After opening the sella floor and dura mater, tumor removal and subsequent exploration of the sella were performed. The repair was performed sequentially using an abdominal fat graft, the nasoseptal flap, and fibrin glue in patients with the observed opening of the sellar diaphragm and cerebrospinal fluid (CSF) drainage. In these cases, at the end of the surgical procedure, a lumbar drain was maintained for 72 hours.

Considering the high number of cases of postoperative leak observed in the early years, the reconstruction technique was modified by adding bone graft or titanium mesh to reconstruct the sella turcica. (►Figure 1). We observed an important decrease in the incidence of postoperative fistula after the routine adoption of this technical modification. The tumor samples collected during the procedures were sent for anatomopathological study and subsequent immunohistochemical analysis.

Postoperative Evaluation
The patients were evaluated postoperatively concerning the neuro-ophthalmological status and endocrinological evaluation. The immunohistochemistry findings were reported, and complications were reviewed and analyzed.
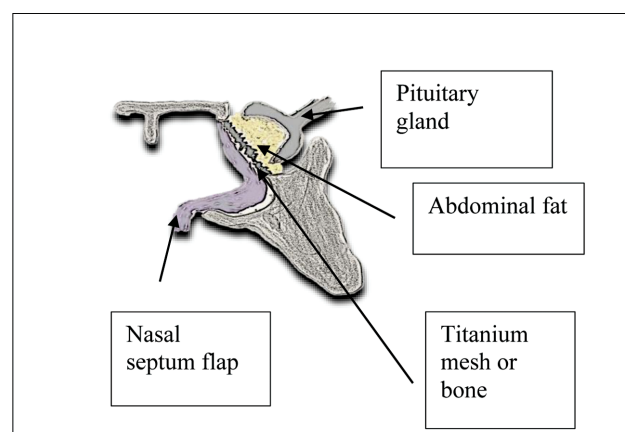

Fig. 1 Schematic drawing of sellar reconstruction using bone or titanium mesh with the application of the nasoseptal graft. Fibrin glue is used to help secure the flap.

During the follow-up, the patients underwent MRI between 3 months and 1 year after the surgery. According to the last control performed, tumor removal was classified as gross total resection or subtotal/partial resection. Patients with functioning tumors were followed up by the endocrinology team using laboratory criteria and clinical symptoms to define the criteria for disease remission.

Results

Overall, we operated 60 patients with pituitary adenomas, 21 male (35%) and 39 female subjects (65%), with a mean age of 54 years: 34 cases were classified as non-functioning adenoma and 26, as functioning.

Hormone changes, with hyperfunction or hypofunction, were often found as the clinical presentation, as well as visual symptoms. Regarding the group with functioning tumors, 11 patients presented acromegaly, 7 subjects had macroprolactinomas, 7 presented Cushing syndrome, and 1 patient had hyperthyroidism/acromegaly syndrome.

Hypogonadism, hypothyroidism, and hypocortisolism were found in 26%, 23%, and 5% of the cases respectively. Panhypopituitarism was found in 5% of the patients, and 78% had preoperative vision disorder manifested by changes in the visual field or loss of visual acuity.

Symptoms such as headache were observed in 18% of the cases, while mental confusion, seizure, and hemiparesthesia were seen in 3%. A total of 3 patients (5%) had undergone previous surgical treatment; all of them underwent transsphenoidal microsurgery in other institutions.

Demographic characteristics, type of tumor, baseline hormonal changes, clinical presentation, and previous surgery history are summarized in ►Table 1.

Suprasellar extension greater than 20 mm was observed in 20 patients (59%) in the non-functioning group and only in 3 patients (12%) in the functioning group. In the functioning group, 18 patients (69%) presented suprasellar extension measuring between 0 mm and 10 mm.

Regarding the Knosp classification, in the non-functioning group, 21 patients (65%) were categorized as grades 0 to 2, and 13 patients (35%), as grades 3 to 4. In the functioning tumor group, 21 patients (81%) were classified as grades 0 to 2, and 5 patients (19%), as grades 3 to 4. The suprasellar extension and degree of cavernous sinus invasion (Knosp scale) of both groups are detailed in ►Table 2 and ►Figures 2, 3, 4 and 5.

According to the Hammer and Radberg classification, 6 patients (10%) had a sinus of the presellar type, equally distributed between the two groups of patients. Most patients had the sellar type, and no cases of sphenoidal sinus of the conchal type were observed.

(►Table 3)

Surgical Results

Regarding the immunohistochemistry results, in the group of non-functioning adenomas, 16 patients (47%) presented "null cell". In the functioning group, the results showed gonadotropin, adrenocorticotropic hor-

Table 1 Baseline characteristics of the patients

Characteristics	N	Percentage
Patients	60	100%
Male	21	35%
Female	39	65%
Mean age	54 years old	
Non-functioning adenomas	34	57%
Functioning adenomas	26	43%
Hyperprolactinemia	7	12%
Growth hormone-secreting adenoma	11	18%
Adrenocorticotropic hormone -secreting adenoma	7	12%
Thyroid-stimulating hormone/ growth hormone-secreting adenoma	1	2%
Hypogonadism	16	26%
Hypothyroidism	14	23%
Hypocortisolism	3	5%
Panhypopituitarism	3	5%
Visual field deficit	26	43%
Abnormal visual acuity	21	35%
Headache	11	18%
Mental confusion	2	3%
Hemiparesthesia	2	3%
Seizure	2	3%
Previous surgery	3	5%

mone (ACTH), and prolactin in 41%, 6%, and 3% of the cases respectively.

Still according to the immunohistochemistry results, in the functioning group, there were 7 patients (27%) with tumors that secreted growth hormone (GH), 7 (27%) patients with prolactin-secreting tumors, 4 patients (15%) with ACTH-secreting tumors, and only 1 patient (4%) with a tumor that secreted thyroid-stimulating hormone (TSH) (►Table 4).

Regarding the visual symptoms 79% of the patients experienced improvement after surgery, while 15% remained stable, and 6% presented worsening of the deficit in the postoperative period.

Hormonal disfunction was found in 55% of the patients, a rate similar to the preoperative rate. None of the patients progressed to panhypopituitarism, and there were no cases of improvement in the pituitary function during the postoperative follow-up period. A total of 54 patients underwent postoperative MRI between 3 months and 1 year, there were 5 cases of loss to outpatient follow-up, and 1 patient died in the first month after surgery.

Overall, GTR was possible in 27 cases (50%). In the non-functioning group, it was achieved in 12 patients (37%), and, in the remaining cases, the resection was subtotal or partial.

Table 2 Size, suprasellar extension and degree of cavernous sinus invasion (Knosp scale) of the tumors

Radiological characteristics	Adenoma	Non-functioning – n (%)	Functioning – n (%)
Number of cases	60	34 (56.6)	26 (43.4)
Size (mm)	0-10	0 (0.0)	3 (11)
	10-20	2 (6)	15 (58)
	20-30	15 (44)	5 (19)
	30-40	11 (32)	2 (8)
	40-50	6 (18)	1 (4)
Median (mm)		32	18
Suprasellar extension	0-10	2 (6)	18 (69)
	10-20	12 (35)	5 (19)
	20-30	17 (50.0)	2 (8)
	> 30	3 (9)	1 (4)
Grade on the Knosp classification	0	5 (15)	15 (58)
	1	5 (15)	5 (19)
	2	11 (35)	1 (4)
	3	7 (19)	3 (11)
	4	6 (16)	2 (8)

The rate of GTR showed a difference when comparing the Knosp 0-2 and Knosp 3-4 patients: it was significantly lower in tumors with a high grade on the Knosp classification ($p < 0.05$).

Complete resection was achieved in 69% of the Knosp 0-2 patients and all Knosp 3-4 subjects underwent subtotal or partial resection. In total, 7 patients (13%) in whom only partial resection was achieved were referred for a new surgery; 3 of them underwent a new endoscopic endonasal procedure, and 4 were referred for craniotomy. After the second procedure, GTR was achieved in 3 (43%) patients, and the 4 (67%) remaining subjects with residual tumors were referred for radiotherapy. The 13 (40%) patients who

remained with subtotal resection showed no progression of the symptoms during the follow-up period and were kept under outpatient observation.

Details of the results found for each functioning tumor subtype are described as follows.

Growth Hormone-Secreting Adenomas

Growth hormone-secreting adenoma was the most common hormone-secreting adenoma found in our series: 4 out of 11 patients were excluded due to loss to follow-up; all the remaining 7 patients had macroadenomas, and 1 of them had a cystic characteristic.
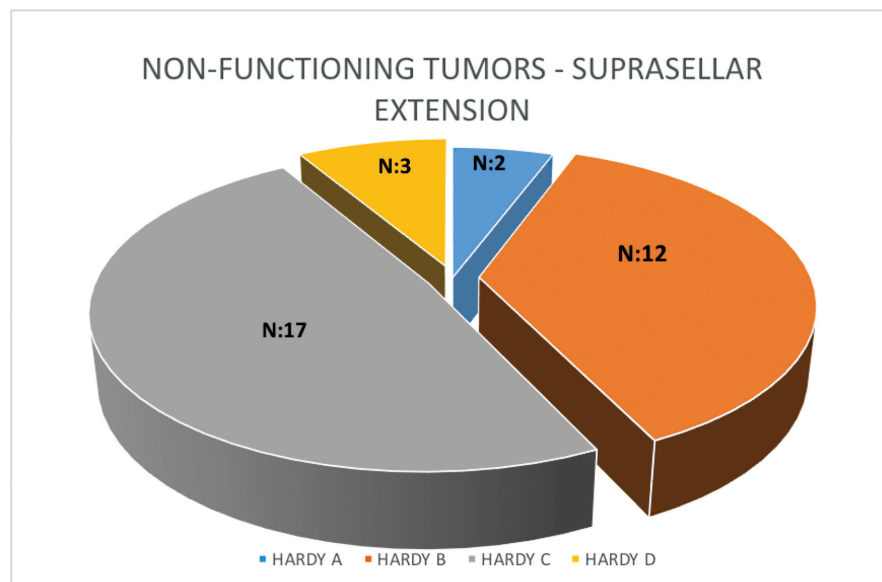

Fig. 2 The graph shows the number of cases of non-functioning tumors classified by the Hardy grade. 17 patients had Hardy grade A, 12 Hardy grade B, 2 Hardy grade C and 3 Hardy grade D.
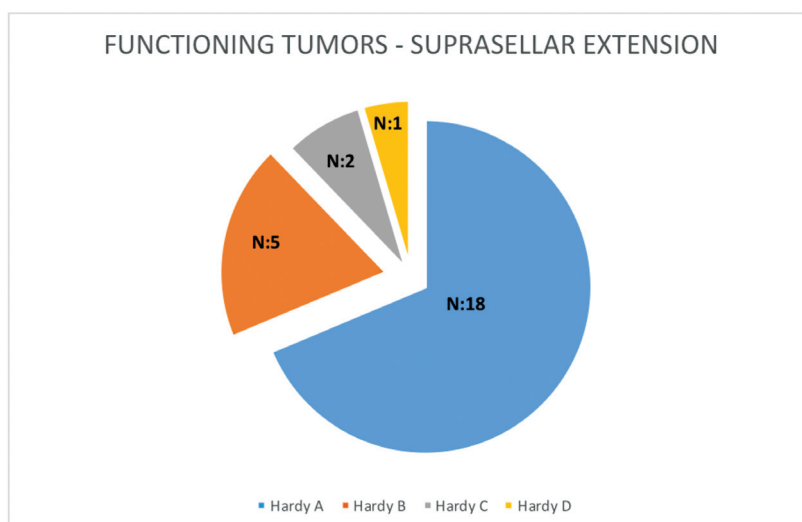
Fig. 3 The graph shows the number of cases of functioning tumors classified by the Hardy grade. 18 patients had Hardy grade A, 5 Hardy grade B, 2 Hardy grade C and 1 Hardy grade D.
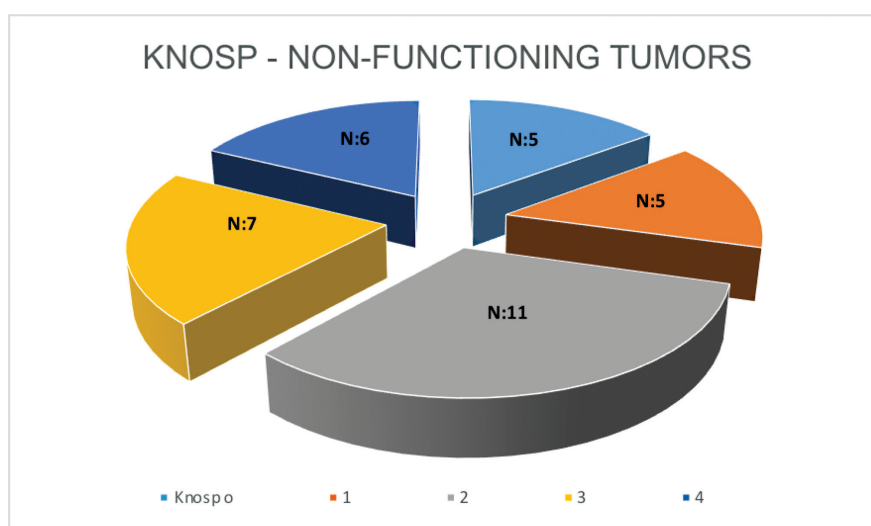

Fig. 4 The graph shows the number of cases of non-functioning tumors classified by the Knosp grade. 5 patients had Knosp grade 0, 5 Knosp grade 1, 11 Knosp grade 2, 7 Knosp grade 7 and 6 Knosp grade 4.
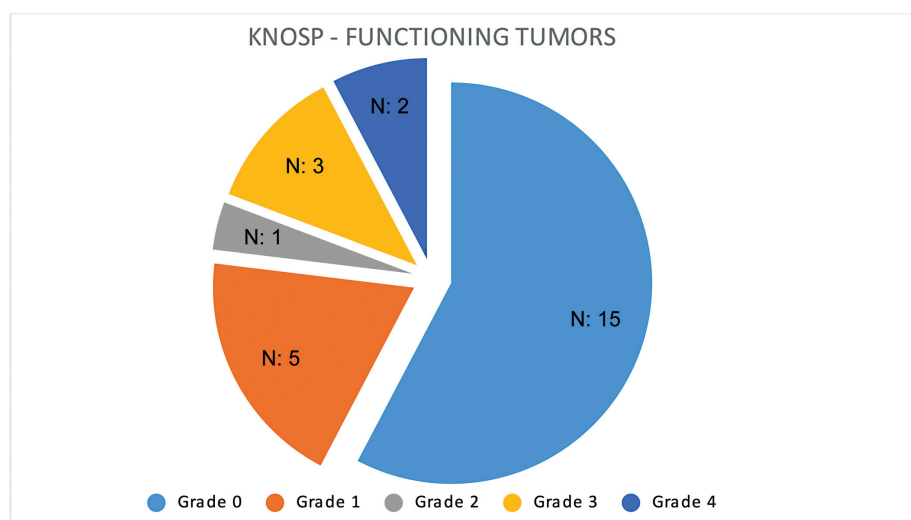

Fig. 5 The graph shows the number of cases of functioning tumors classified by the Knosp grade. 15 patients had Knosp grade 0, 5 Knosp grade 1, 1 Knosp grade 2, 3 Knosp grade 3 and 2 Knosp grade 4.

Table 3 Type of sphenoid sinus for functioning and non-functioning adenoma groups. The sellar type sinus was the most frequent in both groups

Sphenoid sinus type	Non-Functioning adenomas – n (%)	Functioning adenomas – n (%)
Sellar	31 (91)	23 (89)
Presellar	3 (9)	3 (11)
	TOTAL: 34 (100)	TOTAL: 26 (100)

Table 5 Number of complications identified in the sample. The most common were intraoperative CSF leak and transient diabetes insipidus

Complications	n (%)
Intraoperative cerebrospinal fluid leak	13 (24)
Postoperative cerebrospinal fluid leak	6 (11)
Meningitis	4 (7.4)
Intrasellar hematoma	2 (3.6)
Empty sella with downward displacement of suprasellar visual system	1 (1.8)
Transient diabetes insipidus	9 (16.6)
Death	1 (1.8)

In 4 patients (57%), hormonal control was achieved in the postoperative period. The 3 patients without hormonal control after the surgery showed a good clinical response to pharmacological treatment during the follow-up.

Prolactinomas

Of the 7 patients with prolactinomas selected for surgery, 6 had macroadenomas with cystic and/or hemorrhagic characteristics. One patient had a macroadenoma with a high Knosp grade presented with no hormonal control using dopaminergic agonists. We achieved overall hormonal control after surgery in 5 patients (71%).

Table 4 Summary of the immunohistochemistry findings

| Immunohistochemistry	Non-functioning tumors – n (%)	Functioning tumors – n (%)
Null cell	16 (47)	5 (19)
Adrenocorticotropic hormone -secreting adenoma	2 (6)	4 (15)
Gonadotropin-secreting adenoma	14 (41)	1 (4.0)
Prolactin-secreting adenoma	1 (3)	7 (27)
Thyroid-stimulating hormone-secreting adenoma	0 (0)	1 (4.0)
Growth hormone-secreting adenoma	0 (0.0)	7 (27.0)
Multihormonal production	0 (0.0)	1 (4)
Total patients	34 (100)	26 (100)

ACTH-Secreting Adenoma

A total of 6 patients had macroadenomas with sizes ranging from 10 mm to 20 mm, and only 1 patient had a micro-adenoma with a size of 6 mm. No tumor had cystic characteristics, and there was hormonal control after surgery in 6 cases (85%) during the follow-up.

TSH/GH-secreting Adenoma

In the present series, we found one patient with a macroadenoma with lateral extension (Knosp 4) and a plurihormonal profile (GH- and TSH-secreting). After the surgery, the TSH and GH values remained high, although lower than in the preoperative period. A control MRI showed subtotal resection (presence of residual tumor within the cavernous sinus). After introducing the drug treatment, reduction and control of the hormonal levels maintained during the follow-up period were achieved. The mean follow-up time was of 27 months and 32 months in the non-functioning and functioning adenoma groups respectively.

Details of the surgical results for each subgroup are shown in the following organizational chart:
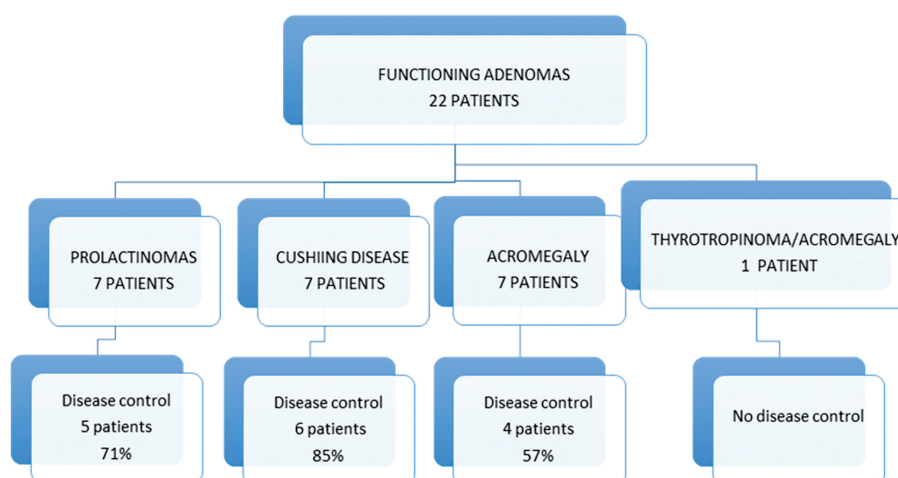
Complications

Intraoperative CSF leak is the most frequent complication, and it was found in 13 patients (24%), followed by postoperative CSF leak in 6 patients (11%).

There were 4 patients (7.4%) with meningitis; 3 of them showed good evolution, but 1 developed severe meningitis and ventriculitis complications and died after a long period of hospitalization. One patient had epistaxis on the first day after surgery and needed to be reoperated.

According to the postoperative tomography, 2 patients (3.6%) with large tumors developed intrasellar hematoma. The management was conservative, given the stability of the visual symptoms. One case of a male patient with late visual deterioration (one year after surgery) was associated with chiasma prolapse in the empty sella. He underwent a transcranial approach for chiasmapexy, and evolved with the improvement in the visual deficit.

Transient diabetes insipidus (DI) was observed in 9 patients (16.6%), but there were no cases of postoperative permanent DI. All of them were managed in the intensive care unit and showed good response to the clinical interventions.

There was a death related to CSF fistula and central nervous system (CSN) infection that occurred within 30 days of the surgery. The complications have been summarized in ►Table 5.

Discussion

Transsphenoidal surgery is considered an excellent alternative to craniotomy in the management of most pituitary adenomas.[34]

Throughout the twentieth century, the technique underwent improvements and modifications,[35] and the use of endoscopy in transsphenoidal surgery is considered a recent breakthrough.[36]

According to Yu et al.,[37] endoscopic endonasal transsphenoidal surgery in the treatment of pituitary adenomas presents results that are similar or better than those of traditional microscopy in terms of mass removal, improvement in visual symptoms, and preservation of endocrine function.

Regarding nasal morbidity and quality of life, it can be said that the endoscopic technique is less morbid because it does not use a sublabial incision or nasal plug, besides producing lower levels of mucosal detachment.[38,39]

The technical advantages of endoscopic endonasal transsphenoidal surgery are related to an increase in the working angle, enabling a close and panoramic view of the anatomical structures.[27,40,41]

In the present study, we performed the isolated or pure endoscopic technique, in which only the endoscope is used in all stages of the procedure, as described by several authors in the 1990s.[15–18]

In the present series, most of the tumors were macroadenomas. Analyzing the groups of patients with non-functioning and functioning adenomas, we observed that the mean sizes of the tumors was of 32 mm and 18 mm respectively, which are larger than the sizes reported in some of the previously described series.[42,43]

Delay in diagnosis due to the difficulty on the part of the patients to access our health system could explain this finding.

Non-Functioning Tumors

The main objectives of the surgical treatment of non-functioning adenomas are to preserve the neighboring neural structures, to prevent functional worsening of the pituitary and visual function, and to revert any functional impact on the surrounding neural structures.[44] Although the improvement in pituitary function in the postoperative period has been reported to range from 16% to 48% of the cases,[45] no improvements were reported in previous series.[46,47] In the present study, pituitary function remained unchanged, with no improvement or worsening observed in any patient.

According to Wichers-Rother et al.,[47] the objective of transsphenoidal surgery is to improve visual field defects rather than to improve the pituitary function. Regarding vision, 79% of our patients showed visual improvement in the postoperative period, a rate similar to that of previous reports.[44,45,48] In the present series, the rate of 37% of GTR in the non-functioning group is lower than the one reported in previous endoscopic series.[49–55] This result is related to the learning curve of the endoscopic technique[56] associated with the findings of large tumors with frequent lateral extension. Patients with high Knosp grades are more likely to present tumor invasion of the parasellar region, which decreases the chance of GTR.[57] Accordingly, we found a statistically significant difference in GTR when comparing patients with Knosp grades 0 to 2 and 3 to 4.

Tumors with Knosp grade 3 or 4 have a greater degree of cavernous sinus invasion and were predictors of greater difficulty in achieving a GTR.

In the present study, the approaches were restricted to the sellar region, which certainly limited the possibility of achieving GTR in tumors of larger size and volume.

Biological factors inherent to the tumor are important in relapse, so not all residual lesions will present a regrowth over time.[46,58] In agreement with this, 13 patients (40%) in whom residual lesions were observed on the postoperative MRI in the present study did not present any changes during the follow-up.

As the postoperative recurrence rate for non-functioning tumors peaks between 1 and 5 years and only reduces after 10 years, it is essential to maintain the follow-up of these patients for longer periods.[59]

Functioning Tumors

Tumors that secrete GH and prolactin are the most common type of functioning pituitary adenomas.[49] In the present series, we found more GH-secreting adenomas (37%) and an equal number of ACTH- and prolactin-secreting adenomas (29%).

Regarding the subjects with GH-secreting tumors, we obtained control of hormonal levels in 4 patients (57%), a rate similar to the 56.4% mean historical control rate for first-time surgery.[60]

According to Nomikos et al.,[61] the remission rate in patients undergoing transsphenoidal surgery tended to decrease in macroadenomas, being of 33.3% for suprasellar tumors with visual impairment and of 44.5% for suprasellar tumors without impairment. In our case series, patients with acromegaly had large lesions, more than 1 cm in diameter, and we achieved a remission rate in 57% of cases.

Managing patients with acromegaly without control of hormonal levels after the first operation is a matter of discussion.[61] Three patients in whom control was not achieved after surgery were referred for drug treatment and showed good clinical response during the follow-up.

Regarding prolactinomas, although we found large tumors (the largest measuring 45 mm), most of them had cystic or hemorrhagic characteristics, increasing the chance of achieving GTR. Our resection rate of 71% for prolactin-secreting macroadenomas is similar to rates in previously described series.[53,62,63]

The surgical treatment of prolactinomas is indicated in patients who have tolerance or resistance to the use of dopaminergic agonists or who have tumors larger than 20 mm with an associated visual deficit.[53] In some countries, the cost of the drug treatment is also considered in this decision.[49] Therefore, there is some controversy about the best management. According to Donoho and Laws (ref [64]), patients with prolactinomas in the subacute evolution and mild early visual changes can be controlled with medication.

There is some controversy about the best management. According to Donoho and Laws,[64] patients with prolactinomas in subacute evolution and mild early visual changes could be managed with medications.

On the other hand, Akinduro et al.[65] report that, given the significant reduction in the largest tumor volume and prolactin levels occurring within six months after starting the treatment, surgery would play an important role in patients with a large tumor and acute visual deterioration.

We agree that patients with prolactin-secreting macroadenomas with cystic/hemorrhagic characteristics, suprasellar growth, and visual loss may actually benefit from the endoscopic endonasal transsphenoidal surgery.

Our disease control rate of 85% for Cushing disease is superior to that of a previous endoscopic series,[66] considering that 6 of the 7 operated patients had macroadenomas.

As previously described, the recurrence rate for Cushing disease can vary from 10% to 30% up to 10 years after surgery,[67,68] with 50% of recurrences occurring during the first 50 months after surgery.[69] Considering that our follow-up was of 32 months, there is a need for longer follow-up periods to confirm the remission rate.

Tumors that secrete TSH (thyrotropinomas) are very rare pituitary tumors, corresponding to 1% to 5% of the cases.[70–72] They often concomitantly secrete other pituitary hormones, such as prolactin, gonadotropins, and GH, which is the most frequently co-secreted hormone.[71]

These tumors show an aggressive growth pattern and are harder to control only with surgery compared with other types of adenomas. Therefore, radiotherapy and drug treatment should be considered in the case of surgical failure.[72]

In the present series, one patient had a macroadenoma that simultaneously secreted TSH and GH. This patient underwent subtotal resection and achieved hormonal control during the follow-up after using long-acting somatostatin analogs.

Complications

The occurrence of intraoperative and postoperative CSF leaks in endoscopic surgery of pituitary adenomas varies from 16% b to 26% and from 1.3% to 10.3% respectively.[73,74]

According to Lobatto et al.,[75] the following preoperative risk factors are associated with a potential higher risk of CSF leak: adenomas with intraventricular extension, age under 65 years, being female, peptic ulcer disease, and high body mass index (BMI). Boling et al.[76] describe intraventricular extension as the main risk factor associated with the occurrence of postoperative fistula, and they suggest aggressive treatment of the intraoperative fistula in these cases.[76]

The learning curve is also considered an important factor associated with the risk of CSF leak and most of the complications described.[73] In the present study, our CSF leak rate of 11% is strongly associated with the learning curve.

In endoscopic pituitary surgery, the incidence of intracranial infection ranges from 0 to 9.8%.[75] Longer operative time, diabetes mellitus, and intraoperative CSF leak are the main factors associated with its occurrence.[77] In the present study, the rate of CNS infection was of 7.4%, which falls within this range. All cases were associated with the occurrence of intraoperative CSF leak.

The occurrence of intratumoral bleeding of large and giant adenomas in the postoperative period has been reported to range from 2.1% to 3.7%.[78–80] Considering the high risk of visual deterioration, emergency craniotomy should always be considered in the management of this complication.[81] In the present study, the rate of intratumoral bleeding of 3.6% is similar to the rates reported in previous series. The patients in the present study who suffered from this complication did not show any visual deterioration, and they were not referred to emergency craniotomy.

The association of an empty sella with visual impairment was described almost 50 years ago.[82] Such a condition is associated with delayed visual deterioration after pituitary surgery.[83] The pathophysiology would be the presence of scar tissue related to the secondary empty sella, causing retraction and lower displacement of the sellar diaphragm and the optic apparatus. The repair of such a condition, known as chiasmapexy, can be performed by the transcranial or transsphenoidal routes.[84]

In the present series the only patient with chiasmapexy needed a transcranial repair in which retraction of the optic apparatus and its lower displacement along with the sellar diaphragm were observed. Release of fibrosis and scar tissue adhered to the optic nerves was achieved, improving visual acuity in the postoperative period.

Although it is a rare condition, the pituitary surgeon must watch out for patients with visual deterioration in the late postoperative period associated with the presence of an empty sella.

The prevalence of temporary and permanent DI is of 9.1 and 2.3% respectively, which is significantly lower when compared to microsurgery.[85] According to Kim et al.,[52] invasive tumors, previous surgery, and radiotherapy can increase its prevalence. In the present series, 9 patients (16.6%) developed transient DI, and none developed permanent DI.

The overall mortality rate in the present series was 1.8% (1 patient), which is higher than the mean rate of 0.5% reported in the literature.[76] The case was directly related to the surgical procedure (CSF leak/meningitis).

There certainly is a learning curve regarding the use of the endoscopic technique. As the experience increases, the incidence of complications as a whole will obviously decrease. This current study describes a small sample submitted to the initial experience with endoscopy in transsphenoidal surgery.

Conclusion

The current study describes a small sample submitted to the initial experience with endoscopy in transsphenoidal surgery in a public tertiary hospital, a reference in neurosurgery in Southern Brazil. We were able to show that the technique can yield good results in the management of pituitary tumors, with acceptable peri- and postoperative morbidity and mortality. Regardless of the technique currently used, the presence of large and giant pituitary adenomas with high Knosp grades represents a great challenge for contemporary neurosurgery.

Conflict of Interests
The authors have no conflict of interests to declare.

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