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ORIGINAL ARTICLE

Endoscopic endonasal transsphenoidal resection of pituitary adenomas: preliminary evaluation of consecutive cases[☆,☆☆]

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Abstract
Introduction: Endoscopic endonasal transsphenoidal surgery has gained increasing acceptance by otolaryngologists and neurosurgeons. In many centers throughout the world, this technique is now routinely used for the same indications as conventional microsurgical technique for pituitary tumors.
Objective: To present a surgical experience of consecutive endoscopic endonasal trans-sphenoi-dal resections of pituitary adenomas.
Methods: In this study, consecutive patients with pituitary adenomas submitted to endoscopic endonasal pituitary surgery were evaluated regarding the rate of residual tumor, functional remission, symptoms relief, complications, and tumor size.
Results: Forty-seven consecutive patients were evaluated; 17 had functioning adenomas, seven had GH producing tumors, five had Cushing's disease, and five had prolactinomas. Of the function-ing adenomas, 12 were macroadenomas and five were microadenomas; 30 cases were non-func-tioning macroadenomas. Of the patients with functioning adenomas, 87% improved. 85% of the patients with visual deficits related to optic nerve compression progressed over time. Most of the patients with complaints of headaches improved (76%). Surgical complications occurred in 10% of patients, which included with two carotid lesions, two cerebrospinal fluid leaks, and one death of a patient with a previous history of complications.
Conclusion: Endoscopic endonasal pituitary surgery is a feasible technique, yielding good surgi-cal and functional outcomes, and low morbidity.
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Ressecção endoscópica transesfenoidal de adenomas de hipófise: avaliação preliminar de pacientes consecutivos

Resumo

Introdução: A cirurgia endoscópica endonasal ganhou aceitação crescente por otorrinolaringologistas e neurocirurgiões. Em muitos centros, esta técnica é agora rotineiramente utilizada para as mesmas indicações que a técnica microcirúrgica convencional.

Objetivo: Descrever resultados cirúrgicos relativos à remissão hormonal, ressecção do tumor e complicações de série consecutiva de pacientes com adenoma da hipófise submetidos à ressecção endoscópica.

Método: Estudo de série de pacientes consecutivos com adenomas da hipófise, submetidos à cirurgia endoscópica endonasal, avaliados quanto à taxa de tumor residual, remissão funcional, sintomas, complicações e o tamanho do tumor.

Resultados: De 47 pacientes consecutivos, 17 eram portadores de adenomas funcionantes, sete produtores de GH, cinco com doença de Cushing e cinco prolactinomas. Dos adenomas funcionantes, 12 foram macroadenomas, cinco microadenomas, e 30 macroadenomas não funcionantes. Dos adenomas funcionantes, 87% melhoraram. Em relação ao déficit visual, 85% melhoraram ao longo do tempo. A maioria dos pacientes que apresentou queixas de cefaléia melhorou (76%). Complicações cirúrgicas ocorreram em 10% dos pacientes, com duas lesões da carótida, duas fístulas liquóricas e uma fatalidade em um paciente com um histórico complicado.

Conclusão: A cirurgia hipofisária endoscópica endonasal é uma técnica viável, rendendo bons resultados cirúrgicos e funcionais e baixa morbidade.

Introduction

The sublabial transsphenoidal approach to the sella turcica, as described by Cushing,[1] has been the primary route for pituitary tumor resection. With the introduction of operative microscopy and radiofluoroscopy, the transsphenoidal approach has gained increased popularity. Subsequent modifications to minimize mucosal trauma and patient discomfort were originally described by Hirsch[2] and popularized by Griffith and Veerapen[3] as the direct endonasal approach. This minimally invasive route to the sella turcica allows for simpler and more rapid nasal dissection, with fewer postoperative nasal complications The endoscope was first employed in 1963 by Guiot to visualize the contents of the sella turcica.[4] Pure endoscopic endonasal transsphenoidal surgery was described in detail by Jho and Carrau;[5] subsequently, outcomes related to the original procedure and extended endoscopic approaches have been reported by other authors.[6-12] Based on data, endoscopic endonasal transsphenoidal surgery has gained increasing acceptance by otolaryngologists and neurosurgeons. In many centers throughout the world, this technique is now routinely used for the same indications as the conventional microsurgical technique. This study aimed to analyze the surgical outcomes and complications in a series of 47 consecutive patients who underwent a purely endoscopic endonasal transsphenoidal approach for treatment of pituitary adenomas.

Patients and method

All consecutive patients who underwent endoscopic transsphenoidal procedures for pituitary adenomas in this center between January of 2009 and December of 2012 were included in this study. All clinical and surgical data were collected regarding tumor size, symptoms, residual tumor after surgery, functional remission, symptom relief, and complications. All patients underwent neurological, ophthalmological, and endocrinological examinations before and after resection. This study was approved by the institutional review board under No. 00803412.9.0000.5404.

Patients with non-functioning adenomas were submitted to surgery in cases of pituitary dysfunction or significant mass effect with chiasm compression. Endoscopic resection of prolactinomas was performed in selected cases: chiasmatic compressive lesions, failed hormonal control with medical therapy, important side effects, or refusal of clinical treatment. Other functioning adenomas were treated primarily by endoscopic surgery. In the cases that did not achieve successful hormonal control after surgery, medical therapy was included as standard of care. The same otolaryngologist and neurosurgeon team operated all patients.

Endocrinological investigation included multiple measurements of plasma GH (range: 1 to 9 ng/mL for males; 1 to 16 ng/mL for females); insulin-like growth factor-I (IGF-I, adjusted for age); GH level after oral glucose tolerance test (OGTT with or without suppression); prolactin (< 20 ng/mL), adrenocorticotrophic hormone (ACTH; 9 to 52 pg/mL); basal cortisol (8 AM) (4 to 19 ug/mL); 24-hour urinary free cortisol (10 to 110 ug/2 4h) when Cushing's disease was suspected; thyroid-stimulating hormone (TSH: 2 to 11 uU/mL); free thyroxine (0.8 to 2.8 ng/dL); luteinizing hormone (LH, adjusted for age and gender); and follicle-stimulating hormone (FSH, adjusted for age and gender); testosterone (adjusted for age and gender) and estradiol (adjusted for gender); levels were studied before surgery and three

months afterwards. As a standard of care, all tumors were submitted for pathological analyses.

All patients with tumors close to the optic chiasm underwent ophtalmologic evaluation with computerized campimetry before and three months after surgery.

All patients underwent tumor evaluation via 1.5 Tesla magnetic resonance imaging (MRI) with T1- and T2-weighted spin echo before and after gadolinium-based contrast medium. Tumor size was determined according to maximum tumor diameter in two categories: microadenoma (< 10 mm) and macroadenomas (> 10 mm). The lesions were also classified, according to their relationship to the sella, as pure intrasellar lesions and lesions with extrasellar components. Paranasal sinus computed tomographic scan was obtained in order to evaluate paranasal sinuses and septal anatomy for surgical planning. The follow-up for MRI studies were at 24 hours, three months, and nine months after surgery, and then annually afterwards.

Under general anesthesia, the patients were placed in supine position on the operating table, with the back elevated at a 30° angle, head tilted back at a 20° angle, and rotated toward the left shoulder at a 25° angle. Rigid fixation of the head was routinely used. The otolaryngologist was positioned on the right side of patient, and the neurosurgeon on left side. All cases were performed by binostril approach. Typically, the surgery began employing the right nostril. A 0° rigid endoscope (180/4 mm) was used with no endoscope holder; infrequently, a 45° endoscope was employed. The endoscope was navigated into the nasal cavity until in proximity of the sphenoid floor, which is located approximately 1 cm above the inferior margin of the middle turbinate. A rescue flap for avoiding injure to the vascular pedicle of the posterior nasoseptal artery was raised on the right in the last 15 cases.[13] The middle turbinate was resected in all cases. A large opening was made in the posterior nasal septum and anterior wall of the sphenoidal sinus, bilaterally, with a high-speed drill with diamond burr. Inside the sphenoidal sinus, the sella and carotid-optic recess were located and the anterior wall and floor of the sella were opened with a drill or Kerrison rongeur. The dura mater was opened and the tumor was removed. Intraoperative image guidance was used in adenomas with a retrosellar component, reoperation, or suprasellar component. For reconstruction of the sellar region, a combination of fascia lata, abdominal fat, and fibrin glue was used. Vascularized nasal septal flap (VNSF), a mucoperichondrial flap based on the posterior nasoseptal artery, was raised as a final layer over the onlay graft, followed by a Foley catheter as a buttress in cases of significant intraoperative cerebrospinal fluid (CSF) leaks.[14] In cases of nontrivial anatomic variations or considerable extrasellar tumor or reoperations, neuronavigation and ultrasonic probes for carotid monitoring were used.

The aim of the treatment was to remove the tumor in its totality without causing hypopituitarism. The criteria for disease control were total tumor removal in nonfunctioning adenomas and hormonal control in functioning adenomas. The tumor was considered to be totally removed when no residual tumor was observed on MRI.

Results

A total of 47 consecutive patients underwent endoscopic transsphenoidal procedures for pituitary adenomas. The age of this patient cohort ranged from 14 to 73 years (mean:54 years). The mean follow-up was of 15 months (range: 2-24 months). Seventeen had functioning adenomas, seven had GH producing tumors, five had Cushing's disease, and five had prolactinomas. Of these functioning adenomas, 12 were macroadenomas and five were microadenomas; 30 cases were non-funtioning macroadenomas. Among macroadenomas, 16 had suprasellar and five had suprasellar and parasellar extension. Two patients had hormone levels at the upper limit of normal range. The mean follow-up of functioning adenomas was eight months (range = 4 - 17 months).

Of the 47 pituitary adenomas, total tumor removal was achieved in 96% of patients. Among patients who presented with non-functioning pituitary adenomas, total tumor removal was achieved in 94%. 87% of the functioning adenomas improved. Compressive symptoms related to optic nerve compression due to macroadenomas were relieved in 85% of these patients. Headache symptoms also improved in 76% of patients with macroadenomas. Hormonal remission was achieved in 87% of patients during this follow-up. Two cases presented failure of hormonal remission; one GH tumor with suprasellar and parasellar extension and cavernous sinus extension, and the other, Cushing's disease with microadenoma not visible during surgery, despite surgical exploration of the pituitary gland with approximately 3 mm of size at MRI.

Surgery-related complications were observed in five cases (10%); most were easily controlled, notwithstanding two carotid injuries. Those cases with carotid injuries were followed-up for 18 and 22 months, with parasellar extension of the tumor to the cavernous sinus.

CSF leakage was the most common complication. In eight patients, some degree of CSF leak was observed during surgery. In all of them, the arachnoid opening was repaired by a routine multilayer closure using fat tissue graft and fascia lata graft fixed with fibrin glue. In cases of high volume CSF leaks, a vascularized nasal septal flap was raised for sellar roof repair. Post-operative CSF occurred in two patients (4%) and were treated with lumbar drains; one of these cases required further surgical exploration of the sphenoid sinus.

Two patients (4%) suffered major bleeding after the opening of the sellar floor due to injury to the internal carotid artery (ICA). All cases occurred during an extended-approach to cavernous sinus, and one of then during a second endoscopic surgery for residual lesion. In both cases, bleeding was controlled by packing the cavity with muscle, fascia, and gauze nasal packing. An angiography was performed, and the carotid lesion was treated with placement of coils into the pseudoaneurysm.

One patient presented with bleeding in the immediate postoperative period, with aspiration of blood, secondary pneumonia, sepsis, and death. This patient had had a previous transcranial approach (2%).

Discussion

Pituitary tumors comprise approximately 15% of intracranial tumors, and the transsphenoidal midline approach has become the standard to access the pituitary and sellar region (> 95% of surgical indications in this region). The endoscope represents one of the latest technique innovations, allowing for a wider panoramic view, regardless of the width and

depth of the access. Jankowski et al.[15] were the first to use endonasal endoscopy for the removal of pituitary adenomas. The technique has subsequently been refined and popularized by Jho et al.[5,16,17] The initial reports on the use of this technique have highlighted the endoscope and its superior visualization, suggesting that this minimally invasive technique might allow for more complete tumor removal and reduced complications.[15-20]

The first principle in both understanding and successfully achieving good results with the endoscopic endonasal approach is a close collaboration between the otolaryngologist with experience in endoscopic sinus surgery/skull base surgery and the neurosurgeon with experience in performing transsphenoidal pituitary and skull base surgery. The approaches derive from the union of these two perspectives.[21]

The previously published complication rate appears to be related to several factors, including anatomical localization and local invasion, extent of tumor removal, biology of the adenoma, adequate preservation of the anatomical structures around the lesion (pituitary stalk and gland, cavernous sinus and its contents, suprasellar cistern, optic apparatus), and previous medical treatment leading to increased technical difficulty. The control offered by the endoscope contributes to a reduction in the rate of complications. Many studies with the endoscopic technique have reported a decrease in the percentage of surgical complications by an experienced surgical team.[10,22-24]

Serious and potentially fatal complications must be reduced as much as possible, although it is not possible to completely eliminate them due to the size of some lesions and their relationship to the surrounding structures.

Previously published endoscopic studies have reported rates of complication ranging from 10% to 26.3%.[10,16,23,25,26] Surgery-related mortality is rare in all previous studies (0% to 0.68%).[10,16,23,25,26] Transphenoidal microsurgical approach presents complication rates of 8.2% to 47% and 0% to 0.9% mortality rates in major large series.[27,28] In the present study, the observed rates of complications were in accordance to those previously described. Comparing the total rate of complications of endoscopy and microsurgery, the results are nearly the same. However, it is important to consider that the microsurgical series and their respective follow-ups are usually larger and longer than those presented regarding the endoscopic approach. Possible explanations for the number of complications associated with the endoscopic approach for resection of pituitary tumors include the better visualization achieved with use of the endoscope, less nasal dissection, and bone resection.[23,29]

Complications usually reported in cases of surgery related to the sphenoidal sinus include mucoceles, fracture of the sphenoidal bone, injury of the optic nerves, lesion of carotid arteries with intrasphenoidal projections, and postoperative infection of the sinus.[23,30-32] In the literature, the rate of such complications varies between 2.0% and 2.05%.[3,33] In microsurgery series, this rate varies from 1.0% to 9.06%.[23,34] Cappabianca et al.[23] explained the reduction of such complications by the wide opening of the sphenoidal ostium area, with respect to the osteomeatal complex.

The most frequent complication associated with the sella in endoscopic endonasal transsphenoidal surgery is CSF leakage. In the present study, eight patients presented some degree of CSF leak during surgery. In most cases, the occurrence of the leaks was associated with large macroadenomas with suprasellar extension, which required the surgeon to work in close proximity to the diaphragma sella. In case of high flow CSF leak, reconstruction of the sella with fat, fascia, and the nasoseptal vascularized flap is important; sometimes, lumbar drainage can be employed to control the leak, in addition to bed rest. In cases of low volume CSF leaks, reconstruction is adequate for control. Previously published endoscopy studies report rates of CSF leaks of 1.2% to 6.0%,[10,16,23,25,26] which are compatible with those of the present study, and similar to rates presented by large microsurgery studies (0.9% to 3.0%).[25,27,28]

Injury to the ICA during transsphenoidal resection of pituitary adenomas typically occurs during aggressive dissection of macroadenomas that extend into the cavernous sinus and encase the ICA, or during reoperations with anatomic alterations of the region. These lesions are relatively rare (0% to 0.68%),[10,16,23,25,26] but are described to be associated with significant morbidity (24%) and mortality (14%).[35] Intracranial hemorrhage from carotid lesions, carotid-cavernous fistulas, or pseudoaneurysms typically occurs during surgery, or within days, weeks, or even years after the procedure; the combined morbidity and mortality rates are similar to sub-arachnoid hemorrhage from saccular aneurysms.[36] Furthermore, patients harboring a pseudoaneurysm may be at risk for stroke caused by thromboembolism originating from the injured parent artery or within the aneurysm.[37,38] If an iatrogenic carotid artery injury is suspected, the hemorrhage must be controlled intraoperatively with tamponade and an immediate cerebral angiographic study is indicated to determine the origin of the bleeding and the nature of the procedure required to control the hemorrhage.

In the present study, two patients suffered major bleeding after opening the sellar floor due to the injury of the carotid artery (4%). This occurred during an extended approach to the parasellar region. One of the cases was associated with drilling of the sphenoidal walls, which must be carefully performed, especially in cases where pre-operative imaging suggests the presence of internal carotid portions in the sphenoidal sinus; the other case presented carotid bleeding during reoperation for pituitary adenoma. At the time, neither a micro-Doppler probe nor a navigation system for carotid localization was routinely used for reoperations and suprasellar/cavernous sinus extent. In reoperations, the midline could be totally distorted and could not be easily found without navigation system, as evaluated in the last 16 consecutive cases with suprasellar or parasellar extension. Also, the carotid artery could be displaced and micro-Doppler is very helpful to identify the exact location of the vessel, especially in cases with anatomical distortions, such as close proximity of both cavernous carotid arteries (kissing carotid arteries) or encasement of the internal carotid artery, as observed in the other three cases with parasellar extension, where probe was very helpful to dissect the tumor from the carotid artery. The importance of anatomical variations of the intrasphenoidal septum is noteworthy. Most patients present with insertion of the septum at one of the carotid prominences. Occasionally, more than one septa is observed, and the sphenoid sinuses are never symmetrical. Usually, the intrasphenoidal septa is not at midline. Overfracture of the septa could result in lesion of bone coverage of the carotid artery and damage to the

wall with major bleeding. It is also important to observe the type of pneumatization of the sphenoid sinus. In the conchal type, the transnasal approach should be avoided; in the presellar type, due to the bulging of the sella into the sphenoid sinus, even if the optic-carotid recess is not visible. In this situation, navigation and micro-Doppler are essential for safe surgery.

Postoperatively, diabetes insipidus (DI) may be transient or permanent, but only permanent DI is regarded as a true surgical complication; temporary DI might be secondary to simple manipulation of the pituitary gland or the skull base. DI is reported as rare complication of pituitary surgery, with reported incidences of the transitory form ranging from 2.5% to 20% in endoscopic series.[25,30] Permanent DI is observed at even lower rates: 1% to 5% in endoscopic series[10,16,23,25,26,30] and 0.9% to 7.6% in microsurgery series. Temporary DI is thought to be caused by temporary dysfunction of vasopressin-producing neurons as a result of surgical trauma.[25,28]

Conclusion

Endoscopic endonasal transsphenoidal surgery for pituitary adenomas was a safe and effective approach in this cohort of patients, and represents a low morbidity approach to patients with pituitary tumor.

Conflicts of interest

The authors declare no conflicts of interest.

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