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Recent Evolution of Endoscopic Endonasal Surgery for Treatment of Pituitary Adenomas

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Abstract

For the treatment of pituitary tumors, microscopic transsphenoidal surgery has been considered the "gold standard" since the late 1960s. Over the last two decades, however, a worldwide shift towards endoscopic endonasal surgery is in progress for many reasons. These include a wide panoramic view, improved illumination, an ability to look around anatomical corners using angled tip and, in addition, application to the extended approaches for parasellar tumors. Both endoscopic and microscopic approaches appear equally effective for nonfunctioning adenomas without significant suprasellar or lateral extensions, whereas the endoscopic approach may improve outcomes associated with the extent of resection and postoperative complications for larger tumors. Despite many theoretical benefits in the endoscopic surgery, remission rates of functioning adenomas do not substantially differ between the approaches in experienced hands. The endoscopic approach is a valid alternative to the microscopic approach for adenomas. The benefits will be more appreciated in the extended surgery for parasellar tumors.

Key words: endoscope, pituitary adenoma, microscope, transsphenoidal surgery

Introduction

Microscopic transsphenoidal surgery has long been considered the "gold standard" in surgical treatment of pituitary tumors. Many large series have reported the efficacy, safety, and limitations of this approach. Over the last two decades, however, endoscopic endonasal surgery has gradually gained favor as a primary approach for sellar and parasellar lesions, primarily due to the wide panoramic, up-close visualization offered by the endoscope. Endoscopic approaches provide many theoretical benefits over standard microscopic techniques, but previous publications had not consistently shown improvement in resection and complication rates in the endoscopic group. In this review, surgical outcomes, complications, and postoperative quality of life (QOL) in microscopic and endoscopic transsphenoidal approaches for pituitary adenoma surgery were evaluated to verify the benefits of the endoscopic endonasal surgery.

History of transsphenoidal pituitary surgery

The first transsphenoidal pituitary surgery is attributed to Hermann Schloffer in 1907. Over the next two decades, the sublabial, transseptal, transsphenoidal technique was developed by Harvey Cushing but was largely abandoned until the 1960s when Jules Hardy popularized the use of operative microscope in transsphenoidal surgery. Since that time, the microscopic transsphenoidal surgery became the "gold standard" for pituitary tumor removal. On the other hand, the endoscope was first introduced to transsphenoidal surgery by Gerard Guiot in the early 1960s. At the beginning, the endoscope was mostly used as a microscope-assisted tool to explore the sella cavity for residual tumor. In 1997, the first clinical series of purely endoscopic pituitary surgery was reported by Jho and Carrau.[1)] Since then, many pituitary surgeons gradually shifted towards an endoscopic endonasal approach for pituitary adenomas and other parasellar tumors. The recent development of endoscopic instrumentations and techniques has contributed in enhancing the efficacy and safety of the endoscopic approach and has further promoted the shift.

General aspects in microscopic versus endoscopic transsphenoidal surgery

Both microscope and endoscope are effective and safe tools to successfully treat most pituitary adenomas. The major benefits of the microscopic approach include maintaining stereoscopic vision, instrument mobility under the direct vision, controlling massive bleeding from the cavernous sinus or arteries, retraction of nasal soft tissue that may at

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times be edematous or vascular, and a more rapid approach to the sella in some cases.[2-8] For most neurosurgeons, this approach is more intuitive and does not require meeting the steep learning curve associated with endoscopic approaches. Zada et al.[8] reported intraoperative conversion from endoscopic to the microscopic approach in 18% of 148 cases. The major reasons for conversion included previous transsphenoidal surgery, tissue hypertrophy due to acromegaly, atypical nasal anatomy, and nasal mucosal bleeding.

On the other hand, for most neurosurgeons who have been able to make the transition to fully endoscopic endonasal surgery, there is little doubt that this technique has many clear advantages. These include a wider, more panoramic field of visualization, improved illumination and mobility of instruments, and an ability to look around anatomical corners using angled lens. Concerns about instrument maneuverability during endoscopic procedures have largely been alleviated with the development of newer endoscope-specific instrumentation and the evolution of endoscopic techniques.[6] A recent study by Elhadi et al.[9] provided quantitative data on the superiority of the binarial endoscopic approach in achieving target surgical freedom and sagittal angular freedom. High definition 3D endoscopic system may resolve the stereoscopic visualization issue.[10]

Surgical outcomes in nonfunctioning adenomas

No class 1 data derived from direct comparisons of microscopic versus endoscopic transsphenoidal approaches in randomized controlled trails is available, and may not be feasible.[6] In a recent report by Dallapiazza et al.[11], microscopic and endoscopic techniques provided similar outcomes in the treatment of nonfunctioning adenomas with Knosp grades 0-2 (i.e. those without marked lateral extension).

In contrast, most meta-analysis and retrospective series converge on the superiority of endoscopic techniques in achieving gross total removal in macroadenomas, especially when these tumors are locally invasive and are not just limited to the sella.[6,12–16] McLaughlin et al.[13] noted the endoscopic visualization led to additional adenoma removal in over one-third of patients after microscope-based tumor removal. Using an intraoperative magnetic resonance imaging (MRI), Theodosopiulos et al.[15] noted a decreased incidence of unexpected residual tumor via an endoscopic approach in their institution. In a large series of nonfunctioning adenomas, Messerer et al.[14] noted the endoscope was more efficient than microscope in terms of the quality of resection and the endocrinological outcome, particularly for large tumors and those with advanced Knosp grade.

In summary, nonfunctioning adenomas without significant suprasellar or lateral extensions can be effectively removed, either using the microscope or the endoscope, with similar results in experienced hands. For larger tumors, the endoscopic approach may improve outcomes associated with the extent of resection and postoperative complications.

Endocrine outcomes in functioning adenomas

The continuous evolution of the endocrinologic remission consensus criteria complicates any attempt to compare old historic microscopic results with those of more recent endoscopic series.[6] Starke et al.[7] and Fathalla et al.[17] noted that the surgical outcome of acromegaly by experienced surgeons do not differ between endoscopic and microscopic techniques. Gondim et al.[18] who use the pure endoscopic approach noted "although presenting better illumination and visualization of the lesions, no report has definitively proved the superiority of endoscopy over microscopy in pituitary surgery". Oldfield[4] noted that the endoscope provides monocular vision, whereas the microscope provides true binocular 3D vision permitting more precise microscopic dissection. The microscopic remission rates of Cushing disease with microadenoma are outstanding in highly experienced hands and have not yet been matched by endoscopic series.[6,19–21] Most authors agree that the remission rates of functioning small adenomas do not differ between the approaches.[22–27] Microscopic procedure probably have more advantage over endoscopic procedure in patients with Cushing's disease with negative MRI.[5,28]

Likewise nonfunctioning adenomas, the advantages of endoscopy might be more appreciated in large functioning adenomas and in those invading the cavernous sinus, although these tumors are usually difficult to achieve endocrinological remission. Some authors noted the endoscopic results in functioning macroadenoma are slightly better than in the microscopic results with similar complication rates.[23,25–27] Wagenmakers et al.[27] noted the endoscopic surgery should be the treatment of choice as remission rates seems to be higher than those reported for microscopic surgery for patients with adrenocorticotropic hormone (ACTH)-producing macroadenoma, although recurrence rates were comparable. Regardless of the approach, however, extensive tumors, i.e. large and/or invasive adenomas, are inherently difficult to achieve endocrinological remission only by surgery.

(1) Endoscopic surgery for giant adenomas

Endoscopic and the extended approaches are replacing open craniotomy as a first-line approach to most large sellar lesions.[29] In a review of 16

studies (478 patients) of giant adenomas, Komotar et al.[30] noted the microscopic transsphenoidal cohort had a lower rate of total resection and worse visual outcome than the endoscopic group. The transcranial group had a higher rate perioperative mortality compared to the transsphenoidal group. Although the endoscopic approach is safe and effective in select cases, they concluded that an individualized surgical approach is wisest for giant adenomas. These include endoscopic and the extended approaches, transcranial (skull base) approaches, and the combined transcranial and transsphenoidal approaches.

The following complex adenomas had been previously considered contraindication by the transsphenoidal approach: adenomas with a dominant extrasellar component in combination with a small, non-enlarged sella, adenomas with a dumbbell configuration which harbor an hourglass constriction, adenomas with multi-lobulated suprasellar extensions, adenomas with a large eccentric extension into the anterior, middle, and posterior cranial fossa, et al.[31,32] Extended approach provides excellent exposure of suprasellar and retrochiasmatic region and, thus, is indicated for some complex adenomas, especially for suprasellar extended tumors invading mainly the midline structure.[33] For few selected patients with more complex adenoma, i.e. large/giant and multi-lobulated adenoma, the simultaneous combined transcranial and transsphenoidal surgery is indicated using combinations of endoscope and microscope.[31,34]

(2) Endoscopic surgery for adenomas invading the cavernous sinus

Cavernous sinus invasion is the most significant, independent predictor of unfavorable outcome in functioning adenomas.[3,16,21,25] For tumors invading the cavernous sinus, many authors noted higher resection rate with an endoscope than microscope indicating the advantage of the panoramic and angled views of cavernous sinus medial wall provided by endoscopes.[35–37]

The prevalence of cavernous sinus invasion varies significantly among the studies. The endoscopic inspection is reported to be the best technique to detect cavernous sinus invasion, whereas microscopy tends to overestimate the invasion.[36] However, histological examination remains necessary for some cases to evaluate "occult invasion", i.e. tumor invasion of the dura or cavernous sinus medial wall that is not evident on imaging studies and is not obvious to the surgeon and, thus, can be the basis of recurrence or persistent tumor and endocrinopathy.[3,27] For the histological verification and complete tumor removal, sharp excision of the medial wall is required particularly for functioning adenomas.

Management of massive venous hemorrhage from the cavernous sinus is one of the most important issues in cavernous sinus surgery. Ceylan et al.[35] noted that they do not consider such hemorrhage to contraindicate the use of the endoscopic approach, but some authors noted that microscopic techniques are superior to endoscopic techniques for meticulous maneuvers including sharp excision of the cavernous sinus medial wall while controlling the massive venous hemorrhage.[3,7,39]

(3) Endoscopic surgery for recurrent adenomas

In general, surgery for the removal of a recurrent (regrowing) adenoma is burdened by an increased risk of morbidity and often, it results in an incomplete resection compared with primary surgery.[40] The main reason that makes the surgery for a recurrence more complex is inherent tumor characteristics, namely a fibrous consistency, an irregular multi-lobulated configuration and/or marked supra/parasellar invasiveness. However, the endoscopic endonasal surgery has been reported to be a valid option in recurrent adenomas.[34,40–42] In addition to the various advantages of the endoscope that has been mentioned, a wider exposure of the sella by the endoscopic approach may contribute to the better outcome, especially when the limited exposure by the previous microscopic surgery had been a major factor of incomplete tumor resection.[40–42]

Complications

The reported incidence of postoperative CSF rhinorrhea following endoscopic pituitary surgery usually ranges between 0.7 and 12%.[6,12,14,43–47] Despite a wider exposure and dissection and, thus, a higher risk of intraoperative CSF leakage in endoscopic approach, the postoperative leak rates are at least equivalent if not superior to lower than those in microscopic surgery in the recent literature. The results of endoscopic series reported in the literature indicate an amount of new adenohypophysial dysfunction between 2.1 and 14.6%.[6,12,14,15,43,47] The risk for permanent diabetes insipidus with endoscopic surgery accounted for between 0.7 and 8.5%.[6,14,22,43,47] Injury of the carotid artery is a rare but severe and potentially fatal complication and is reported with a rate of less than 1%.[6,15,42,44–46] In general, the surgical complication rates of endoscopic procedure are either equivocal or slightly superior to those of microscopic procedure.[6,12,15,22,43–46] However, Ammitirati M et al.[43] noted a higher incidence of vascular complications with endoscopic technique.

These results are based on retrospective review of nonrandomized study. In an international survey by de Divitis et al.[48], concerns yet exist in the neurosurgical community regarding the safety of the procedure, and a potential risk of vascular injuries and CSF leak substantiates this concern.

In a multi-institutional study of risk factors for perioperative morbidity following endoscopic pituitary surgery reported by Boling et al.[45], adverse events including intracranial/systemic complications, reoperation, readmission, and death occurred in 23.8% of 982 patients. Most commonly, these events were readmission in 15.4% of cases and reoperation in 6.5% of cases. These rates compare favorably when contrasted with microscopic estimates (8.2–47%). The endoscopic surgery complications were associated with tumors with intraventricular extension, preoperative radiation, as well as common patient comorbidities.

Nasal morbidity and Quality of life

Reported nasal morbidities following transsphenoidal surgery include sinusitis, anosmia, epistaxis, nasal congestion, septal perforation and deviation, and mucosal synechiae. Postoperative epistaxis due to bleeding of the sphenopalatine artery or from one of the septal branches may develop in 1-2% of cases.[12,14,47] Sinonasal QOL following endoscopic pituitary surgery reaches a nadir at 2 to 3 weeks and recovers by 6 weeks to 3 months postoperatively.[49–51] Sinonasal QOL and overall health status are well correlated in the postoperative period, suggesting the importance of sinonasal QOL on the patient experience.[49] Many authors noted better sinonasal QOL after endoscopic approach than microscopic approach at least in short-term period after surgery.[49–54] However, Pledger et al.[51] reported that although patients who underwent endoscopic surgery experienced significantly fewer nasal symptoms during the first 8 weeks, by 1 year after surgery, there were no significant differences between the endoscopic and microscopic groups.

In a qualitative study of postoperative QOL by Lwu et al.[52], the endoscopic approach was well tolerated by patients and was the preferred procedures for most patients over the traditional microscopic approach. Compared with the sublabial route, the endonasal approach was associated with less pain, better nasal airfow, and a shorter hospital stay.[53] Massimi et al.[54] noted endoscopic surgery improve the quality of the postoperative course in children regardless of the type of lesions treated and the surgical complications. They suggested that the reasons for this more comfortable postoperative course are related to some specific advantages offered by endoscopic surgery, namely: (1) less mucosal detachment, (2) absence of sublabial incision, (3) absence of routine nasal packing. These may contribute to the reduction of the pain, quicker recovery, and a shorter hospital stay.

Economics

One of the previous criticisms on endoscopic pituitary surgery was the cost per procedure since it was considered to require two surgeons and longer surgical time.[2] In the recent reports, however, many authors noted the endoscopic pituitary surgery is the more cost-effective intervention compared to the microscopic surgery.[55–57] The overall lower complication rates and shorter hospital stay might have contributed to this result. According to multivariate analysis by Little et al.[55], hospital charges were on average 2% lower for the endoscopic technique patients than for the microscopic technique patients. They noted the primary drivers of hospital charges, in order of importance, were length of stay, a diagnosis of Cushing's disease, and, to a lesser extent, use of the endoscopic technique.

Learning curve and training programs

For every neurosurgeon, a learning curve is necessary to increase the effectiveness of endoscopic surgery and decrease operation time.[58,59] Some reluctance persists with its adoption, especially among microscopically trained neurosurgeon, as they are legitimately unwilling to accept the complications that might results as part of the learning curve.[6] Interestingly, Zaidi et al.[60] noted a less experienced surgeon using a fully endoscopic technique was able to achieve outcomes similar to those of a very experienced surgeon using a microscopic technique in a cohort of patients with nonfunctioning tumors smaller than 60 cm^3. This may indicate certain advantages of endoscopic surgery can help a less experienced surgeon achieve outcomes similar to those of a very experienced surgeon.

Although much learning occurs in the operating theater, it is necessary that sufficient time be spent in the classroom or dissection laboratory to acquire sufficient anatomic knowledge and familiarity with endoscopic techniques before proceeding to live surgeries. The Pittsburgh group has provided a structured approach to endoscopic endonasal skull base surgery training based on level of difficulty of the procedures and perceived neurologic risks.[61]

Future perspectives

Over the past several years, endoscopic technology, instrumentation, and relevant anatomical

mastery have promoted many innovative methods and approaches to the extrasellar regions. The new developed instrumentations include high definition 3D endoscopic system,[10] endoscopic augmented reality navigation system,[62] ultrasonography-assisted endoscope,[63] the indocyanine green fluorescence endoscope,[64] and use of high-field intraoperative MRI,[65] et al. These are reported to increase the safety and reduce the risk of the endoscopic approach. Recently, an experimental feasibility study on robotic endonasal telesurgery was reported.[66] 4K (and 8K) ultra-high definition endoscopes are likely to be introduced to this field in the near future.[67]

The extended endoscopic surgery to the midline ventral skull base have been extensively developed and refined for removal of parasellar tumors including supasesellar adenomas[33], craniopharyngiomas, chordomas, chondrosarcomas, meningiomas, et al. The advantages and benefits of the endoscope can be more appreciated in the extended surgery for these parasellar tumors than the pituitary surgery.

Conclusion

Although there are some circumstances in which the microscopic technique has advantages in pituitary surgery, the endoscopic pituitary surgery may provide several advantages over the microscopic surgery in terms of removal of tumors with suprasellar or lateral extensions and postoperative complications. The endoscopic pituitary surgery is a valid alternative to the microscopic surgery and the worldwide shift towards the endoscopic approach is quite reasonable. The benefits of the endoscopic approach will be more appreciated in the extended surgery for parasellar tumors. Since the adoption of endoscope requires a learning curve, every neurosurgeon who uses the endoscope should use it exclusively for all endonasal surgeries.

Conflicts of Interest Disclosure

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