J Neurooncol (2016) 130:309–317
DOI 10.1007/s11060-016-2124-y

TOPIC REVIEW

Resection of pituitary tumors: endoscopic versus microscopic

Harminder Singh[1,2] · Walid I. Essayed[1] · Aaron Cohen-Gadol[3] · Gabriel Zada[4] · Theodore H. Schwartz[1]

Received: 23 January 2016 / Accepted: 7 April 2016 / Published online: 9 May 2016

Abstract Transsphenoidal microscopic pituitary surgery has long been considered the gold standard in surgical treatment of pituitary tumors. Endonasal endoscopic pituitary surgery has come into prominence over the last two decades as an alternative to microscopic surgery. In this review, we use recent literature to discuss the advantages and disadvantages of each approach. Our review shows that for small intrasellar tumors, both approaches appear equally effective in experienced hands. For larger tumors with extrasellar extension, the endoscopic approach offers several advantages and may improve outcomes associated with the extent of resection and postoperative complications.

Keywords Endoscopic · Endonasal · Skull base surgery · Microscopic · Transsphenoidal · Pituitary adenoma

Harminder Singh and Walid I. Essayed contributed equally to this work

✉ Theodore H. Schwartz
schwarh@med.cornell.edu

[1] New York Prebyterian - Weill Cornell Medical Center, New York, NY, USA

[2] Stanford University School of Medicine, Stanford, CA, USA

[3] Goodman Campbell Brain and Spine, Indiana University School of Medicine, Indianapolis, IN, USA

[4] Keck School of Medicine of USC, Los Angeles, CA, USA

Abbreviations

ETPS	Endoscopic trans-sphenoidal pituitary surgery
QOL	Quality of life

Introduction

Transsphenoidal microscopic pituitary surgery has long been considered the gold standard in surgical treatment of pituitary tumors. Endonasal endoscopic pituitary surgery has come into prominence over the last two decades as an alternative to microscopic surgery. Each technique has its advantages and disadvantages; yet, for multiple reasons, a worldwide shift towards endonasal endoscopic surgery is in progress [1–5]. In recent years, multiple teams have published their experience with this transition [1, 2, 4, 6], and multiple systematic reviews and meta-analyses have been conducted on the comparison of these two techniques [7–13]. Though sometimes discordant on some issues, a global consensus favoring endoscopic surgery in most circumstances is slowly being reached. In this review, we use recent literature to discuss the advantages and pitfalls of both techniques.

Technically, the microscopic approach can be realized in two different fashions, through a sublabial incision or via an endonasal transseptal approach. Both routes involve the use of speculums to fracture the nasal septum and retract soft tissue. A sphenoidotomy is then performed using a self-retaining speculum that initially straddles the bony midline keel and retracts the nasal mucosa laterally [14]. Some extended microscopic transsphenoidal approaches have also been developed and have reported satisfying results [15–17]. Multiple nuances are also possible with endoscopic surgery. Depending on the case, the procedure can be performed through one or both nostrils following a posterior

septectomy. While some authors use the endoscope holder at a certain stage of the surgery, others prefer a four handed technique [14], with two surgeons operating simultaneously.

Discussion

General principles of microscopic versus endoscopic transsphenoidal surgery

Both the microscope and endoscope have been used successfully to approach the sellar region and treat a wide variety of pathology encountered in this region. The large surgical series of microscopic approaches that emerged in the 1980s and 1990s defined surgical outcomes for pituitary adenomas, craniopharyngiomas, Rathke Cleft Cysts and a variety of additional pathology for decades to come [18–23]. Many of these outcomes still are considered the gold standard, and for many surgeons who are familiar with the microscope, it remains a viable tool with several major benefits. These benefits include maintaining stereoscopic vision, retraction of soft tissue that may at times be edematous or vascular, and in some cases a more rapid approach to the sella. For many neurosurgeons, using the microscope is more intuitive and does not require meeting the steep learning curve associated with endoscopic approaches. Finally, fully endoscopic approaches require multiple critical technological components that have to all be working properly, including the endoscope itself, camera, fiberoptic light cable, and video tower.

For a majority of surgeons who have been able to make the transition to fully endoscopic endonasal surgery, there is little doubt that this technique offers several key advantages that, upon surpassing the learning curve associated with endoscopic skull base surgery, make this technique clearly advantageous. 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 lenses. In addition, the ability to safely target regions of the skull base outside of the sella have paved the way for extended transcribriform, transplanum, transtuberculum, and transclival approaches, among others. High definition 3D endoscopic system usage is on the rise, which resolves the stereoscopic visualization issue [24].

The endoscopic approach offers two separate, but complementary, technical improvements over the microscope that improves anatomic visualization. The first involves the bony opening. The endoscopic approach requires a larger sphenoidotomy to permit the endoscope to be adequately positioned in the sinus along with two working instruments. This allows the endoscope to be moved around the sinus cavity to visualize larger areas of the skull base. In a complementary fashion, the endoscope lens provides a wider panoramic view, which is not confined by a direct linear viewing trajectory through a speculum as is the microscopic view. Moreover, endoscopes can have angled tips which can provide lateral exposure around anatomical corners that are not possible with the microscope [25, 26].

The microscope, on the other hand, provides stereoscopic vision not available with the endoscope, unless a 3D endoscopic system is used [24]. 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. These generally involve a requirement for instruments with low-profile, straight handles and mobile or curved tips to reach areas visualized using the endoscope. The requirement for bayoneted instruments used during microscopic approaches is obviated by a transition to fully endoscopic approaches. A recent report by Elhadi et al. provided quantitative data on the superiority of the binarial endoscopic approach in achieving *target surgical freedom* and *sagittal angular freedom* [14]. Varying degrees of "hybrid" endoscope-assisted microscopic surgery has been reported in the literature, with a unanimous observation that the endoscope not only allows better visualization of the sellar region, but also frequently helps in identifying small areas of residual tumor [27–31]. Improved visualization augments the confidence of the surgeon to be aggressive in resection of more fibrous tumors.

Surgical results

Gross total removal (GTR)

Studies comparing the extent of resection between endoscopic and microscopic surgery require very large numbers of patients to reach statistical significance since the results of microscopic surgery are already quite good. Furthermore, no class I data derived from direct comparisons of microscopic versus endoscopic approaches in randomized controlled trials is available, and may not be feasible. Therefore, surgeons have had to rely on comparisons of historical data to draw conclusions pertaining to the effectiveness and possible superiority of one technique over another, which have been classically skewed by selection bias and comparisons of surgical outcomes series that are decades apart. Nevertheless, the majority of meta-analysis and retrospective series converge on the slight superiority of endoscopic techniques in achieving gross total removal in pituitary tumors, especially when these tumors are locally invasive or are not just limited to the sella [1, 4, 7–10, 12, 13, 32].

In a recent study by Dallapiaza et al., tumors with Knosp grades 0–2 (i.e. those without cavernous sinus extension) underwent a similar extent of resection when approached via either approach [33]. However, in another paper by Messerer et al., a statistical difference emerged when comparing Knosp grade 2 and 3 patients. In the microscopy group, the GTR percentages for Knosp grade 2 and 3 patients were 47.8 and 16.7 % respectively, whereas endoscopy achieved much higher GTR rates of 88 and 69.9 % [32].

Significant suprasellar extension limits GTR rates achieved by both microsurgical [20] and endoscopic techniques [34]. However, when the height of the adenoma surpasses 30 mm, current data supports the superiority of endoscopic surgery to microscopic resection [20, 32, 35]. These results are likely associated with better visualization provided by the endoscope within the deeper operative blind spots beyond the edges of the bone work.

Overall, it is safe to say that the majority of pituitary and skull base surgeons find superiority in the endoscopic approach on account of its advantages in visualization, illumination, access, and mobility, as supported by the worldwide transition to the endoscopic approach.

Endocrinologic cure

The continuous evolution of the endocrinologic remission consensus criteria complicates any attempt to compare old historic microscopic results with those of more recent endoscopic patient series. The superiority of endoscopic surgery is still under investigation, but some early evidence already suggests better endocrinologic cure rates associated with endoscopic surgery. [4, 36] For functional adenomas, Razak et al. reported a remission rate of 57 % in the microscopic group and 94 % in the endoscopic group ($p = 0.018$). [4] Nevertheless, microsurgical results for surgical cure of microadenomas causing Cushing's disease in highly experienced hands are outstanding and have not yet been matched by endoscopic series [37–39]. With respect to Cushing's disease, it can be argued that one of the greatest advancement has been the pseudocapsular resection technique. To achieve this technique, Oldfield [37, 38] utilized a sublabial microscopic approach specifically to gain a wide surgical corridor, and more panoramic visualization of the sella. However, there is nothing specific about the microscopic approach that lends itself more to this technique. As more endoscopic surgeons adopt this technique the results should be comparable.

Visual outcome

Pre-operative visual disturbance is a frequent symptom and sign in patients with pituitary adenomas, particularly in those with suprasellar tumor extension. In a meta-analysis, DeKoltz et al. observed a statistically higher rate of visual improvement in the endoscopically treated patients when compared with the microsurgical group (71 vs. 56 %, respectively) [8]. This difference has not been substantiated by multiple other reports, which found comparable outcomes for both techniques [1, 8, 11, 13, 32].

These similar results are probably explained by the fact that the visual outcome primarily depends on the timing and decompression of the optic apparatus, rather than the extent of resection itself. The favorable visual results achieved by both techniques necessitates further study with precise pre- and post-operative visual evaluation in a large number of patients to uncover any statistical differences.

Quality of life (QOL)

When postoperative recovery is compared in patients who had endoscopic surgery subsequent to their initial microscopic sublabial transsphenoidal surgery, the endoscopic approach was associated with less post-operative pain, better airflow and a shorter hospital stay [40–42]. Notably, Lwu et al. found that when their patients were asked about their preference regarding an endoscopic or microscopic procedure for a future procedure, they favored the endoscopic option [42]. Current validated predictors of a better QOL are the extent of resection and the use of packing and nasal splints [43, 44], both of which are better managed via endoscopic surgery. Endoscopy appears to provide better post-operative olfactory function and endocrinological outcome, both of which play an important role in long-term QOL [45, 46].

Complications

CSF leaks

Since post-operative CSF leak was believed to be the "Achilles heel" of endoscopic endonasal surgery, abundant data is available on its comparison with that of the classic microscopic approach. Multiple systematic reviews compared the CSF leak rates associated with endoscopic surgery, finding a higher but statistically insignificant rate when compared to those of microscopic surgery [7, 10, 13]. The reported incidence of postoperative CSF rhinorrhea in microscopic surgery series usually ranges between 1 and 3 % [21, 47]. The greater visualization of the sella with the endoscope encourages more exposure, dissection and is likely to cause a higher rate of intraoperative CSF leakage, thereby counterbalancing the potential for improved reconstructive closure through endoscopy.

While reconstructive techniques during microscopic surgery are limited, successive improvements in endoscopic endonasal closure techniques, including the use of

pedicled nasoseptal flap and multi-layer reconstruction protocols (e.g., gasket seal and bilayer button closure techniques), have improved postoperative CSF leak rates to less than 5 % in extended approaches to non-adenomatous lesions [48–50]. Pituitary adenoma surgery is classically associated with fewer post-operative leaks. The selective use of lumbar drainage for larger adenomas, together with administration of intrathecal fluorescein for identification of intraoperative CSF leaks, have further diminished the CSF leak rate to less than 1 % in the recent literature. These results are at least equivalent if not superior to the traditional microscopic outcomes [11, 12, 51–54].

Meningitis

Postoperative meningitis risk is broadly considered equivalent between endoscopic and microscopic surgery at around 1 % [2, 8, 10, 13, 46, 55]. A meta-analysis by Ammirati et al. found statistically less meningitis rates in endoscopic patients compared to microscopic: 1 vs. 2 % [7]. These results may be related to the better intra-operative identification and repair of CSF leaks offered by endoscopy [51].

Posterior pituitary dysfunction: diabetes insipidus

Disruption and manipulation of the posterior pituitary gland, pituitary stalk, or other fibers arising from the hypothalamus are frequently responsible for transient postoperative diabetes insipidus (DI) that might persist as a permanent deficiency. The majority of reports suggest that endoscopic resection results in less transient and postoperative permanent DI [7, 10–13]. The rate of transient DI ranges from 4–14 % for endoscopic resection, and 7.6–19.5 % for microscopic approaches. Similarly, for permanent DI, these rates range from 0–2 and 2–10 % for endoscopic and microscopic resection, respectively (Table 1). The risk for permanent DI with endoscopic procedures is less than 1 % in the recent literature [12, 55]. These results are based on retrospective review of nonrandomized studies. The enhanced visualization of the different structures, decreasing blind manoeuvers and inadvertent resection the posterior pituitary gland, plays an important role in improving the endoscopic results.

Anterior pituitary dysfunction

The reported rate of post-operative anterior pituitary dysfunction after microscopic endonasal surgery is around 3 % [9, 56]. Multiple reports suggest a lower rate of postoperative hypopituitarism linked to endoscopic surgery, though more data need to be gathered to reach sufficient statistical significance [7, 9, 10]. Recent results support the excellence of endoscopic techniques, with a reported anterior pituitary dysfunction rate of only 1.29 % in a large series of 1166 patients [55].

Visual complications

No statistically significant difference between the two techniques has been reported in the literature [7, 8, 10–12, 46, 57] for this parameter, although a trend of fewer visual complications is noticeable with endoscopic surgery (0.3–0.6 %) [7, 10, 55], compared to microscopic surgery 0.5–0.9 % [21, 23].

Vascular complications

Depending on the definition of a vascular complication, the rate might be discordant between the reviews. Still, these complications are sporadic in pituitary surgery, with rates less than 0.5 % [12, 56]. Even though some authors noticed an increase in vascular complications with endoscopic procedures [7], global consensus of the risk remains equivocal between the two techniques [2, 8–11, 13, 57–59]. Plausibly, endoscopic surgery provides better visualization laterally into the cavernous sinus, which encourages manipulation of its contents, leading to eventual vascular injury. This risk is balanced by the avoidance of any intrasellar blind instrument maneuvering performed during microsurgical approaches.

Rhinological complications

Multiple sino-nasal complications can shadow pituitary surgery. Sinusitis and nasal septal perforation are the most reported complications. Endoscopic surgery offers excellent results for postoperative sino-nasal QOL [43, 44], and these results are significantly superior to those achieved via microscopic surgery [8–10, 36, 40–42], which is more frequently associated with postoperative epistaxis, lip and nasal anesthesia, septum deviation, and postoperative synechiae [10]. The overall sino-nasal complication rate of microscopic surgery can reach 13 %, while only 1.2 % of patients developed such complications in the endoscopic surgery group [10]. There is evidence showing, however, that at 1 year after surgery, the results are equivalent [60]. The superior rhinological results achieved endoscopically are probably associated with the better visualization during all surgical steps, and minimizing any blunt or blind instrument manoeuvers. The close pre, intra, and post-operative collaboration with experienced otorhinolaryngologists also plays a crucial role in decreasing rhinological complications.

Table 1 Surgical results and complications from systematic reviews, meta-analysis, and single centers' transition experiences, analyzing microscopic versus endoscopic pituitary surgery

	Systematic reviews and meta-analysis												Single center transition experiences			
	Rotenberg		Goudakos		Strychowsky		DeKlotz		Ammirati		Gao		O'Malley		Karppinen	
	2010 [11]		2011 [10]		2011 [13]		2012 [8]		2013 [7]		2014 [9]		2008 [3]		2015 [1]	
Number of studies	11		11		10		22		38		15		–		–	
	Micro	Endo	Micro	Endo	Micro	Endo	Micro	Endo	Micro	Endo	Micro	Endo	Micro	Endo	Micro	Endo
Cases	313	234	437	369	353	314	479	1701	3518	2125	527	487	25	25	144	41
Results																
Gross total removal	No difference		Favoring Endo*		Favoring Endo*		**65 %**	**79 %**	64 %	68 %	**58 %**	**71 %**	77 %	66 %	45 %	56 %
Endocrinological cure	No difference		Favoring Endo*		Favoring Endo*		71 %	71 %	-		-		-		-	
Visual improvement	No difference		-		No difference		**56 %**	**71 %**	-		-		-		No difference	
Complications																
CSF leak	No difference		No Difference		Favoring Endo*		**7 %**	**5 %**	6 %	7 %	12 %	12 %	24 %	28 %	3.50 %	2.40 %
Meningitis	No difference		No Difference		No difference		1 %	1 %	2 %	1 %	No difference		1 %	0 %	0.70 %	0.00 %
Transient DI	Higher	Lower	**19.50 %**	**14 %**	-		-		10.20 %	9.10 %	-		**16 %**	**4 %**	7.60 %	4.90 %
Permanent DI	Higher	Lower	**10 %**	**2 %**	Favoring Endo*		3 %	2 %	4 %	2 %	Favoring Endo*		**8 %**	**0 %**	2 %	0 %
Ant. pituitary dysfunction	No difference		Favoring Endo*		Favoring Endo*		-		12 %	9 %	6 %	3 %	-		13 %	9 %
Visual	-		0.78 %*	0.3 %*	Favoring Endo*		-		0.60 %	0.70 %	-		-		No difference	
Vascular	-		Favoring Endo*		-		-		**0.50 %**	**1.50 %**	-		-		Favoring Endo*	
Rhinological	Favoring Endo*		**13 %**	**1.20 %**	**Favoring Endo**		-		-		-		-		-	

* Statistically insignificant

\- Not reported

Bold Statistically significant

Economics

One of the old criticisms of endoscopic surgery was its economical weight. Current reports are converging to conclude that the overall cost per patient per procedure and global cost-effectiveness of endoscopic endonasal surgery is significantly more optimized when compared to the classic microscopic procedures [59, 61]. Although some authors report shorter operating time [11, 13], the use of two surgeons and the time it takes for the otolaryngologist to perform the approach may increase the operative time for the endoscopic approach. The endoscopic approach, however, is associated with shorter hospital stays with lower hospital resource consumption [11, 13, 57, 61].

The overall lower complication rate, extent of resection and adjunctive treatments (e.g., radiosurgery, medications, additional operations) and the less frequent need for short- and long -term endocrinologic replacement therapy are other factors to consider when evaluating the long-term cost effectiveness [8, 61]. Using a variety of economic models, a statistical difference favoring endoscopic surgery is noticeable [59, 61, 62] (Fig. 1). These results indicate that in large academic centers, endoscopic endonasal surgery is less costly 94–98 % of time [59].

Surgeon skillset

Learning curve

Learning curves are an inevitable part of any new technique [1–3, 54, 63, 64]. In its infancy, endoscopic endonasal surgery was associated with mixed results, longer operating times and higher complications, particularly when compared to the good results achieved by the well-established standard microsurgical procedures. Currently, in specialized hands, endoscopic endonasal surgery results are equivalent or superior to microsurgery for almost all parasellar tumor extension, and equivalent to microsurgery for sellar pathology. Yet, some reluctance persists with its adoption, especially among microscopically trained neurosurgeons, as they are legitimately unwilling to accept the complications that might result as part of the learning curve.

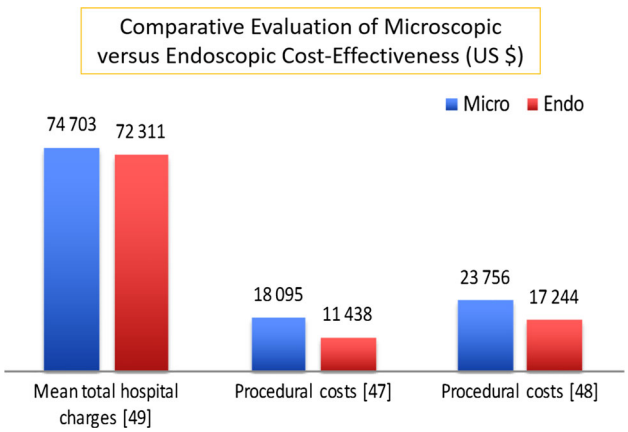

Fig. 1 Comparative Evaluation of Microscopic versus Endoscopic Cost-Effectiveness for a trans-sphenoidal procedure (US $)

Multiple experienced teams in microsurgery have now published their transition to endoscopy with unanimous results showing the safety of endoscopic endonasal surgery though the transition phase [1–3, 6]. However, comparison between results achieved sequentially must always be looked at skeptically due to the element of reporting bias. Interestingly, a recent report found similar surgical results when comparing the outcome of a less-experienced surgeon using a fully endoscopic technique to the outcome achieved by a very experienced surgeon using the microscopic transsphenoidal technique [65].

Beyond the sella: extended approaches

Extended microscopic approaches have been described by some authors. Even though some positive results were achieved in experienced hands [15–17], the degree of technical difficulty and the associated high morbidity rates prevented the spread of such techniques [15–17]. The concomitant development of standard and extended endoscopic approaches also prevented the wide development of such extended microscopic approaches.

Through the strong collaboration between neurosurgeons and otorhinolaryngologists and the modern improvement of endoscopic instruments and techniques, endoscopic endonasal surgery is succeeding in tackling an increasing array of pathologies ranging from simple CSF leaks to complex skull base tumors [66, 67]. Successive reports are progressively expanding the range of endoscopic surgery; from midline transclival approaches to brain stem tumors, including lateral approaches to the cervico-occipital junction and jugular foramen [66–68].

The continuous development of endonasal techniques also pushes the boundaries of other endoscopic-assisted cranial, skull base and neuro-endoscopic procedures. As a versatile technique, endonasal endoscopic surgery is an indispensable tool in the armamentarium of the contemporary skull base surgeon.

Conclusion

For many surgeons, the endoscopic transsphenoidal approach offers several advantages over the microscopic approach, particularly for removal of the extra- and parasellar tumor extension. Purely intrasellar adenomas can be removed, either using the microscope or the endoscope, with similar results.

Since there is a learning curve associated with the adoption of endoscopy, the selective use of the endoscope with only extrasellar tumors will prolong this learning curve. Therefore, most centers who use the endoscope use it exclusively for all endonasal tumor resections, and in doing so, have all abandoned the microscope.

References

1. Karppinen A, Kivipelto L, Vehkavaara S, Ritvonen E, Tikkanen E, Kivisaari R, Hernesniemi J, Setala K, Schalin-Jantti C, Niemela M (2015) Transition from microscopic to endoscopic transsphenoidal surgery for nonfunctional pituitary adenomas. World Neurosurg 84:48–57. doi:10.1016/j.wneu.2015.02.024
2. Laws ER Jr, Barkhoudarian G (2014) The transition from microscopic to endoscopic transsphenoidal surgery: the experience at Brigham and Women's Hospital. World Neurosurg 82:S152–S154. doi:10.1016/j.wneu.2014.07.035
3. O'Malley BW Jr, Grady MS, Gabel BC, Cohen MA, Heuer GG, Pisapia J, Bohman LE, Leibowitz JM (2008) Comparison of endoscopic and microscopic removal of pituitary adenomas: single-surgeon experience and the learning curve. Neurosurg Focus 25:E10. doi:10.3171/foc.2008.25.12.e10
4. Razak AA, Horridge M, Connolly DJ, Warren DJ, Mirza S, Muraleedharan V, Sinha S (2013) Comparison of endoscopic and microscopic trans-sphenoidal pituitary surgery: early results in a single centre. Br J Neurosurg 27:40–43. doi:10.3109/02688697.2012.703353
5. Rolston JD, Han SJ, Aghi MK (2015) Nationwide shift from microscopic to endoscopic transsphenoidal pituitary surgery. Pituitary. doi:10.1007/s11102-015-0685-y
6. Yang I, Wang MB, Bergsneider M (2010) Making the transition from microsurgery to endoscopic trans-sphenoidal pituitary neurosurgery. Neurosurg Clin N Am 21:643–651. doi:10.1016/j.nec.2010.07.008 **(vi)**
7. Ammirati M, Wei L, Ciric I (2013) Short-term outcome of endoscopic versus microscopic pituitary adenoma surgery: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry 84:843–849. doi:10.1136/jnnp-2012-303194
8. DeKlotz TR, Chia SH, Lu W, Makambi KH, Aulisi E, Deeb Z (2012) Meta-analysis of endoscopic versus sublabial pituitary surgery. Laryngoscope 122:511–518. doi:10.1002/lary.22479
9. Gao Y, Zhong C, Wang Y, Xu S, Guo Y, Dai C, Zheng Y, Wang Y, Luo Q, Jiang J (2014) Endoscopic versus microscopic transsphenoidal pituitary adenoma surgery: a meta-analysis. World J Surg Oncol 12:94. doi:10.1186/1477-7819-12-94
10. Goudakos JK, Markou KD, Georgalas C (2011) Endoscopic versus microscopic trans-sphenoidal pituitary surgery: a systematic review and meta-analysis. Clin Otolaryngol 36:212–220. doi:10.1111/j.1749-4486.2011.02331.x
11. Rotenberg B, Tam S, Ryu WH, Duggal N (2010) Microscopic versus endoscopic pituitary surgery: a systematic review. Laryngoscope 120:1292–1297. doi:10.1002/lary.20949
12. Tabaee A, Anand VK, Barron Y, Hiltzik DH, Brown SM, Kacker A, Mazumdar M, Schwartz TH (2009) Endoscopic pituitary surgery: a systematic review and meta-analysis. J Neurosurg 111:545–554. doi:10.3171/2007.12.17635
13. Strychowsky J, Nayan S, Reddy K, Farrokhyar F, Sommer D (2011) Purely endoscopic transsphenoidal surgery versus traditional microsurgery for resection of pituitary adenomas: systematic review. J Otolaryngol Head Neck Surg 40:175–185
14. Elhadi AM, Hardesty DA, Zaidi HA, Kalani MY, Nakaji P, White WL, Preul MC, Little AS (2015) Evaluation of surgical freedom for microscopic and endoscopic transsphenoidal approaches to the sella. Neurosurgery 11(Suppl 2):69–78. doi:10.1227/neu.0000000000000601 **(discussion 78–69)**
15. Couldwell WT, Weiss MH, Rabb C, Liu JK, Apfelbaum RI, Fukushima T (2004) Variations on the standard transsphenoidal approach to the sellar region, with emphasis on the extended approaches and parasellar approaches: surgical experience in 105 cases. Neurosurgery 55:539–547 **(discussion 547–550)**
16. Laws ER, Kanter AS, Jane JA Jr, Dumont AS (2005) Extended transsphenoidal approach. J Neurosurg 102:825–827. doi:10.3171/jns.2005.102.5.0825 **(discussion 827–828)**
17. Dumont AS, Kanter AS, Jane JA Jr, Laws ER Jr (2006) Extended transsphenoidal approach. Front Horm Res 34:29–45. doi:10.1159/000091570
18. Laws ER Jr, Fode NC, Redmond MJ (1985) Transsphenoidal surgery following unsuccessful prior therapy. An assessment of benefits and risks in 158 patients. J Neurosurg 63:823–829. doi:10.3171/jns.1985.63.6.0823
19. Eisele DW, Flint PW, Janas JD, Kelly WA, Weymuller EA Jr, Cummings CW (1988) The sublabial transseptal transsphenoidal approach to sellar and parasellar lesions. Laryngoscope 98:1301–1308. doi:10.1288/00005537-198812000-00005
20. Saito K, Kuwayama A, Yamamoto N, Sugita K (1995) The transsphenoidal removal of nonfunctioning pituitary adenomas with suprasellar extensions: the open sella method and intentionally staged operation. Neurosurgery 36:668–675 **(discussion 675–666)**
21. Ciric I, Ragin A, Baumgartner C, Pierce D (1997) Complications of transsphenoidal surgery: results of a national survey, review of the literature, and personal experience. Neurosurgery 40:225–236 **(discussion 236–227)**
22. Abosch A, Tyrrell JB, Lamborn KR, Hannegan LT, Applebury CB, Wilson CB (1998) Transsphenoidal microsurgery for growth hormone-secreting pituitary adenomas: initial outcome and long-term results. J Clin Endocrinol Metab 83:3411–3418. doi:10.1210/jcem.83.10.5111
23. Semple PL, Laws ER Jr (1999) Complications in a contemporary series of patients who underwent transsphenoidal surgery for Cushing's disease. J Neurosurg 91:175–179. doi:10.3171/jns.1999.91.2.0175
24. Fraser JF, Allen B, Anand VK, Schwartz TH (2009) Three-dimensional neurostereoendoscopy: subjective and objective comparison to 2D. Minim Invasive Neurosurg 52:25–31. doi:10.1055/s-0028-1104567
25. Catapano D, Sloffer CA, Frank G, Pasquini E, D'Angelo VA, Lanzino G (2006) Comparison between the microscope and endoscope in the direct endonasal extended transsphenoidal approach: anatomical study. J Neurosurg 104:419–425. doi:10.3171/jns.2006.104.3.419
26. Spencer WR, Das K, Nwagu C, Wenk E, Schaefer SD, Moscatello A, Couldwell WT (1999) Approaches to the sellar and parasellar region: anatomic comparison of the microscope versus endoscope. Laryngoscope 109:791–794
27. Baussart B, Aghakhani N, Portier F, Chanson P, Tadie M, Parker F (2005) Endoscope-assisted microsurgery for invasive endo- and suprasellar pituitary macroadenomas: a consecutive retrospective study with 13 patients. Neurochirurgie 51:455–463
28. Jarrahy R, Berci G, Shahinian HK (2000) Assessment of the efficacy of endoscopy in pituitary adenoma resection. Arch Otolaryngol Head Neck Surg 126:1487–1490
29. Kim EY, Park HS, Kim JJ, Han HS, Nam MS, Kim YS, Park HC (2001) Endoscopic transsphenoidal approach through a widened nasal cavity for pituitary lesions. J Clin Neurosci 8:437–441. doi:10.1054/jocn.2000.0851

30. Frazier JL, Chaichana K, Jallo GI, Quinones-Hinojosa A (2008) Combined endoscopic and microscopic management of pediatric pituitary region tumors through one nostril: technical note with case illustrations. Childs Nerv Syst 24:1469–1478. doi:10.1007/s00381-008-0710-9
31. McLaughlin N, Eisenberg AA, Cohan P, Chaloner CB, Kelly DF (2013) Value of endoscopy for maximizing tumor removal in endonasal transsphenoidal pituitary adenoma surgery. J Neurosurg 118:613–620. doi:10.3171/2012.11.jns112020
32. Messerer M, De Battista JC, Raverot G, Kassis S, Dubourg J, Lapras V, Trouillas J, Perrin G, Jouanneau E (2011) Evidence of improved surgical outcome following endoscopy for nonfunctioning pituitary adenoma removal. Neurosurg Focus 30:E11. doi:10.3171/2011.1.focus10308
33. Dallapiazza R, Bond AE, Grober Y, Louis RG, Payne SC, Oldfield EH, Jane JA Jr (2014) Retrospective analysis of a concurrent series of microscopic versus endoscopic transsphenoidal surgeries for Knosp Grades 0-2 nonfunctioning pituitary macroadenomas at a single institution. J Neurosurg 121:511–517. doi:10.3171/2014.6.jns131321
34. Hofstetter CP, Nanaszko MJ, Mubita LL, Tsiouris J, Anand VK, Schwartz TH (2012) Volumetric classification of pituitary macroadenomas predicts outcome and morbidity following endoscopic endonasal transsphenoidal surgery. Pituitary 15:450–463. doi:10.1007/s11102-011-0350-z
35. Komotar RJ, Starke RM, Raper DM, Anand VK, Schwartz TH (2012) Endoscopic endonasal compared with microscopic transsphenoidal and open transcranial resection of giant pituitary adenomas. Pituitary 15:150–159. doi:10.1007/s11102-011-0359-3
36. Lenzi J, Lapadula G, D'Amico T, Delfinis CP, Iuorio R, Caporlingua F, Mecca N, Mercuri V, Bassotti G, Rillo M, Santoro F, Tamburrano G, Santoro A, Gargiulo P (2015) Evaluation of trans-sphenoidal surgery in pituitary GH-secreting micro- and macroadenomas: a comparison between microsurgical and endoscopic approach. J Neurosurg Sci 59:11–18
37. Jagannathan J, Smith R, DeVroom HL, Vortmeyer AO, Stratakis CA, Nieman LK, Oldfield EH (2009) Outcome of using the histological pseudocapsule as a surgical capsule in Cushing disease. J Neurosurg 111:531–539. doi:10.3171/2008.8.jns08339
38. Starke RM, Raper DM, Payne SC, Vance ML, Oldfield EH, Jane JA Jr (2013) Endoscopic vs microsurgical transsphenoidal surgery for acromegaly: outcomes in a concurrent series of patients using modern criteria for remission. J Clin Endocrinol Metab 98:3190–3198. doi:10.1210/jc.2013-1036
39. Honegger J, Schmalisch K, Beuschlein F, Kaufmann S, Schnauder G, Naegele T, Psaras T (2012) Contemporary microsurgical concept for the treatment of Cushing's disease: endocrine outcome in 83 consecutive patients. Clin Endocrinol 76:560–567. doi:10.1111/j.1365-2265.2011.04268.x
40. Dusick JR, Esposito F, Mattozo CA, Chaloner C, McArthur DL, Kelly DF (2006) Endonasal transsphenoidal surgery: the patient's perspective-survey results from 259 patients. Surg Neurol 65:332–341. doi:10.1016/j.surneu.2005.12.010 **discussion 341–332**
41. Karabatsou K, O'Kelly C, Ganna A, Dehdashti AR, Gentili F (2008) Outcomes and quality of life assessment in patients undergoing endoscopic surgery for pituitary adenomas. Br J Neurosurg 22:630–635. doi:10.1080/02688690802220379
42. Lwu S, Edem I, Banton B, Bernstein M, Vescan A, Gentili F, Zadeh G (2012) Quality of life after transsphenoidal pituitary surgery: a qualitative study. Acta Neurochir (Wien) 154:1917–1922. doi:10.1007/s00701-012-1455-5
43. Little AS, Kelly D, Milligan J, Griffiths C, Prevedello DM, Carrau RL, Rosseau G, Barkhoudarian G, Otto BA, Jahnke H, Chaloner C, Jelinek KL, Chapple K, White WL (2015) Predictors of sinonasal quality of life and nasal morbidity after fully endoscopic transsphenoidal surgery. J Neurosurg 122:1458–1465. doi:10.3171/2014.10.jns141624
44. McCoul ED, Bedrosian JC, Akselrod O, Anand VK, Schwartz TH (2015) Preservation of multidimensional quality of life after endoscopic pituitary adenoma resection. J Neurosurg 123:813–820. doi:10.3171/2014.11.jns14559
45. Kahilogullari G, Beton S, Al-Beyati ES, Kantarcioglu O, Bozkurt M, Kantarcioglu E, Comert A, Unlu MA, Meco C (2013) Olfactory functions after transsphenoidal pituitary surgery: endoscopic versus microscopic approach. Laryngoscope 123:2112–2119. doi:10.1002/lary.24037
46. Simal-Julian JA, Miranda-Lloret P, Pancucci G, Evangelista-Zamora R, Perez-Borreda P, Sanroman-Alvarez P, Camara-Gomez R, Botella-Asuncion C (2014) Microscopic versus endoscopic pituitary surgery. Neurocirugia (Astur) 25:170–178. doi:10.1016/j.neucir.2013.12.001
47. Zada G, Kelly DF, Cohan P, Wang C, Swerdloff R (2003) Endonasal transsphenoidal approach for pituitary adenomas and other sellar lesions: an assessment of efficacy, safety, and patient impressions. J Neurosurg 98:350–358. doi:10.3171/jns.2003.98.2.0350
48. Garcia-Navarro V, Anand VK, Schwartz TH (2013) Gasket seal closure for extended endonasal endoscopic skull base surgery: efficacy in a large case series. World Neurosurg 80:563–568. doi:10.1016/j.wneu.2011.08.034
49. Raza SM, Schwartz TH (2015) Multi-layer reconstruction during endoscopic endonasal surgery: how much is necessary? World Neurosurg 83:138–139. doi:10.1016/j.wneu.2014.07.004
50. Luginbuhl AJ, Campbell PG, Evans J, Rosen M (2010) Endoscopic repair of high-flow cranial base defects using a bilayer button. Laryngoscope 120:876–880. doi:10.1002/lary.20861
51. Banu MA, Kim JH, Shin BJ, Woodworth GF, Anand VK, Schwartz TH (2014) Low-dose intrathecal fluorescein and etiology-based graft choice in endoscopic endonasal closure of CSF leaks. Clin Neurol Neurosurg 116:28–34. doi:10.1016/j.clineuro.2013.11.006
52. Patel KS, Komotar RJ, Szentirmai O, Moussazadeh N, Raper DM, Starke RM, Anand VK, Schwartz TH (2013) Case-specific protocol to reduce cerebrospinal fluid leakage after endonasal endoscopic surgery. J Neurosurg 119:661–668. doi:10.3171/2013.4.jns13124
53. Maric A, Kruljac I, Cerina V, Pecina HI, Sulentic P, Vrkljan M (2012) Endocrinological outcomes of pure endoscopic transsphenoidal surgery: a Croatian Referral Pituitary Center experience. Croat Med J 53:224–233
54. Jakimovski D, Bonci G, Attia M, Shao H, Hofstetter C, Tsiouris AJ, Anand VK, Schwartz TH (2014) Incidence and significance of intraoperative cerebrospinal fluid leak in endoscopic pituitary surgery using intrathecal fluorescein. World Neurosurg 82:e513–e523. doi:10.1016/j.wneu.2013.06.005
55. Wang F, Zhou T, Wei S, Meng X, Zhang J, Hou Y, Sun G (2015) Endoscopic endonasal transsphenoidal surgery of 1,166 pituitary adenomas. Surg Endosc 29:1270–1280. doi:10.1007/s00464-014-3815-0
56. Paluzzi A, Fernandez-Miranda JC, Tonya Stefko S, Challinor S, Snyderman CH, Gardner PA (2014) Endoscopic endonasal approach for pituitary adenomas: a series of 555 patients. Pituitary 17:307–319. doi:10.1007/s11102-013-0502-4
57. Schaberg MR, Anand VK, Schwartz TH, Cobb W (2010) Microscopic versus endoscopic transnasal pituitary surgery. Curr Opin Otolaryngol Head Neck Surg 18:8–14. doi:10.1097/MOO.0b013e328334db5b
58. Komotar RJ, Starke RM, Raper DM, Anand VK, Schwartz TH (2012) Endoscopic endonasal compared with microscopic transsphenoidal and open transcranial resection of craniopharyngiomas. World Neurosurg 77:329–341. doi:10.1016/j.wneu.2011.07.011

59. Oosmanally N, Paul JE, Zanation AM, Ewend MG, Senior BA, Ebert CS Jr (2011) Comparative analysis of cost of endoscopic endonasal minimally invasive and sublabial-transseptal approaches to the pituitary. Int Forum Allergy Rhinol 1:242–249. doi:10.1002/alr.20048
60. Pledger CL, Elzoghby MA, Oldfield EH, Payne SC, Jane JA Jr (2015) Prospective comparison of sinonasal outcomes after microscopic sublabial or endoscopic endonasal transsphenoidal surgery for nonfunctioning pituitary adenomas. J Neurosurg 11:1–11. doi:10.3171/2015.6.jns142695
61. Rudmik L, Starreveld YP, Vandergrift WA, Banglawala SM, Soler ZM (2015) Cost-effectiveness of the endoscopic versus microscopic approach for pituitary adenoma resection. Laryngoscope 125:16–24. doi:10.1002/lary.24780
62. Little AS, Chapple K, Jahnke H, White WL (2014) Comparative inpatient resource utilization for patients undergoing endoscopic or microscopic transsphenoidal surgery for pituitary lesions. J Neurosurg 121:84–90. doi:10.3171/2014.2.jns132095
63. Cappabianca P, Cavallo LM, Colao A, de Divitiis E (2002) Surgical complications associated with the endoscopic endonasal transsphenoidal approach for pituitary adenomas. J Neurosurg 97:293–298. doi:10.3171/jns.2002.97.2.0293
64. Koutourousiou M, Gardner PA, Tormenti MJ, Henry SL, Stefko ST, Kassam AB, Fernandez-Miranda JC, Snyderman CH (2012) Endoscopic endonasal approach for resection of cranial base chordomas: outcomes and learning curve. Neurosurgery 71:614–624. doi:10.1227/NEU.0b013e31825ea3e0 **(discussion 624–615)**
65. Zaidi HA, Awad AW, Bohl MA, Chapple K, Knecht L, Jahnke H, White WL, Little AS (2015) Comparison of outcomes between a less experienced surgeon using a fully endoscopic technique and a very experienced surgeon using a microscopic transsphenoidal technique for pituitary adenoma. J Neurosurg. doi:10.3171/2015.4.jns15102
66. Leng LZ, Anand VK, Hartl R, Schwartz TH (2009) Endonasal endoscopic resection of an os odontoideum to decompress the cervicomedullary junction: a minimal access surgical technique. Spine 34:E139–E143. doi:10.1097/BRS.0b013e31818e344d
67. Lee DL, McCoul ED, Anand VK, Schwartz TH (2012) Endoscopic endonasal access to the jugular foramen: defining the surgical approach. J Neurol Surg B Skull Base 73:342–351. doi:10.1055/s-0032-1322796
68. Rajappa P, Margetis K, Sigounas D, Anand V, Schwartz TH, Greenfield JP (2013) Endoscopic endonasal transclival approach to a ventral pontine pediatric ependymoma. J Neurosurg Pediatr 12:465–468. doi:10.3171/2013.8.peds12183