The role of outcomes data for assessing the expertise of a pituitary surgeon

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Purpose of review

Over the past four decades, advances in surgical technique, instrumentation, and anatomical knowledge have fueled the evolution and sophistication of transsphenoidal pituitary surgery. Paralleling these advances have been major improvements in endocrinological and overall clinical outcomes in patients with pituitary adenomas and other parasellar lesions such as Rathke's cleft cysts and craniopharyngiomas. In this review, we assess the impact of neurosurgeon expertise as a determinant of outcome in pituitary surgery.

Recent findings

Published data since the 1980s indicate that remission rates, overall clinical outcomes and surgical complication rates in pituitary and parasellar surgery are related to neurosurgeon practice volume and cumulative clinical experience. More recently, pituitary surgery has been increasingly performed using an endonasal endoscopic approach. Reports over the last decade suggest when an experienced pituitary neurosurgeon performs a fully endoscopic or endoscope-assisted tumor removal; outcomes are similar if not better than when performed by a traditional microscopic transsphenoidal approach.

Summary

A focused clinical practice and large transsphenoidal surgical volume appear to be important outcome determinants for patients with pituitary and parasellar tumors. Strategies that may further improve patient outcomes include establishing guidelines for pituitary tumor centers of excellence and more focused residency and fellowship training in endonasal endoscopic transsphenoidal surgery. Encouraging regionalization of care to higher volume pituitary tumor centers of excellence and promoting patient education on the importance of surgical expertise may further enhance pituitary patient outcomes.

Keywords

complication, endonasal, endoscopy, pituitary adenoma, transsphenoidal surgery

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Introduction

Many factors influence outcomes from pituitary surgery, including disease severity, tumor characteristics, and patient comorbidities. Surgeon experience and hospital volume have been previously shown to affect outcomes in a variety of disciplines [1•] including neurosurgery [2–4,5•,6,7], and appear to play an important role in influencing outcomes after pituitary tumor surgery [8–12,13•–15•,16–19]. In this review, we evaluate pituitary surgery outcomes data to determine how to best define success in various types of pituitary tumor surgery, if surgical experience and expertise is associated with outcome, what factors may explain relationships between pituitary surgery expertise and outcome, and how this data should be applied to management of patients with pituitary region tumors.

History of transsphenoidal surgery

Transsphenoidal surgery is considered the first-line treatment for all clinically significant endocrine-inactive and endocrine-active pituitary adenomas except prolactinomas, which are typically treated with dopamine agonists. Transsphenoidal surgery is also the primary treatment for Rathke's cleft cysts and for many craniopharyngiomas. The transsphenoidal approach to the pituitary gland was first developed in the early 1900s by Schloffer, Cushing, and Hirsch [20], and in the 1950s and 1960s the sublabial route was further described by Dott, Guiot, and Hardy.

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Introduction of the operating microscope by Jules Hardy in the 1960s propelled pituitary surgery into the modern microsurgical era [21], with subsequent improvements in surgical safety and efficacy established by Wilson, Weiss, Laws, and others in the 1980s. A direct endonasal approach described by Griffith and Veerapen in 1987 and Cooke and Jones in 1994 significantly reduced mucosal trauma and improved patient comfort, and has become the most commonly used approach in present day pituitary surgery. Endoscopy as a primary or assisting tool represents the latest major advancement in transsphenoidal surgery technique, and in the past decade has dramatically expanded the surgical access of pituitary surgeons to tumors that were previously considered beyond the reach of conventional microscopic transsphenoidal operations [22,23]. Ongoing advancements such as improved surgical instrumentation, [24,25•], high definition and virtual [26] endoscopy, frameless neuronavigation [27], and intraoperative MRI [28,29], continue to fuel the evolution of pituitary surgery.

Outcomes data in pituitary surgery

Outcomes data play a key role in supporting the development of pituitary surgery as a field of expertise in neurosurgery, and have been reported by different groups using varying techniques. In general, the goals of pituitary surgery include rapid resolution of tumor mass effect, including decompression of the optic apparatus and of the normal pituitary gland and stalk, and elimination of hormonal hypersecretion syndromes. Therefore, outcomes can be measured using a combination of imaging, endocrine, and clinical parameters, and have varying importance based on tumor type and patient presentation. For example, extent of tumor resection and restoration of visual fields and visual acuity are key outcome determinants for endocrine-inactive macroadenomas. In contrast, resolution of endocrinopathy and quality of life are key parameters for patients with Cushing's disease (CD), acromegaly and prolactinomas [30–32]. Many factors influence pituitary surgery outcome data, including tumor size [14•,33,34••,35], reoperation [36], magnitude of endocrinopathy [37], and patient factors such as age and sex [38•]. Success rates can also differ based on treatment goal; subtotal resection represents failure in a patient with CD but can be successful in enhancing response to medical therapy in a patient with acromegaly [39,40].

Surgical approach and outcome

The development of transsphenoidal approaches to the sella was a major advancement in pituitary surgery, and now well over 95% of tumors are resected using variations of this technique [34••,41–43]. In comparison to transcranial operations, the transsphenoidal approach has been associated with better recovery of visual deficits [44–47] and postoperative hormonal function [48,49]. The direct endonasal transsphenoidal approach has many advantages over sublabial or transseptal techniques, which are associated with increased risk of nasoseptal perforations, synechiae, upper limb numbness, anosmia, and septal abscess [50–53]. In a survey of 30 patients that underwent initial sublabial surgery followed by redo transsphenoidal surgery via a direct endonasal route, hospital stay was significantly shorter and 87% reported easier recovery, 80% less pain, and 79% better postoperative nasal airflow [54].

Although direct endonasal transsphenoidal approaches are generally preferable to transcranial pituitary surgery, this does not imply that the latter has no place in the armamentarium of pituitary surgery. Data from transcranial clinical series are strongly biased towards factors that worsen clinical outcome (large tumor size, significant suprasellar extension, and worse preoperative clinical status), and these studies are limited by significant heterogeneity in patient characteristics and outcome measurements. As has been previously described, craniopharyngiomas with little to no intrasellar component or with lateral suprasellar extension, or the rare pituitary adenoma with minimal sellar component, may be appropriate candidates for transcranial or a combined surgical approach [34••,42,55]. Expertise in pituitary surgery, therefore, does not imply exclusive transsphenoidal operations, but, instead, sound clinical judgment in identifying select cases of pituitary region tumors that could be resected via a transsphenoidal, transcranial, or combined route.

Endoscopic techniques and outcomes

Endoscopy represents one of the latest major advancements in the evolution of pituitary surgical techniques, and has the advantages of expanded surgical visual field, panoramic images of sphenoid sinus and sella anatomy, and improved identification of tumor tissue and the interface between pituitary adenomas and the pituitary gland and medial wall of the cavernous sinus. With purely endoscopic transsphenoidal approaches there is generally less anterior nasoseptal dissection and less need for postoperative nasal packing, resulting in improved patient comfort and decreased hospital length of stay. Potential disadvantages of endoscopy include the loss of stereoscopic view and technical challenges associated with learning a new surgical technique, including difficulty with bimanual approaches and increased operating time. Some authors have described these disadvantages as transient, suggesting that after 17–50 [56•,57,58•] procedures one can overcome these challenges and progress to more difficult variations [56•]. Others [59•] have suggested that they are insignificant if the transition to

endoscopic pituitary surgery is made by a dedicated otolaryngology/neurosurgery team with significant endoscopic and pituitary surgery experience.

Over the last decade, there have been an increasing number of publications related to endoscopic pituitary surgery. The effect of the 'endoscopic learning curve' on surgical outcomes has been previously reported from various institutions. For example, O'Malley *et al.* [58•] reviewed their experience with the first 25 pituitary surgeries performed with the endoscope, and reported improvements in operating time (3.4 to 2.2 h) and hospital length of stay (4.7 to 3.9 days) when comparing the last eight cases to the initial 17. Koc *et al.* [57] reviewed their experience in 78 patients treated with pure endoscopic resection and found that the second half of the study group had decreased operating time (130 vs. 175 min for macroadenomas, 95 vs. 130 min for microadenomas), increased GTR rate (66–75% vs. 50–55%), and increased likelihood of remission (66% vs. 50–55%).

Many groups [60••,61•,62•,63,64•] have compared outcomes between microscopic and endoscopic pituitary surgery series, supporting the proposed benefits of pure endoscopic operations. Graham *et al.* [62•] recently compared 122 microscopic procedures to 71 endoscopic operations and reported reduced recurrence rate (18.2 vs. 28.4%), shorter hospital stay (4.1 vs. 6.0 days), greater visual improvement rates (53.8 vs. 46.7%), and improved sinonasal outcome scores in patients undergoing endoscopic surgery. Gondim *et al.* [61•] reviewed gross total resection rates and endocrine remission in 228 consecutive patients with various types of pituitary adenomas, demonstrating remission data that was equal to or better than historical data from microsurgical series. Dehdashti *et al.* [64•] demonstrated similar results in 200 patients treated endoscopically, with GTR rates of 96–98% and remission rates at 19 months of 71, 81, and 88% in acromegaly, CD, and prolactinoma, respectively. In a recent meta-analysis of 821 patients from nine published studies, Tabaee *et al.* [65••] reported an average GTR rate of 78%, remission rates of 81–84%, and CSF leak, permanent diabetes insipidus, and mortality rates of 2, 1, and 0.2%, respectively.

Randomized clinical trials comparing standard microsurgical techniques to endoscopy are limited [66••], but there is sufficient evidence to suggest that endoscopic techniques result in similar, if not better, surgical outcomes and are particularly advantageous for tumors that are difficult to visualize or access with standard microscopy [67–69]. As has occurred in other surgical fields, expertise in pituitary surgery will likely require incorporation of endoscopic techniques into the majority of transsphenoidal operations.

Surgical expertise and outcome

Surgeon experience and hospital volume is associated with 'better outcomes across a wide range of procedures and conditions' [1•], including neurosurgical diseases such as meningioma [5•], intraoperative aneurysm rupture [6,7], subarachnoid hemorrhage [3,4] and microvascular decompression of cranial nerves [2]. A similar association has been described for pituitary tumor operations as well [8–10,13•–15•,16–19,57,58•,70–73] (Tables 1 and 2). In a large US survey of 958 neurosurgeons conducted by Ciric *et al.* [15•], complications from pituitary surgery were significantly more common in respondents with less experience. A series of studies

Table 1 Select studies relating pituitary surgeon experience to outcome

Author	Surgeon	Pathology, technique	Outcome variable	Early in series (*n*)	Late in series (*n*)
Ahmed [14•]	Adams (England)	Acromegaly, microscopic	Remission (all); remission (micro); improved pit fcn	48%; 50%; 16% ($n=25$)	73%; 100%; 41% ($n=32$)
Trepp [9]	Seiler (Switzerland)	Acromegaly, unspecified	Remission	33% ($n=38$)	55% ($n=31$)
Abbassioun 2006 [10]	Abbassioun (Iran)	Acromegaly, microscopic	Recurrence	5.6% ($n=126$)	0% ($n=25$)
Koc [57]	Various surgeons (Turkey)	Various, endoscopic	OR time; GTR rate; remission	175/130 min[a]; 66–75%; 66%	130/95 min; 50–55%; 50–55%
Fatemi [72]	Kelly (USA)	Various, micro/endo	CSF leak; hematoma; ICA injury; neuro def	3%; 1%; 0.6%; 0.8% ($n=500$)	1%; 0.3%; 0.3%; 0% ($n=312$)
Gardner [71]	Kassam, Gardner, Snyderman, Carrau (USA)	Cranioph, Endoscopic	CSF leak	69% ($n=13$)	20% ($n=3$)
O'Malley 2008 [58•]	Grady, O'Malley (USA)	Various, endoscopic	OR time; LOS	3.4 h; 4.7 days ($n=17$)	2.2 h; 3.9 days ($n=8$)

Cranioph, craniopharyngioma; CSF, cerebrospinal fluid; GTR, gross total resection; ICA, internal carotid artery; LOS, length of (hospital) stay; pit fcn, pituitary function.
[a] Microadenoma/macroadenoma.

Table 2 Select studies demonstrating benefits of 'single surgeon' strategy

Author/(country)	Pathology, technique	Outcome variable	Less experienced/ multiple surgeons	More experienced/ single surgeon	Comments
Yamada (Japan) [18]	Acromegaly, microsurgery	Remission	29–37% ($n=30$)	77–81% ($n=31$)	Transitioned to single surgeon strategy
Gittoes (UK) [16]	Acromegaly, microsurgery	Remission	33% ($n=78$)	64% ($n=66$)	Transitioned to single surgeon strategy
Erturk (Turkey) [8]	Acromegaly	Remission	33% ($n=30$)	–	Treated by seven different surgeons
Boeving (Brazil) [70]	Acromegaly, microsurgery	Remission	49% ($n=?$)	66% ($n=?$)	Combined own series ($n=28$) with 10 other studies ($n=1632$)
Bates (UK) [73]	Acromegaly, microsurgery	Remission	31% ($n=77$)	53% ($n=136$)	Improved outcomes in last 4 years of study, when care was transitioned to experts

from the UK on acromegaly has confirmed a relationship between surgeon volume and patient outcome. Centers in Manchester [17] and Birmingham [74] reported data from 73 patients operated by nine surgeons and 89 patients operated by eight surgeons, resulting in remission rates of 20 and 33%, respectively. On the other hand, centers in Oxford [14•], Newcastle [75], and London [76] had remission rates of 42–56% using a 'one pituitary surgeon strategy'. At Queen Elizabeth hospital in Birmingham, remission rates for acromegaly nearly doubled from 33 to 64% when a single surgeon performed all operations [16]. In a review of 1215 cases of acromegaly treated at 22 centers in the UK, Bates *et al.* [73] confirmed that surgical outcome significantly improved in the last 4 years of the study after directing care to a small number of subspecialists [77]. Yamada *et al.* [18] reported a similar phenomenon in Japan, with an increase in surgical success for acromegaly from 37 to 81% with transition to a single surgeon strategy.

Clinical series data from highly experienced surgeons [43,71,78,79] further support this association between expertise and clinical outcomes. For example, Fatemi *et al.* [72] reported data from our 10-year experience with endonasal transsphenoidal resection of 812 pituitary region tumors, including 605 pituitary adenomas. Comparing the first 500 cases to the last 312, we found decreases in postoperative CSF leak rates (3 vs. 0.8%), hematomas (1 vs. 0.3%), carotid artery injuries (0.6% vs. 0.3%), and neurological deficits (0.8 vs. 0%) with increasing surgical experience. Ahmed *et al.* [14•] reviewed their 20-year experience with 139 patients treated for acromegaly; remission was achieved in 48% of patients during the first 15 years and 74% in the last 5 years (microadenoma success rates increased from 50 to 100%). Improvement in pituitary function was achieved in 16% early in the series and 34% with increasing experience. The authors did not find temporal relationships in complication or recurrence rates, but clearly demonstrated improved outcomes with increasing surgical experience. Hofmann *et al.* [80] reported their 35-year experience with primary surgery for cardiac disease in 426 patients. All but two patients were treated with a transsphenoidal approach, and outcome data of at least 3 months duration was available in all but 64 patients. The authors reported significant improvements in complication rates with increasing experience, but found no relationship with remission of hypercortisolemia (overall 75.9%).

Why experience improves outcome

Various reports have shed light on factors associated with improved outcome in experienced surgical series. In our early experience with pituitary region tumors, advancements in instrumentation and surgical techniques were coincident with improved outcomes. For example, we transitioned to a short trapezoidal speculum that improves microscopic visualization and facilitates instrument maneuverability [81]. We also began to routinely use a micro-Doppler probe and hook blade to better identify the cavernous carotid artery and more safely open the sellar dura [25•]. Improved outcomes also coincided with increased use of direct endonasal (versus sublabial and transseptal) [54] approaches and the endoscope (both endoscopic-assisted and pure endoscopic approaches) [72]. Adoption of a graded CSF leak repair protocol also resulted in a decreased postoperative CSF leak rate from 4 to 1% between the first 328 cases and the last 340 cases [82•]. In another series of expanded endonasal approaches to sellar region tumors, CSF leak rates decreased from 69 to 20% [71] to below 5% [83•] with the use of modified techniques such as balloon buttresses and a vascularized, nasoseptal flap [84•]. Improved outcomes with increased surgical experience, therefore, may be due to modified surgical techniques [85,86], adoption of new instrumentation [87] and, perhaps most importantly, by simply gaining altitude on the learning curve of knowing how to maximize outcomes and avoid complications.

Surgical series of patients undergoing reoperations for residual or recurrent tumors [88•,89,90] may shed

additional light on factors that predispose to surgical failure. In our experience [88•] of 30 repeat operations for patients with residual endocrine-inactive adenomas from a series of 188 consecutive patients, suboptimal bony exposure was a consistent finding in all cases. Inadequate removal of the sphenoid keel or suboptimal exposure of the sella was present in 97 and 93% of cases, respectively. We also found that reoperations were more common for adenomas with cavernous sinus invasion (53%) or those that had a fibrous or rubbery consistency (40%). Surgeon experience was a significant factor in all 30 cases; 27 of 30 patients had their initial operation at centers not recognized for pituitary tumor surgery, and the other three were done by the senior author early in his transsphenoidal surgical experience.

The experience of the treating hospital may also play a role independent of surgeon experience, a phenomenon that has been previously implicated in outcome of ruptured aneurysms [91] and brain tumors [92]. In a review of over 38 000 admissions for biopsy or resection of primary brain tumors, large-volume centers had decreased adverse discharge disposition and lower mortality rates [92]. With increasing institutional experience managing patients with brain tumors, mortality rates at high volume centers decreased from 4.8 to 1.8% over 12 years. A similar phenomenon was reported by Barker *et al.* [13•] in a review of transsphenoidal surgery outcomes in the USA between 1996 and 2000, confirming that high-volume centers had lower complication rates and superior clinical outcomes. In a recent review [38•] of 3525 cases of CD treated with transsphenoidal surgery between 1993 and 2002 in the USA, there was a non-significant trend towards lower complication rates at high-volume hospitals. Improved outcome for pituitary tumors treated at high-volume centers may be due to a variety of factors, including the critical influence that strong collaborative efforts among neurosurgery, otolaryngology, endocrinology, and radiation oncology have on patient management [93,94•].

Implications

Regionalization of care has been established for pediatric critical care and management of burn patients, and has been proposed for neurosurgical disorders such as cerebral aneurysms [4,91]. On the basis of the literature, a similar strategy for management of pituitary adenomas has been proposed [11,77] and may be appropriate. Extensive pituitary surgery outcome data from various centers in the UK [14•,16,17,74–76] has strongly supported a proposed policy [77] of focusing pituitary surgery to a small number of referral centers with established surgical experts and allied expertise in pituitary endocrinology, which has coincided with improved outcomes [73]. Development of 'pituitary tumor centers of excellence' has many theoretical advantages, but regionalization of care faces significant practical [95], political, and philosophical obstacles [96] that make it difficult to adopt in most practice environments.

An alternative strategy is increased emphasis on achieving a higher degree of pituitary surgery expertise and clinical education. Studies [97•,98•] of neurological surgery training at US centers have revealed significant differences in pituitary surgery experience. In a detailed review of primary brain tumor surgical experience at 94 ACGME approved neurosurgery residency programs in the USA, Jane *et al.* [98•] found that 30.9% of institutions performed at least 20 pituitary operations per year and 79.8% performed less than 50 each year (only 7.4% performed more than 100 cases annually) [98•]. It is not known what proportion of these centers routinely use advanced techniques such as endoscopy, which may improve outcomes but is associated with a significant learning curve. Therefore, many graduating neurosurgery residents likely lack sufficient advanced endonasal transsphenoidal surgical experience. Whether such trainees should consider subspecialty fellowship training prior to establishing a pituitary surgery practice remains open to debate.

Survey data also suggest that most neurosurgeons in clinical practice perform pituitary surgery infrequently, and are unable to develop the type of clinical experience associated with improved outcomes. In a study by the Neurosurgery Executives' Resource Value & Education Society (NERVES) published in 2005 [99], the mean number of pituitary tumor operations performed by neurosurgeons was 4.45 per year. With or without subspecialty training, neurosurgeons with limited pituitary surgery experience should consider working with more experienced colleagues, adopting a step-wise progression in case type and difficulty, and a policy of referring more challenging cases to established, high-volume centers with experienced multidisciplinary pituitary teams. In a detailed report by one of the world's most experienced groups in endoscopic transsphenoidal surgery, present and former colleagues from the Minimally Invasive endo-Neurosurgery Center at the University of Pittsburgh [56•] discussed the importance of fellowship education for mastery of endoscopic surgery and proposed an incremental training program that 'requires mastery of simpler procedures [30–50 cases] before proceeding to the next level of difficulty'. The authors state '... it is important for surgeons to recognize their own limitations and not attempt procedures that are beyond their capabilities' to 'avoid unnecessary complications and minimize patient morbidity and mortality' [56•], a conclusion that is strongly supported by the literature on pituitary surgery expertise and outcomes.

Conclusion

Pituitary surgery has significantly evolved in technique and instrumentation over the last 40 years with major resultant improvements in clinical outcome. A review of the recent literature indicates that expertise in transsphenoidal surgery gained from specialized training and a high-volume clinical practice, is a key determinant of surgical success and patient outcomes. To further improve patient care and reduce complication risks in pituitary surgery, careful consideration should be given to establishment of guidelines for subspecialization in endonasal transsphenoidal surgery through intensified residency and fellowship training, and designation of pituitary tumor centers of excellence with regionalization of care. Practicing neurosurgeons should also be encouraged to work closely with colleagues in endocrinology, and to adopt a step-wise progression in case complexity, including consideration of referral of highly challenging cases to more experienced colleagues at centers of excellence.

References and recommended reading

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