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Review Article

The expanding role of the endonasal endoscopic approach in pituitary and skull base surgery: A 2014 perspective

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Abstract

Background: The past two decades have been the setting for remarkable advancement in endonasal endoscopic neurosurgery. Refinements in camera definition, surgical instrumentation, navigation, and surgical technique, including the dual surgeon team, have facilitated purely endonasal endoscopic approaches to the majority of the midline skull base that were previously difficult to access through the transsphenoidal microscopic approach.

Methods: This review article looks at many of the articles from 2011 to 2014 citing endonasal endoscopic surgery with regard to approaches and reconstructive techniques, pathologies treated and outcomes, and new technologies under consideration.

Results: Refinements in approach and closure techniques have reduced the risk of cerebrospinal fluid leak and infection. This has allowed surgeons to more aggressively treat a variety of pathologies. Four main pathologies with outcomes after treatment were identified for discussion: pituitary adenomas, craniopharyngiomas, anterior skull base meningiomas, and chordomas. Within all four of these tumor types, articles have demonstrated the efficacy, and in certain cases, the advantages over more traditional microscope-based techniques, of the endonasal endoscopic technique.

Conclusions: The endonasal endoscopic approach is a necessary tool in the modern skull base surgeon's armamentarium. Its efficacy for treatment of a wide variety of skull base pathologies has been repeatedly demonstrated. In the experienced surgeon's hands, this technique may offer the advantage of greater tumor removal with reduced overall complications over traditional craniotomies for select tumor pathologies centered near the midline skull base.

Key Words: Craniopharyngioma, chordoma, endoscopic skull base surgery, endoscopic endonasal surgery, endoscopic pituitary surgery, tuberculum sella meningioma

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INTRODUCTION

In traditional transsphenoidal surgery, the operating microscope provides a clear view of the sella through a corridor created by a nasal speculum. While this approach has been a highly effective technique for most midline sellar pathology for over five decades, the "tunnel vision" and restricted maneuverability provided by this approach led neurosurgeons to seek better modes of visualizing and accessing the parasellar region.[34] The first applications of the endoscope in transsphenoidal surgery were described by Apuzzo *et al*.[4] in 1977 and Bushe and Halves[10] in 1978 as an adjunct to the microscope for tumors extending outside of the confines of the sella. In the mid-1990s, surgeons began reporting their experience with endoscope assisted transsphenoidal microsurgery for pituitary adenomas and concluded that it facilitated greater tumor resection by allowing better differentiation of tumor from the normal gland[33] and visualization of tumor hidden in the presellar and parasellar regions with angled endoscopes.[44] Pioneers in endoscopic pituitary surgery, Jho and Carrau, reported their technique[49] and results[46] utilizing a fully endoscopic approach for tumor resection in 1997 and 1998, respectively. With further refinements in camera definition and surgical instrumentation, fully endoscopic endonasal pituitary and sella surgery became a mainstay. The experience gained with operating in this region, coupled with a better understanding of the surgical anatomy, improved surgical navigation systems, and the implementation of a surgical team composed of an experienced rhinologist and neurosurgeon,[52,57] led to expanded approaches outside the confines of the sella.

To date, the fully endonasal endoscopic approach (EEA) has been described to access the anterior middle fossa through the cribriform plate,[47,54] the suprasellar cistern through the planum sphenoidale and tuberculum sellae,[35,54,87] the prepontine and premedullary cisterns through the clivus,[48,55,78] the ventral cervicomedullary junction,[53,74] Meckel's cave,[58,59] the middle cranial fossa,[57] the petrous apex,[90] the jugular foramen,[32,52] and the pterygopalatine[9] and infratemporal fossae.[6,59] Although benign tumors represent the majority of pathology addressed with the fully EEAs, malignant tumors,[6,58] congenital lesions,[74,85] inflammatory processes,[74] and vascular lesions[23,29] have been reported. The following review provides an update on the indications and outcomes of endoscopic endonasal skull base surgery with coverage of the most relevant and impactful articles from 2011 to 2014.

Given the complex nature of many if not most midline skull base lesions and the fact that a majority may have sellar and pituitary gland involvement, the use of a multidisciplinary team is strongly advocated to optimize outcomes. This team approach should include specialists in neurosurgery, otorhinolaryngology (ENT), endocrinology, radiation oncology, medical oncology, neuro-ophthalmology, diagnostic and interventional neuroradiology, and neuropathology.[77]

ENDONASAL ENDOSCOPIC APPROACH AND SKULL BASE RECONSTRUCTION

History

Jho and Carrau's first description of their fully endoscopic endonasal technique utilized a single nostril, single surgeon approach with an endoscope holder in the majority of cases.[49] They noted the steeper learning curve associated with the technique and also the frustration an inexperienced surgeon may have with two instruments consistently striking each other in a small enclosed area. Kassam *et al*. advocated for the bimanual-binasal, two surgeon technique to overcome this drawback of the single nostril approach especially in cases of expanded endoscopic approaches.[54] This improved freedom of movement facilitated the ability to treat surgical pathology outside the sella. However, with the forthcoming expanded EEAs, the need to prevent problematic postoperative cerebrospinal fluid (CSF) leaks through large dural openings by reconstructing the skull base floor became readily apparent.[56] In 2006, Hadad *et al*. described using the septal mucosa as a rotational flap based off of the posterior nasoseptal artery branches to reconstruct the skull base and concluded that it "resulted in a sharp decrease in the incidence of postoperative CSF leaks after expanded endonasal approaches."[40] Soon after, Rivera-Serrano *et al*. described the "rescue" flap, in which the vascular pedicle of the nasoseptal flap, which may otherwise be injured during sphenoidotomy, is preserved without the need to raise an entire flap at the beginning of the case.[84] The need to preserve the posterior septal artery branches that this article addressed exemplifies an important principle in modern expanded endonasal approaches: A viable salvage plan for skull base reconstruction is a prerequisite to undertaking an operation in which a CSF leak may be encountered.

Approach

In our center, we utilize a bimanual-binasal, two surgeon technique for all endonasal surgeries. All operations are performed using neuronavigation with face mask registration (Stryker Inc, Kalamazoo, Michigan, USA).[75] For the majority of the procedure, a 0-degree 4 mm rigid endoscope is used for visualization. However, 30° and 45° endoscopes should also be available and are very useful at various stages of the procedure particularly for lateral and suprasellar visualization. Additionally, with the use of newer high definition and enhanced video processing technology (e.g. 'HD Image 1 Spies' system, Karl Storz-America: El Segundo, California, USA) visualization may be further enhanced.

The initial transnasal approach is performed by a single surgeon, usually an otolaryngologist with skull base endoscopic experience, by out-fracturing the middle and inferior turbinates bilaterally. The right middle turbinate is usually preserved to maintain endonasal physiologic function but in select rare cases removal is performed to facilitate movement of instruments and expose more lateral pathology. If a high flow CSF leak is expected, a full nasoseptal flap is raised at the beginning of the operation and placed in the nasopharynx during the main portion of the operation. Some centers raise a unilateral "rescue" flap and sacrifice the contralateral posterior nasoseptal pedicle prior to performing sphenoidotomies. A modification of the "rescue" flap may be made by placing the horizontal cut lower along the septum to spare the olfactory fibers within the superior strip of septum. We recently published a technique in which we perform bilateral olfactory fiber sparing modified "rescue" flaps in cases when a CSF leak is not expected. This technique preserves both posterior septal artery pedicles and promotes rapid healing while reducing the incidence of postoperative epistaxis and olfactory dysfunction.[39] Olfaction has been identified as a major determinant of quality of life,[8] which this technique ensures in the great majority of cases. After the "rescue" flaps have been raised, large posterior sphenoidotomies are created to provide access the sphenoid sinus. The posterior septum is then removed to create a single posterior working corridor for the surgical instruments. Depending on anatomical variations, removal of sphenoid septations and posterior ethmoidectomies are variably performed to widen the exposure to sellar face. The internal carotid arteries are then identified with neuronavigation and confirmed with Doppler ultrasonography for a flow signal.[24] At this time, the dual surgeon technique is employed with one surgeon "driving" the endoscope and irrigating with warm saline to clean the endoscope lens and operative field, and the other surgeon utilizing a bimanual technique to perform the necessary bone drilling and removal followed by the main portion of the surgery. After the primary goal of surgery has been accomplished, skull base reconstruction may be performed in a single surgeon or dual surgeon fashion.

Reconstruction

High rates of postoperative CSF leakage following initial expanded endonasal approaches lead to the trials of several multilayered closure techniques[56,73,80] and was modified to incorporate the nasoseptal flap after its advent.[40,70] At our center, we frequently perform multi-layer closure. The composite of the closure is primarily dependent on the dead space created by the surgery and intraoperative CSF leak grade. In cases of a small dead space and no CSF leak, the dead space is filled with a small piece of collagen sponge followed by a larger piece of collagen sponge over the dural opening. This may be secured in place with fibrin glue or an autologous bone graft fitted in the epidural space to act as a buttress. In cases of small dead space and a low flow CSF leak, the above closure technique may be used with a possible autologous abdominal fat graft to plug any dural hole seen or between the layers of the collagen sponges. In cases of a large dead space created after the resection of a large tumor, we frequently obliterate this space with autologous fat obtained from the abdomen. This fat may be covered with a large collagen sponge if there is no CSF leak or a low flow CSF leak is present and a vascularized flap if a high flow CSF leak is present. If a flap is used, it is buttressed with Merocel packs (Medtronic, Inc., Minneapolis, Minnesota, USA) for 5 days. Recently, Koutourousiou *et al.*[66] reviewed 103 posterior fossa cases in which a transclival EEA was utilized and found a 13.6% incidence of postoperative posterior fossa changes including ventral pontine displacement. They found that all patients who developed these changes had undergone greater than 50% of the clival resection and use of a fat graft was the single significant factor that prevented pontine dislocation ($P = 0.02$).[66]

Since its advent, the nasoseptal flap has become the work-horse for skull base reconstruction following expanded EEAs. Its centralized vascular pedicle and large surface area makes it ideal for coverage of nearly all central skull base defects. However, in some patients, the nasoseptal flap may not be an option because of prior surgery or involvement of the flap by tumor. In cases of an anterior fossa defect, the endoscopicaly harvested pericranial flap[92] and anteriorly based lateral nasal sidewall flap[41] have been described. For small planum and anterior skull base defects, the middle turbinate flap may be used.[82] For larger transplanum defects, the posterior pedicle lateral nasal wall flap was recently described.[84] Smaller clival defects may be covered by an inferior turbinate flap and larger defects may be reconstructed with a tunneled temporoparietal fascia flap.[81] These flaps play a crucial role in the rhinologists and neurosurgeons' armamentarium when the nasoseptal flap is unavailable.

INDICATIONS AND OUTCOMES OF THE FULLY ENDONASAL ENDOSCOPIC APPROACH BY PATHOLOGY

Pituitary adenomas

Pituitary adenomas are the third most common intracranial neoplasm in adults after gliomas and meningiomas.[79] At most centers performing endoscopic endonasal skull base surgery, pituitary adenomas are the most frequent skull base pathology treated. The utility of the endoscope versus the microscope is still being studied. At our center, we assessed if the endoscope provided additional value to microscopic endonasal pituitary surgery.[76] We found that use of the endoscope following maximal microscopic resection in 140 patients allowed for additional tumor resection secondary to endoscopic identification in 36% of cases. In subset analysis, the endoscope provided further identification of tumor leading to additional resection in 54% of cases with tumors greater than 2 cm and 57% of cases with cavernous sinus invasion. Similarly, Komotar *et al*.[61] reported a greater rate of gross total resection (GTR) in the endoscopic cohort of as systematic literature review assessing the endoscope versus the microscope in patients undergoing transsphenoidal surgery for giant pituitary macroadenomas (tumors measuring greater than 40 mm). The endoscopic cohort also had better rates of visual improvement and a lower incidence in postoperative CSF leaks.[61]

Interestingly, a recent study published by Dallapiazza *et al*.[20] reviewing concurrent endoscopic and microscopic transsphenoidal surgeries at a single institution for nonfunctioning adenomas with no cavernous sinus invasion, or cavernous sinus invasion limited to the medial limit of the cavernous carotid arteries, found no significant difference in the rate of GTR, postoperative CSF leakage, and postoperative new transient or permanent endocrinopathy. Patients who underwent endoscopic surgery did have a significantly shorter hospitalization than patients who underwent microscopic surgery (2.4 vs. 3.0 days, $P = 0.04$). Within sub-group analysis of tumors with cavernous sinus invasion, there was no difference in GTR rate between endoscopic and microscopic groups.

Dallapiazza *et al*.[21] assessed the long-term (greater than 5 years follow-up) outcomes in 80 patients who had undergone endoscopic transsphenoidal surgery for nonsecretory pituitary adenomas. GTR was achieved in 71% of patients, and long-term progression-free survival was 80% at 10 years in this cohort. Among the patients who did not have GTR, progression-free survival was 21% at 10 years. Risk factors for tumor progression were preoperative visual deficits and higher Knosp grades, which measure the extent of cavernous sinus invasion. Persistent new diabetes insipidus requiring medication was found in 6% and persistent new hypocortisolism in 7.5%. Major postoperative complications included postoperative CSF leaks in 2.5%, and carotid artery injury in 1.3%. The authors concluded that the incidence of tumor recurrence and progression were similar to microscopic surgical series with long-term follow-up.

Regarding functional adenomas, a recent paper by Starke *et al*. retrospectively reviewed a series of 113 patients treated by a fully endoscopic removal versus microscopic removal of a growth hormone secreting adenomas by two experienced pituitary surgeons.[88] The overall remission rate was 70% and was significantly higher for microadenomas versus macroadenomas (87% vs. 66%, respectively) regardless of which technique was used. No significant superiority in terms of remission rate was found for either technique. Endoscopic surgery was associated with higher rates patient-reported sinusitis and alteration in sense of smell or taste. Similarly, another study assessing endoscopic versus microscopic transsphenoidal surgery for Cushing disease found no significant difference in rates of remission or major perioperative complications.[2]

At this time, one can conclude the results from the endoscopic transsphenoidal surgical technique for pituitary adenomas is comparable to microscopic transsphenoidal surgery for the majority of endocrine-active and endocrine-inactive adenomas. The benefit of the endoscope may be for macroadenomas over 2 cm in maximal diameter and those with significant lateral and/or suprasellar extension: Areas for which the

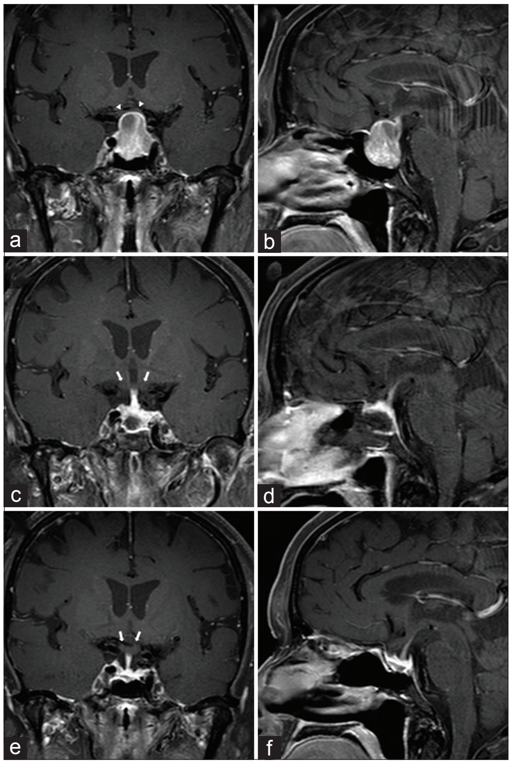

Figure 1: A 71-year-old female who developed progressive vision loss in the left eye over 6 months. Because of her worsening vision she underwent a brain MRI with gadolinium (a and b) revealing a 24 × 19 × 16 mm sellar mass with suprasellar extension. The chiasm was markedly compressed (white arrowheads). The normal gland was thinned and pushed superiorly toward the right. Formal neuro-ophthalmologic visual field testing confirmed severe global decreased acuity in the left eye, and a superior temporal quadrant defect in the right eye. Her preoperative prolactin level was 41.5 ng/ml indicating the tumor was not a prolactinoma. The patient underwent endonasal endoscopic tumor removal. The patient's immediate postoperative MRI (c and d) and 1 year postoperative MRI (e and f) revealed a GTR of the tumor and decompression of the optic apparatus (white arrows)

microscope has limited visualization. Such a case is demonstrated by [Figure 1], in which a large adenoma with significant suprasellar extension was completely removed utilizing a fully EEA.

At our center, most pituitary adenoma patients are hospitalized for 1–2 nights depending on the extent of the procedure and have outpatient neurosurgical follow-up and their first nasal debridement at 7–10 days after surgery. They then typically have two additional nasal debridements at 2-week intervals and magnetic resonance imaging (MRI) at 3 months. Additional MRI and clinical follow-up are typically completed at 6 months or 12-month intervals to monitor for possible tumor recurrence or progression. All patients also have follow-up pituitary hormonal testing typically within 4–6 weeks of surgery and long-term endocrinology follow-up is arranged depending upon perioperative pituitary hormonal function and tumor subtype.

Craniopharyngiomas

Craniopharyngiomas represent the second most common neoplasm in the sellar/suprasellar region after pituitary adenomas.[11,79] Although considered benign, surgical resection is made particularly difficult by their potentially calcified nature, close proximity and tendency to tightly adhere to the optic nerves, infundibulum, hypothalamus, pituitary gland, small perforating vessels and larger local vessels. As such, aggressive resection carries significant risk of causing neurologic morbidity.[42] Even after GTR, recurrence rates range from 7% to 50% in modern studies with over 5 years mean follow-up.[26-28,83,93] On the other hand, higher recurrence rates after subtotal resection[11,28,93] and potential long-term risks of adjuvant radiation make management particularly challenging, especially in the pediatric population.

Both transcranial[37,38,91] and transnasal[12,50,63,69,71] techniques have been described for surgical approaches. Zygourikas *et al*. reviewed their single institution experience with craniopharyngiomas utilizing various surgical approaches including unilateral craniotomy, bifrontal craniotomy with subfrontal approach, and transsphenoidal approaches, and found patients undergoing craniotomies to be 1.5 times more likely to develop complications such as hematoma, stroke, or wound infection, but no correlation between surgical approach and outcome at last visit.[93] On the other hand, microscopic transnasal approaches are often limited in terms of visualizing lateral extensions of tumor and deeper seated portions of tumor because of the narrow surgical corridor and the loss of light intensity at required higher magnifications, respectively. This has led some to adopt an EEA for these lesions.[19,36]

Recently, two larger case series have demonstrated the efficacy of the EEA for treatment of craniopharyngiomas.[11,67] In their review of 64 patients treated with the EEA at a single institution, Koutourousiou *et al*. showed a GTR rate and near total removal rate of 37.5% and 34.4%, respectively. Visual improvement was achieved in 86.4% of patients with preoperative visual disturbance. The most common complication following surgery was CSF leak in 23.4% of cases, but the authors reported that the rate had been decreased to 10.6% in recent years after introduction of the vascularized nasoseptal flap in reconstruction.[67] Cavallo *et al*. reported in their series of 103 craniopharyngiomas treated with an EEA a GTR in 68.9% of cases with 74.7% overall improvement in vision.[11]

Komotar *et al*.[60] performed a meta-analysis to compare the efficacy of the EEA to traditional microscopic and open treatments for craniopharyngiomas in 88 studies published between 1995 and 2010 and found higher rates of both GTR (66.9% vs. 48.3%) and improved visual outcome (56.2% vs. 33.1%) in the endoscopic cohorts. Nonetheless, the EEA is limited by certain anatomical and pathological considerations including small sellas with a narrow corridor between the carotid arteries, particularly solid tumors with significant calcifications and multilobulated tumors involving multiple compartments.[18] Furthermore, the relation of the tumor to optic chiasm as described by Hoffman,[45] plays an important part in the ability of the surgeon to achieve a GTR utilizing an EEA. For instance, Cavallo *et al*. found a higher rate of GTR in tumors that were supradiaphragmatic retrochiasmatic (80%) compared with tumors that were pre- and retrochiasmatic (39.1%).[11] Given these considerations, our group reported our experience in selecting an endonasal approach versus a supra-orbital craniotomy for craniopharyngioma resection and found that the EEA afforded good access for tumors with a significant retrochiasmatic component, and the unilateral supraorbital approach was useful for tumors that were pre- or suprachiasmatic lesions or suprasellar/sellar lesions with significant lateral extension.[31] In our view, the endonasal trajectory is naturally suited for tumors arising behind the optic chiasm and extending into the third ventricle [Figure 2], whereas a supraorbital approach may be needed to address tumors with significant pre- or suprachiasmatic components.

Anterior skull base meningiomas

After the experience gained with endonasal endoscopic pituitary surgery, surgeons recognized several theoretical benefits of the EEA for anterior skull base meningiomas: Bilateral access to the tumor, removal of involved hypertrophied bone at the origin site of the tumor, early dural devascularization, and no required brain retraction. Koutourousiou *et al*. recently published the largest single institution series on olfactory groove[65] and suprasellar meningiomas[64] and achieved GTR rates of 66–76%, but found significant rates of CSF leak from

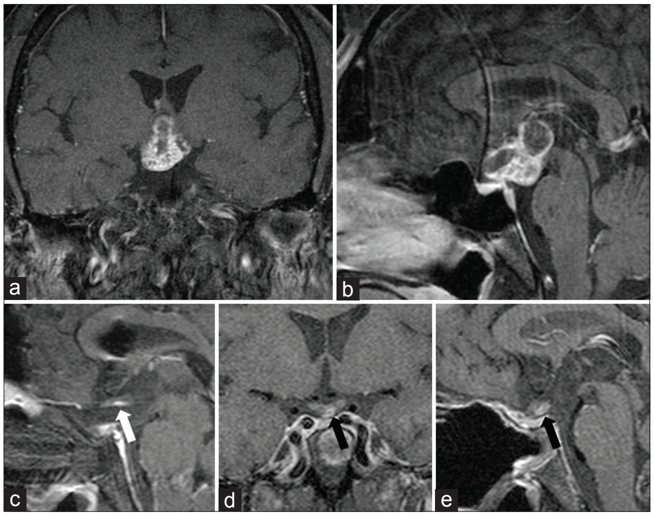

Figure 2: A 52-year-old male who presented with worsening bouts of cold intolerance, 18 kg weight gain over 2 years, fatigue, decreased libido, polyuria, and 6 months of worsening vision. Endocrinological workup revealed central hypothyroidism, hypogonadotropic hypotestosteronism. T1 MRI with gadolinium (a and b) demonstrated a heterogeneously enhancing cystic suprasellar retrochiasmatic mass. The patient underwent an endonasal endoscopic transsellar, transplanum resection of the tumor. The pathology was consistent with craniopharyngioma. The postoperative MRI with gadolinium 1 day after surgery (c) demonstrated near total removal of the tumor with a small amount of tumor purposefully left along the posterior edge of the optic chiasm given its dense adhesions to the optic apparatus (white arrow). MRI with gadolinium 6 months after surgery (d and e) reveals residual tumor along the chiasm that was followed with serial MRIs

25% to 30%. Ottenhausen *et al*. found a similarly high rate of CSF leak in the early part of their series of tuberculum sellae meningiomas treated with EEA,[80] but were able to reduce it to 0% utilizing 24 h of postoperative lumbar CSF drainage and a surgical closure with an onlay fascia lata graft that was buttressed with a countersunk piece of Medpor (Porex, Newnan, Georgia, USA), then covered with a vascularized nasoseptal flap and held in place with Duraseal (Covidien, Dublin, Ireland).[73,80]

Komotar *et al*. performed a meta-analysis of 60 studies published between 2001 and 2010 to assess the EEA versus traditional transcranial approaches for midline anterior cranial fossa meningiomas.[62] Higher rates of GTR were found in the transcranial cohort (84.1% vs. 74.7%) with significantly lower rates of CSF leak (4.3% vs. 21.3%). Slightly higher rates of visual improvement were reported for the endoscopic cohort (69.1% vs. 58.7%), but was not found to be statistically significant. Clark *et al*. performed a meta-analysis specifically assessing the EEA versus open transcranial approaches for tuberculum sellae meningiomas and also found significantly higher rates of CSF leak (21% vs. 5%) but significantly higher rates of visual improvement (87% vs. 59%) in the endoscopic cohort.[15] In their study, no significant difference existed in GTR rates between the endoscopic and open cohorts (88% vs. 87%, respectively). Although both of these meta-analysis have reported higher CSF leaks in the endoscopic cohort of series, which included data from 2002 to 2010, it should be noted that several studies have shown improved rate of CSF with refinement of closure techniques[64,65,80] including the vascularized nasoseptal flap, which only became more widely utilized after its description in 2006.[40]

Based on this information and our own experience [Figure 3], the EEA is likely better suited for smaller midline anterior cranial fossa meningiomas[30] and may have a selective benefit for tumors causing vision impairment.[15] The barriers to achieving a GTR through a purely EEA are tumor size,[64,65] vascular encasement,[64] loss of a cortical cuff,[65] and tumor calcification.[65]

Skull base chordomas

Chordomas are low grade malignant neoplasms that arise from notochordal remnants[7] and predominantly occur in the clivus and the sacrum. Given their high-recurrence rate and local invasiveness to neurovascular structures, these tumors pose a significant challenge in management. Many authors have shown improved rates of progression-free survival with GTR.[3,14,68,86] Improved rates of progression-free survival with adjuvant radiotherapy has also been demonstrated,[16,22,89] however, a superior rate of progression-free survival with GTR and adjuvant radiation compared with subtotal resection and adjuvant radiation[3] have maintained GTR, when safely possible, as the primary mode of treatment. Surgical management via lateral and midline microsurgical approaches have been described.[1,16,17] Although midline approaches afford direct access to the tumor origin in most cases, a benefit in terms of rate of complete removal and progression-free survival has not been demonstrated.[86] Furthermore, in cases of tumors with extensive lateral invasion, a lateral approach may be required to achieve a GTR.[1,68]

For midline approaches, the EEA offers the benefit of better illumination and visualization of tumor in deeper seated areas as well as tumor within the lateral extremes via angled endoscopes over traditional midline microscopic approaches. [Figure 4] illustrates a case in which the EEA was utilized to achieve a near total removal of clival chordoma. Koutourousiou *et al*. reported the largest series of skull base chordomas managed with the EEA.[68] An overall GTR rate of 66.7% was achieved in a group of 60 patients. Notably, a significantly higher GTR rate of 82.9% was achieved in patients without prior surgery compared with 44% in patients previously treated with surgery at other institutions ($P = 0.002$). The EEA was used as the initial approach in all 60 patients; however, in 6 patients, an additional transcranial approach was also needed. Barriers for achieving a GTR were tumor volume greater than 20 cm^3 ($P = 0.042$) and lower clival lesions with lateral extension ($P = 0.022$). Significant complications were CSF leakage (20%), which the authors noted had decreased in recent years with the

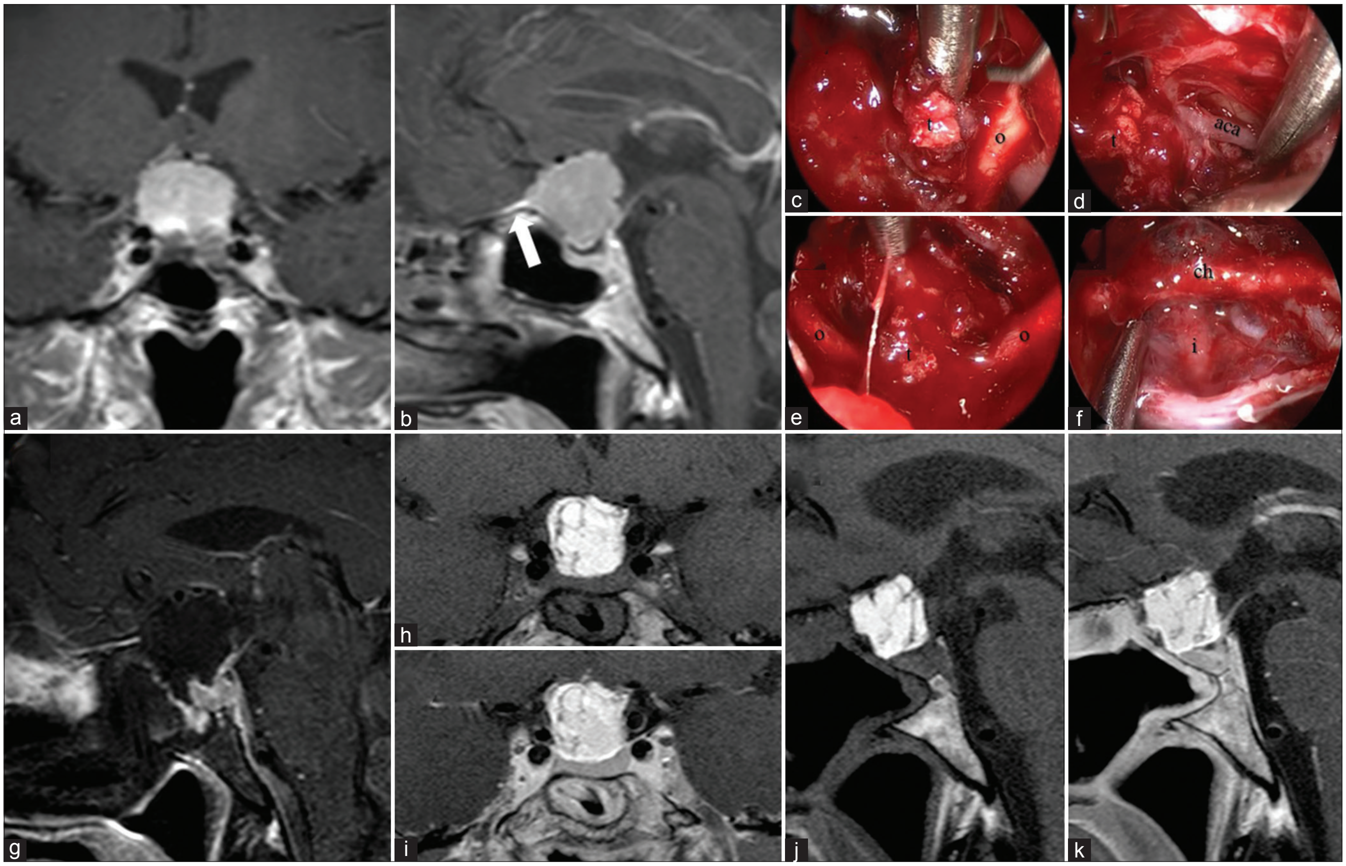

Figure 3: A 65-year-old female with gradual visual deterioration. The preoperative T1 MRI with gadolinium (a and b) demonstrated an extra-axial mass arising from the tuberculum sella dura with dural tail (white arrow). The patient underwent an endonasal endoscopic transplanum, transsellar skull base approach for resection of the mass. Pathology was consistent with a benign meningioma. Intraoperative views (c,d,e,f) of tumor (t) removal with separation away from the optic nerves (o), chiasm (ch), anterior cerebral artery (aca), and infundibulum (i). The immediate postoperative T1 MRI with fat suppression and gadolinium (g) demonstrated a GTR of the tumor. The 3-month postoperative T1 MRI without gadolinium (h and j) and with gadolinium (i and k) demonstrate fat graft in the resection cavity without evidence of tumor recurrence

use of a vascularized nasoseptal flap, new permanent cranial neuropathy (6.7%), and one patient experienced a delayed pontine hemorrhage resulting in lower cranial neuropathy and quadriparesis. Furthermore, the authors assessed the role of experience in obtaining a GTR and noted that in recent years a GTR rate of 88.9% had been achieved compared with 36.4% in early years ($P < 0.0001$) without any significant increase in surgical complications.

In the second largest reported series of chordomas managed with the EEA, Chibbaro *et al*. reported a similarly high rate of overall GTR of 65% in 54 patients, with a GTR rate of 88% in the subset of 32 patients with in newly diagnosed tumors.[14] All patients were treated by the endonasal route, although the authors noted that four patients required an additional operation. One surgical mortality was noted from a delayed rupture of an internal carotid artery pseudoaneurysm. Other significant complications were CSF leak in 8% and meningitis in 14%. No new focal neurological deficits were noted.

Recently, Amit *et al*. completed a meta-analysis to assess the efficacy of different surgical approaches for patients harboring chordomas.[3] The analysis identified 467 patients from 28 published studies and complete individual data was available for compiled data analysis for 165 cases. For open (transcranial) surgery versus endoscopic surgery, no significant difference was found in the 5-year disease specific survival rate (45% vs. 49%, $P = 0.07$), and the progression-free survival rate (94% vs. 79%, $P = 0.11$). Interestingly, the transcranial group had a 20% rate of cranial nerve injury versus a rate of 3.7% in the endoscopic group, although this only trended toward significance ($P = 0.07$). No significant difference was found in rates of CSF leakage or endocrine disorders among the transcranial and endoscopic groups.

Based on these studies, the EEA provides an efficacious surgical management for patients with skull base chordomas with high rates of GTR in experienced hands. Given the relatively modern application of this approach, studies with long-term assessment of disease-free survival and overall survival will be needed to properly compare them with more traditional open surgical approaches. Nonetheless, in cases of large tumors and tumors with

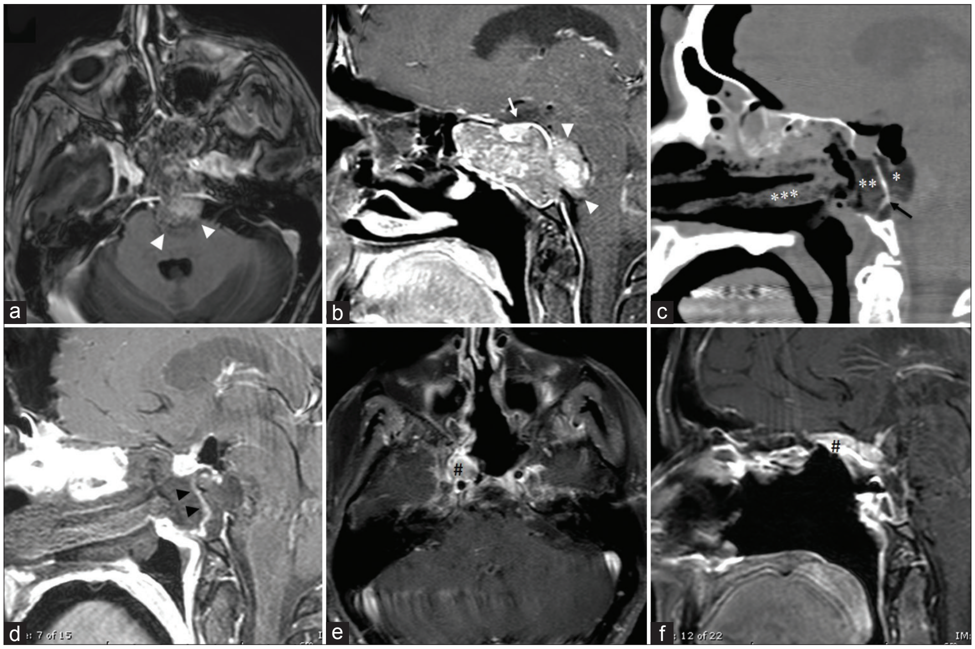

Figure 4: A 61-year-old female who presented with headaches. Her MRI with gadolinium (a and b) revealed a sphenoclival mass with preservation of sellar contents (white arrow) and intradural invasion and compression of the brain stem (white arrowheads). The patient underwent a transsphenoidal, transclival EEA for resection of the tumor. The pathology was consistent with chordoma. A postoperative CT (c) was completed immediately after surgery to assure no dislodgment of her multilayered skull base reconstruction with intradural fat graft (*), bone (black arrow), extradural fat graft (**), and right nasoseptal flap, which were buttressed with Merocel packs (***). Fat suppression T1 MRI with gadolinium was completed on postoperative day 1 (d) with clear enhancement of the nasoseptal flap (black arrowheads). Her fat suppression MRI with gadolinium 3 months after surgery (e and f) demonstrate no definitive tumor enhancement. The enhancement along the right posterior and superior nasal cavity (#) is consistent with the right nasoseptal flap enhancement

significant lateral extension, both an EEA and lateral approach may be needed to properly manage these tumors and achieve a GTR.

FUTURE ENDEAVORS

Three-dimensional neuroendoscopy

A notable limitation of current neuroendoscopy has been the loss of three-dimensional (3D) visuospatial orientation and depth perception with standard endoscopes. Although this can be recreated with dynamic movement of standard endoscopes, it may in part account for the significant learning curve when transitioning from a microscopic to a fully endoscopic technique. With laparoscopic surgery, earlier 3D endoscopes were noted to help with improved depth perception but were also associated with more vision strain and headaches over conventional endoscopes.[13,43] Currently, one 3D system (VisionSense 3D, VisionSense Corp., Orangeburg, New York, USA) is commercially available for endonasal endoscopic use. Kari *et al.* retrospectively compared this system in a small cohort of patients with a standard endoscope for routine pituitary surgery and found no significant difference in surgical time, estimated blood loss, and postoperative complications.[51] A preference was noted by the senior neurosurgical author for utilizing the 3D endoscope for tumor resection, where it allowed for a better subjective assessment of multiple tissue layers and appreciation of the neurovascular relation. A more significant, and harder to assess advantage of the 3D endoscope may be for the novice surgeon transitioning to neuroendoscopy after training with a surgical microscope. In a study of surgeons with limited neuroendoscopic experience, task performance was assessed in a skull base model utilizing 3D endoscopes, standard definition endoscopes, and high definition endoscopes.[72] Time to task completion was significantly shorter in the 3D endoscope group (P = 0.001). Barkhoudarian *et al.* compared 3D endoscopic and two-dimensional high definition endoscopic resection of pituitary tumors at an academic teaching hospital with residents and fellows. They noted that there was significant decrease in surgical time for similarly sized adenomas with the 3D endoscope (174 vs. 147 min, P = 0.03).[5] One may extrapolate that this difference may help partially with overcoming the learning curve associated with the learning endoscopy. Notable disadvantages of the 3D endoscope are a sense of disequilibrium for some users and significant red saturation variations in which a minute amount of blood on the camera lens may disrupt the color balance and image clarity.

Malleable endoscopes

A common problem experienced by many surgeons is the collision of the endoscope with surgical instrumentation resulting in limited surgical freedom. Although with experience this problem is surmountable, frustration and inadvertent collision with the endoscope during a critical surgical moment has potential for resulting in a significant complication. Sources for collision of the surgical instrument with the endoscope are extranasaly at the site of the camera head and light cord, within the nasal cavity along the shaft of the endoscope, and at the tip of the endoscope. A further source of limited surgical freedom occurs when advancement of endoscope for visualization of deeper structures results in the camera head, lighting cord, and hand of endoscope driver obstructing the movement of lead surgeon's hands. Malleable endoscopes offer the potential advantage of reducing surgical collision by adjusting the camera head out of the way from entrance of the nasal cavity. Elhadi *et al*. assessed surgical freedom of the VisionSense 3D malleable endoscope with the VisionSense 3D rigid endoscope utilizing a cadaver model.[25] The malleable endoscope measures 4.7 mm in diameter compared with the 4.9 mm rigid endoscope, retains its shape after initially bent, and produces the same quality of image as its rigid counterpart. Elhadi *et al*. demonstrated significantly improved surgical freedom utilizing both uninostril and binostril techniques. Furthermore, they noted that surgical collisions were diminished at two points: The extranasal entry zone and at the tip of the endoscope since this could be displaced by surgical dissectors and then return to position given the memory property of malleable metal. One limitation of the malleable endoscope was noted during initial surgical approach when precise movements of the surgeons hand did not translate to the tip movement. Currently surgeons utilize various surgical techniques to improve surgical freedom such as selective middle turbinectomy and binostril technique. A potential unstudied advantage of the malleable endoscope may be in reducing the extent of surgical dissection currently needed to accommodate the rigid endoscope.

CONCLUSION

Significant advances over the past two decades in imaging technology, surgical instrumentation, skull base anatomical knowledge, and reconstructive techniques have resulted in the extended EEA becoming an integral part of the modern skull base surgeon's armamentarium. With growing use and greater experience, surgical outcomes continue to incrementally improve across many skull base pathologies, both benign and malignant. However, the importance of the learning curve in endoscopic surgery and use of a multi-disciplinary approach cannot be over-emphasized. As with any new surgical tool and technique, a firm foundation built on basic surgical technique and anatomical knowledge should be obtained prior to advancing to more complex surgical approaches and pathology. Additionally, realizing the limits of the endonasal approach and the reasonable use of transcranial approaches is critical. Finally, understanding the indications for radiosurgery, stereotactic radiotherapy, and medical treatment options within the treatment armamentarium for skull base pathology is also essential to optimize outcomes and reduce risk of surgical complications.

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