SKULL BASE SURGERY (CH SYNDERMAN AND EW WANG, SECTION EDITORS)

# Quality of Life Outcomes and Approach-Specific Morbidities in Endoscopic Endonasal Skull Base Surgery

Nicholas R. Rowan<sup>1</sup> · Debraj Mukherjee<sup>2</sup>

Published online: 19 March 2020 © Springer Science+Business Media, LLC, part of Springer Nature 2020

#### Abstract



**Purpose of Review** Endoscopic endonasal skull base surgery (EESBS) has many advantages compared with traditional approaches. Recently, there is an increasing focus on patient-centered, quality of life (QOL), and approach-specific outcomes. This review seeks to illuminate our current understanding and knowledge gaps in EESBS-specific QOL outcomes.

**Recent Findings** In an effort to capture the most relevant QOL implications for patients undergoing EESBS, three comprehensive, validated, QOL instruments have been created. These instruments are often supplemented by sinonasal-specific outcome measures, given the potentially significant sinonasal repercussions incurred with the use of the endonasal corridor. To date, most EESBS QOL investigations include patients with sellar-based pathology, though series with patients undergoing more extensive approaches are emerging.

**Summary** Generally, patients experience transient postoperative worsening of skull base– and sinonasal-specific QOL. Larger series, with validated QOL outcome measures, are needed to better understand patient outcomes and the morbidities of EESBS, especially those that relate to olfaction and surgery beyond the sella.

Keywords Skull base · Quality of life · Sinonasal morbidity · Endoscopic endonasal skull base surgery · Olfaction · Pituitary

# Introduction

Over the past 2 decades, the combination of technological advancements, improved endoscopic techniques and surgeon comfort, has made the utility of endoscopic endonasal corridor for a variety of skull base pathologies commonplace. The advent of endoscopic endonasal skull base surgery (EESBS) has afforded surgeons and patients many benefits; including similar, if not improved surgical outcomes, improved

This article is part of the Topical Collection on Skull Base Surgery

Nicholas R. Rowan nrowan1@jhmi.edu

Debraj Mukherjee dmukher1@jhmi.edu

- <sup>1</sup> Department of Otolaryngology-Head and Neck Surgery, The Johns Hopkins University School of Medicine, 601 N Caroline St, Suite 6164, Baltimore, MD 21287, USA
- <sup>2</sup> Department of Neurosurgery, The Johns Hopkins University School of Medicine, 600 N Wolfe St, Phipps 124, Baltimore, MD 21287, USA

intraoperative visualization, decreased perioperative complications, and decreased postoperative length of stay as compared with traditional approaches [1–4]. In light of these advances, along with the proximity of skull base pathologies to critical anatomical structures, and the fact that many skull base pathologies are benign, there is an increasing focus on quality of life (QOL) outcomes in skull base surgery and in surgical decision-making.

Despite the many advantages of EESBS, the use of the endonasal corridor introduces unique morbidities and quality of life (QOL) perturbations not experienced by patients undergoing, traditional, transcranial surgery. In particular, accompanying the inherent risk to sinonasal structures with this approach, patients undergoing EESBS are at risk for a variety of sinonasal-related morbidities with a potentially profound impact on patient QOL. In an effort to elucidate the impact of EESBS on patient QOL, several authors have created comprehensive, skull base-specific QOL instruments [5••, 6••, 7••, 8••]. Nonetheless, these instruments are not universally adopted, and oftentimes, rhinologic-specific QOL questionnaires with intrinsic shortcomings for this patient population, are used to assess the influence of EESBS on patient QOL instead [9••].

Overall, though there is increasing recognition of the QOL implications and morbidities incurred for patients undergoing EESBS, there continue to be substantial shortcomings in our understanding. As such, this report will first review some of the instruments available for QOL assessment in patients undergoing EESBS. Next, we seek to illuminate unique sinonasal consequences and sinonasal-specific outcomes associated with EESBS. Finally, we will review morbidities of specific EESBS approaches and surgical techniques.

# Measurement of Skull Base–Specific QOL Outcomes in EESBS

The importance of health-related QOL outcomes is increasingly recognized. In patients undergoing EESBS, the proximity of an oftentimes benign pathology to critical neurovascular structures must be considered in shared surgical decision-making and patient counseling, given the potentially profound morbidities of these surgeries. Surgeons and patients alike should consider the extent of tumor resection and surgical complications, as well as a variety of other clinical outcomes including visual, hormonal, and sinonasal consequences. Moreover, QOL instruments should further characterize outcomes with additional physical, psychosocial and cognitive domains [10].

A variety of tools exist for measuring patient QOL in EESBS, ranging from symptom-specific or skull base– specific instruments to generalized QOL measures. Disease-, or skull base–specific QOL is particularly important in this patient population given the wide variety of skull base pathologies, as well as the range of potentially involved anatomical structures. Meanwhile, symptom-specific instruments, in particular those that assess sinonasal QOL, are paramount in assessing approach-related morbidities and will be reviewed in a forthcoming section. An ideal, comprehensive, QOL instrument should also incorporate aspects of general health outcomes. Currently, several comprehensive EESBS QOL instruments exist.

#### Anterior Skull Base Questionnaire

The Anterior Skull Base Questionnaire (ASBQ) was the first skull base, site-specific QOL instrument. This tool is a validated, multidimensional, site-specific instrument with high internal consistency and test-retest reliability that was created in a cohort of patients with malignant pathologies who had undergone traditional, open approaches [5••]. The ASBQ was then later validated in a population of patients with both benign and malignant pathologies who underwent EESBS [11]. This questionnaire includes six domains: performance, physical function, vitality, pain, specific symptoms, and influence on emotions. There are 35 questions in total, each with a Likert scale of 1 to 5, with 5 representing the highest quality of life, and a total possible score of 175. This instrument has 7 disease-specific questions and 3 questions that relate to sinonasal functioning. The ASBQ benefits from a defined minimal clinically important difference (MCID), defined as a change of 0.4 [12].

#### **Skull Base Inventory**

Next, the Skull Base Inventory (SBI) was developed in 2012 in an attempt to incorporate additional disease-specific items. The SBI is a multidimensional, disease-specific instrument created for patients with both benign and malignant pathologies of the anterior and central skull base, undergoing open or endoscopic approaches [6..]. The instrument consists of 41 total questions, with Likert scale responses ranging from 0 to 6, for a total possible score of 246 with lower scores representing worse QOL. The questionnaire contains 26 disease-specific items and includes 11 specific domains including social, emotional, physical, cognitive, family, financial, spiritual, endocrine, nasal, neurologic, and visual, which demonstrate some differences in the degree of internal consistency. Though the instrument has excellent content validity and follow-up psychometric testing including cross-sectional validity and reliability was demonstrated in 2016, this instrument has yet to be broadly adopted [13].

# Endoscopic Endonasal Sinus and Skull Base Surgery Questionnaire

Most recently, the Endoscopic Endonasal Sinus and Skull Base Surgery Questionnaire (EES-Q) has been proposed as a comprehensive tool for the measurement of health-related QOL in patients with skull base and sinonasal pathology [7••]. The EES-Q is a multidimensional, disease-specific instrument with 3 domains: physical, psychosocial, and social functioning. The instrument has excellent consistency, is validated, and reliable [7.., 14]. It consists of 30 total questions, answered on a 5-choice Likert scale, and has significant positive correlations with the 22-item Sino-Nasal Outcome Test (SNOT-22) and a well-accepted, validated, general healthrelated QOL measure. Similar to the SBI, this instrument has yet to be widely adopted. It is worth noting that the EES-Q was defined in a patient population somewhat different than both the ASBQ and SBI, including almost entirely patients with benign pathology and a subset of patients undergoing limited functional endoscopic sinus surgery for chronic rhinosinusitis.

A summary of the above measures is listed in Table 1. Each instrument presents its own set of advantages and disadvantages. Moreover, though multiple authors have attempted to quantify both disease-specific and general QOL outcomes in patients undergoing EESBS, relatively few studies have utilized these EESBS-specific instruments. The most rigorous investigations have been performed in patients with pituitary

Instrument	Target (defined) patient population pathology	Target (defined) surgical approach	Domains	Type of questionnaire	Number ] of items	Number Interpretation of items	Advantages and disadvantages
Anterior Skull Base Questionnaire (ASBQ)	Malignancy of anterior skull base <sup>a</sup>	Open, transcranial approach <sup>a</sup>	Performance, physical function, vitality, pain, specific symptoms, influence on emotions	5-item Likert questionnaire	35	Higher score corresponds to improved QOL	Advantages: - Most widely used comprehensive instrument - Defined MCID Disadvantages: - Originally defined in patients undergoing open surgery for malignancy - Only 3 questions that directly relate to sinonasal functioning
Skull Base Inventory (SBI)	Benign and malignant pathology of anterior and central skull base	Open and endoscopic approaches	Social, emotional, physical, cognitive, family, financial, spiritual, endocrine, nasal, neurologic, visual	7-item Likert questionnaire	41	Higher score corresponds to improved QOL	Advantages: - Designed for patients with open or endoscopic approaches - 26 disease-specific items - Additional psychometric testing planned Disadvantages: - Not broadly used despite being originally defined 8 years previously
Endoscopic Endonasal Sinus and Skull Base Surgery Questionnaire (EES-Q)	Benign and malignant <sup>b</sup> anterior skull base and paranasal sinus pathology	Endoscopic endonasal surgery	Physical, psychosocial, social functioning	5-item Likert questionnaire	30	Higher score corresponds to worse QOL	Advantages: - Easy to use - Corresponds well with other QOL measures (sinonasal and general) Disadvantages: - New; not broadly used - Limited description in patients with malignancies or more involved skull base approaches

 Table 1
 Comparison of EESBS-specific QOL instruments

<sup>a</sup>Later validated in patients undergoing endoscopic endonasal skull base surgery with combination of benign and malignant pathology

 $^{\rm b}$  Less than 5% of total population with malignant skull base or paranasal sinus pathology

QOL, quality of life; MCID, minimal clinically important difference

pathology. Approach- and disease-specific QOL outcomes using these metrics will be reviewed in the ensuing sections.

# Measurement of Sinonasal QOL Outcomes in EESBS

The sinonasal morbidities of EESBS have long been recognized [15–17]. Direct surgical insults to the sinonasal corridor and alteration of sinonasal anatomy may result in a variety of sequelae including, but not limited to, nasal crusting, nasal obstruction, anosmia, rhinosinusitis, mucocele formation, and cosmetic deformities. Of note, the importance of olfaction cannot be overstated, and is an included item in all OOL instruments detailed in this current report; it is increasingly studied [18, 19•, 20•, 21]. Beyond the obvious important qualities of olfaction, such as the ability to detect potential health hazards (e.g. fire), or create social awareness (e.g., perceive body odor), olfactory dysfunction itself can result in significant health impacts, substantially affecting overall wellbeing and QOL [22-24]. Two rhinologic-specific instruments are commonly used to measure sinonasal QOL outcomes in the EESBS patient population.

The most common instruments used to assess sinonasal QOL is the SNOT-22. Though this instrument has not been validated in the EESBS patient population and has inherent shortcomings of its use, the robustness, reliability, and familiarity of this instrument in the rhinologic community has made this tool an intuitive choice to serve as an indicator of sinonasal-specific symptomatology and QOL. The SNOT-22 questionnaire is composed of 22 questions presented on a Likert scale, scored from 0 to 5, with a maximum possible score of 110 and higher scores representing a more severe impact on sinonasal QOL [25]. This instrument is robust and benefits from wide use, an established MCID, comparative control data, and subdomain scores (rhinologic, extranasal rhinologic, ear/facial symptoms, and psychological and sleep dysfunction) [26, 27].

In addition to the SNOT-22 questionnaire, the Anterior Skull Base Nasal Inventory-12 (ASK Nasal-12) is a validated, site-specific, unidimensional rhinologic outcome tool sensitive to clinical change examining the effect of EESBS on nasal-related morbidities [8••]. It has both symptom and sensory subdomains, and a total of 12 questions. Each question includes a 6-point Likert scale ranging from 0 (no problem) to 5 (severe problem). The ASK Nasal-12 score is reported as a mean of all 12 equally weighted items, thus a total score ranging from 0 to 5. Though this metric benefits from simplicity and rigorous validation, an established MCID, and is EESBS-specific, it has not been extensively reported in the literature [28].

# Sinonasal Morbidities and QOL Outcomes in EESBS

Many studies have attempted to quantify the impacts of EESBS on sinonasal QOL [29–32, 33•, 34, 35]. Though these studies provide meaningful QOL data, they are limited by variable study size, mixed pathologies, and different QOL instruments. The first studies to detail sinonasal morbidities of EESBS emphasized the incidence of nasal crusting, nasal drainage, nasal obstruction, and septal perforations [15–17, 36]. Rates of nasal crusting and nasal drainage have been reported as high as 98% and 46% respectively, whereas published rates of septal perforations in the setting of nasoseptal reconstruction range from none to 14% in the largest series [17, 37–39].

Over time, along with the creation of validated QOL measures and larger patient cohorts, comprehensive data collection has improved the understanding of the durability of these postoperative changes. The Cornell group has several studies that specifically examine sinonasal QOL outcomes in the EESBS population [32, 33•, 40]. The study by McCoul et al. prospectively demonstrated a transient decrease in sinonasal QOL, but no significant long-term sinonasal QOL sequelae [33•]. Several other studies corroborate the findings of relatively transient nasal morbidities following EESBS, most of which include predominantly pituitary pathology [18, 41–45]. Though debated, and some conflicting reports exist, a more extensive surgical approach may not necessarily correlate with worse sinonasal QOL outcomes [18, 46•].

In an effort to comprehensively analyze sinonasal-specific QOL following EESBS, a recent systematic review with metaanalysis reviewed 19 unique studies with a total of 1025 patients with SNOT-22 questionnaire outcome data [9...]. This robust analysis demonstrated temporary worsening of sinonasal QOL at 1 month postoperatively in all patients undergoing EESBS, followed by statistically significant improvements in SNOT-22 scores at 6- and 12-months postoperatively, beyond baseline scores. The authors also demonstrate that whereas patients who are asymptomatic preoperatively do not experience long-term negative impacts, patients with worse preoperative sinonasal QOL demonstrate significant and sustained improvements in SNOT-22 scores as early as 12-weeks postoperatively, and continue through long-term follow-up. Finally, patients with intracranial pathology were compared with those with intranasal pathology. While both populations experienced improvements in SNOT-22 scores by 3-months postoperatively, patients with intranasal pathology had stability in scores thereafter, while patients with intracranial pathology experienced continued improvement.

Beyond broad sinonasal outcomes, olfactory dysfunction is one of the most potentially disruptive sinonasal-specific morbidities of EESBS. Patients with disruptions in their ability to smell, commonly experience weight loss, decreased social interaction, and are at increased risk for major depressive disorder and generalized anxiety [47–50]. Olfactory dysfunction has been directly associated, in a "dose-dependent" fashion with increases in all-cause mortality, reduced overall QOL, productivity, and even cognitive function [51–54].

The degree of olfactory dysfunction experienced by EESBS likely directly correlates with the amount of disease or surgical involvement of the olfactory tract. While a transsellar approach that preserves the olfactory mucosa is less likely to result in severe, permanent olfactory dysfunction, pathology directly involving olfactory structures, such as olfactory groove meningioma or esthesioneuroblastoma, are more likely to result in permanent anosmia [19•, 55-57]. Several studies have attempted to quantify the impact of EESBS on objective olfactory function, most of which include patients with sellar or parasellar pathology. The results of such studies are variable and oftentimes use somewhat abbreviated olfactory testing, which fails to detail both the extent and mechanism of the olfactory insult [18, 19•, 20•, 58•]. The recent report by Griffiths et al. suggests that in a population of patients with predominantly pituitary or other sellar pathology, a small percentage of patients (5.5%) of patients will have objective postoperative hyposmia, but olfaction is generally maintained in the setting of superior olfactory strip preservation [20•].

# Morbidities of Specific Approaches and Surgical Techniques

#### **Sellar and Parasellar Region**

As noted above, several mostly transient sequelae, such as nasal crusting and discharge, may be observed following EESBS for lesions of the sella and parasellar region. Suberman et al. reported no significant long-term detriment in sinonasal QOL among a single-center series of 50 patients undergoing EESBS for pituitary adenomas with an average follow-up of 24 months [59]. McCoul et al. demonstrated transient worsening in ASBQ and SNOT-22 scores in 81 pituitary adenoma patients at 3 weeks postoperatively; starting at 12 weeks postoperatively, SNOT-22 scores normalized to their preoperative baseline while ASBQ improved beyond their preoperative baseline [33•]. In a larger, multi-institutional series of 100 postoperative pituitary adenoma patients, Little et al. found sinonasal QOL to nadir at 2 weeks with recovery at 3 months following EESBS [42].

Beyond pituitary adenomas, postoperative QOL among patients with parasellar lesions has been relatively poorly studied. The Cornell group performed a comparative analysis of QOL between 31 postoperative patients with craniopharyngiomas and 62 postoperative patients with pituitary adenomas [34]. Using the ASBQ and SNOT-22 instruments, the authors found that, among craniopharyngioma patients, those who achieved an operative gross total resection were more likely to have improved postoperative QOL, mirroring their results among patients with pituitary adenomas [32]. The subset of craniopharyngioma patients with worse postoperative vision or endocrine deficits relative to their preoperative baseline drove the cohort of craniopharyngioma patients to have overall worse QOL relative to the pituitary adenomas [34]. Reports focusing on postoperative QOL in patients with parasellar meningiomas are sparse, though the series by Jones et al. reviewed long-term outcomes in 14 patients with ASBQ data and 19 patients with SNOT-22 data and demonstrated a modest improvement in postoperative QOL in this patient population, particularly in patients aged < 55 years old [60].

#### **Anterior Cranial Fossa**

EESBS for resection of anterior cranial fossa lesions, inclusive of esthesioneuroblastoma, meningiomas, and sinonasal malignancies, is prone to many of the nasal morbidities encountered following resection of sellar and parasellar lesions. A recent review found the average complication rate following EESBS for anterior cranial fossa pathology to approximate 17% [61]. Endoscopic endonasal resection of anterior cranial fossa lesions are more likely than parasellar counterparts to be complicated by cerebrospinal fluid leak and associated sequela including pneumocephalus and meningitis, though rates of these complications have significantly decreased following the advent of the vascularized nasoseptal flap [62, 63].

Among case series solely including patients with anterior skull base pathologies, Castelnuovo et al. found a significant decline in ASBQ scores within the first month of surgery, followed by a return to baseline over the first year following surgery. Within this cohort of 153 patients, those aged greater than 60 years old and undergoing radiation were found to be least likely to return to preoperative baseline ASBQ scores [29]. In a similar series of 250 patients with mixed anterior skull base pathologies, Ahn et al. found SNOT-22 scores returned to preoperative baseline scores within 6 months of EESBS, and that patients with significant postoperative mucosal edema demonstrating worse recovery [44]. Within a smaller series of 10 patients with esthesioneuroblastoma, a decrease in sinonasal QOL was noted 3 months postoperatively, though patients returned to their baseline sinonasal QOL scores by 6 months postoperatively [64].

Various operative techniques and approaches have also been associated with variable postoperative morbidity profiles for anterior skull base pathologies. For instance, in a recent series of 14 esthesioneuroblastoma patients with preservation of one olfactory bulb, 43% of patients were found to have residual smell function including 14% of patients with normal or only mildly reduced smell following unilateral endoscopic tumor resection. Of note, all 14 patients in this series received postoperative radiation and none have yet had tumor recurrence, with a mean follow-up of 51.7 months [65]. In contrast, a recent systematic review of EESBS versus open cranial approaches for resection of olfactory groove meningiomas found less postoperative anosmia in patients undergoing open craniotomy (37.4%) relative to the EESBS cohort (95.9%), suggesting the need for further investigation of the most optimal surgical approaches to treat anterior skull base pathologies while minimizing patient morbidity and maximizing QOL [55].

#### Middle Cranial Fossa

The EESBS approach for middle cranial fossa lesions is often employed to treat encephaloceles, spontaneous cerebrospinal fluid leaks, and various skull base tumors including nasopharyngeal carcinomas. An approach to such pathologies often includes an endoscopic endonasal transpterygoid approach, with subsequent risk to the vidian and V2 nerves. As such, operative morbidity from this approach may include hypesthesia, paresthesia, and dry eye. In a recent small series of 8 patients treated with an EESBS approach for repair of lateral pterygoid recess encephaloceles, a majority of patients developed at least transient hypesthesia (75%), paresthesia (62.5%), and dry eye (50%), with a reported 10% incidence of long-term ongoing sequela [66]. In a larger series of 37 patients undergoing EESBS with a transpterygoid approach for tumor resection, 26 patients (70.3%) had sacrifice of the vidian nerve, although only 38.5% of these patients complained of postoperative dry eye [67].

Dependent upon the pathology being surgically treated, the vidian and V2 nerve often must be resected. However, in select instances, it may be possible to avoid injury to these structures. For instance, Geltzeiler et al. recently published an anatomic study highlighting a vidian and greater palatine nerve–sparing transpterygoid approach for nasopharyngeal tumors, and Alves-Belo espoused the potential benefits of a lateral trans-orbital approach over an EESBS transpterygoid approach for repair of lateral encephaloceles [68, 69]. While large clinical series have yet to be published using these novel operative corridors, such approaches may be useful in patients particularly at risk of sequela from trauma to or resection of the vidian and V2 nerves.

# **Posterior Cranial Fossa**

Use of the endoscopic endonasal corridor to approach skull base pathology within the posterior cranial fossa continues to evolve, with this operative corridor being increasingly used to resect chordomas, chondosarcomas, and other lesions involving the clivus and petrous bones. While data on QOL outcomes in these patients is generally lacking, several series have been published highlighting operative morbidity in the patient population, including rates of cerebrospinal fluid leak, abducens nerve palsy, carotid artery injury, atlantoaxial instability, and iatrogenic seeding of tumor.

For instance, in a series of 65 consecutive skull base chordoma patients, Zoli et al. reported an overall complication rate of 15%, including a 2.5% rate of CSF leak rate, 6.2% rate of abducens palsy, and 2.5% of carotid artery injury rate [70]. Rates of perioperative complications vary widely in the literature and are based, in part, upon surgeon experience and operative technique. For instance, in another large series of 60 chordoma patients, with 25 such patients being operated upon for recurrent disease, the CSF leak rate totaled 20% with an associated meningitis rate of 3.3%, and the rate of new abducens nerve palsy was 6.7% [71]. Among the most devastating complications from EESBS for posterior fossa lesions is carotid artery injury. One of the largest series to investigate this complication found a 2% risk of carotid artery injury among 142 cases of chordoma and chondrosarcoma [72]. Additionally, aggressive resection of bony elements within the posterior fossa may be associated with instability at the skull base. A series of 212 patients with lower clival lesions inclusive of chordomas, chondrosarcomas, and osteosarcomas found that 7 patients (3.3%) required atlanto-occipital fusion for instability, with the primary risk factor for instability being greater than 75% resection of the occipital condyle, which is often not possible to achieve without a combined EESBS/ open craniotomy approach for tumor resection [73]. Lastly, a recent series of 173 chordoma patients found a 1.2% rate of iatrogenic seeding of tumor cells along the operative corridor; additional studies are required to help determine whether operative adjuncts, such as pathway protection devices, may help prevent such seeding within the endonasal corridor [74].

Among the most difficult to reach lesions via the EESBS approach, new approaches to access tumors within the petrous ridge and to address resultant CSF leaks continue to push the boundaries of endoscopic skull base surgery. The contralateral transmaxillary approach has expanded the EESBS corridor to allow the skull base surgeon greater ease of access to the petrous ridge posterior to the petrous segment of the carotid artery, permitting greater extent of resection for chondrosarcomas in this region without significantly increased risk of injury to the carotid artery [75]. The use of pericranial flaps has also been found to be useful in patients with recurrent tumors of the posterior fossa requiring complex reconstruction involving fresh, vascularized flaps [76].

#### **Reconstructive Methods**

In addition to morbidities imposed by specific surgical approaches, reconstructive methods in EESBS, in particular the use of the nasoseptal flap (NSF), may be associated with disruptions in QOL and pose their own unique postoperative sequelae. While broadly acknowledged that the NSF incurs additional postoperative septal healing and nasal crusting, the degree to which NSF impacts postoperative outcomes is debated [17]. Though an evidence-based review suggests that NSF usage leads to olfactory impairment and a recent report in a very large cohort of patients undergoing EESBS suggests that the use of a NSF is the only prognosticator of worse sinonasal QOL, other reports fail to demonstrate a difference between populations of patients undergoing NSF reconstruction to those without [43, 77–80]. Meanwhile, a recent report specifically investigating NSF upper limb incision techniques failed to demonstrate a difference in olfactory outcomes between cold knife and monopolar cautery [58•].

Sequelae specific to NSF reconstruction include nasal crusting, mucocele formation, septal perforation, external nasal deformities, septal flap necrosis, and changes in olfaction [81•]. Mucocele formation is thought to be secondary to incomplete sinonasal mucosal removal at the recipient bed, while septal perforation is likely secondary to avascular necrosis. Moreover, prior surgery or a thin NSF pedicle may increase the risk for septal flap necrosis. Perhaps the most interesting unique morbidity of NSF usage is the occurrence of postoperative external nasal deformities, specifically nasal dorsum collapse. Three studies have identified this occurrence, including a large retrospective review with a followup prospective study that included detailed facial analysis [37, 39, 82•]. Though the mechanism of nasal dorsum collapse is not entirely known, it may be related to surgical technique and could potentially be avoided if additional septal mucosa along the dorsum is preserved.

Several techniques exist to potentially minimize the associated comorbidities of NSF usage include Silastic splinting, donor site free mucosal grafts, the "reverse flap" technique, or xenoplastic grafting [83–86]. The use of an endonasal sheath during EESBS may also help to limit the amount of intranasal trauma to the nasal septum and other sinonasal structures typically encountered during passage of instruments repeatedly in and out of the endonasal corridor. Though there is a varying degree of efficacy of each of these techniques, studies specifically evaluating objective sinonasal functional and the QOL implications following the employment of these strategies are lacking.

# Conclusion

There is increasing recognition of the importance of QOL outcomes in EESBS. Though a single comprehensive QOL instrument familiar to skull base surgeons is lacking, it is clear that both EESBS-specific and sinonasal-focused metrics are vital in our understanding of the QOL implications in this ever-growing patient population. There is tremendous opportunity for future study in more diverse skull base pathologies beyond pituitary neoplasms, as well as novel interventions to minimize the morbidities and QOL repercussions of EESBS.

#### **Compliance with Ethical Standards**

**Conflict of Interest** Nicholas R. Rowan and Debraj Mukherjee declare that they have no conflict of interest.

Human and Animal Rights All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

# References

Papers of particular interest, published recently, have been highlighted as:

- · Of importance
- •• Of major importance
- Komotar RJ, Starke RM, Raper DM, Anand VK, Schwartz TH. Endoscopic skull base surgery: a comprehensive comparison with open transcranial approaches. Br J Neurosurg. 2012;26(5):637–48. https://doi.org/10.3109/02688697.2012.654837.
- Cho J, Grayson JW, Christensen J, Winder MJ, Sheehy J, Steel T, et al. Long-term Sinonasal function following transnasal pituitary surgery: a comparison of surgical approach. Am J Rhinol Allergy. 2020;1945892419896788:194589241989678. https://doi.org/10. 1177/1945892419896788.
- Neal JG, Patel SJ, Kulbersh JS, Osguthorpe JD, Schlosser RJ. Comparison of techniques for transsphenoidal pituitary surgery. Am J Rhinol. 2007;21(2):203–6.
- DeKlotz TR, Chia SH, Lu W, Makambi KH, Aulisi E, Deeb Z. Meta-analysis of endoscopic versus sublabial pituitary surgery. Laryngoscope. 2012;122(3):511–8. https://doi.org/10.1002/lary. 22479.
- 5.•• Gil Z, Abergel A, Spektor S, Shabtai E, Khafif A, Fliss DM. Development of a cancer-specific anterior skull base quality-oflife questionnaire. J Neurosurg. 2004;100(5):813–9. https://doi. org/10.3171/jns.2004.100.5.0813. Original description of the ASBO.
- 6.•• de Almeida JR, Vescan AD, Gullane PJ, Gentili F, Lee JM, Lohfeld L, et al. Development of a disease-specific quality-of-life questionnaire for anterior and central skull base pathology-the skull base inventory. Laryngoscope. 2012;122(9):1933–42. https://doi.org/10. 1002/lary.23426. Original description of the SBI.
- 7.•• Ten Dam E, Feijen RA, van den Berge MJC, Hoving EW, Kuijlen JM, van der Laan B, et al. Development of the Endoscopic Endonasal Sinus and Skull Base Surgery Questionnaire. Int Forum Allergy Rhinol. 2017;7(11):1076–84. https://doi.org/10. 1002/alr.22000 Original description of the EES-Q.
- 8.•• Little AS, Kelly D, Milligan J, Griffiths C, Rosseau G, Prevedello DM, et al. Prospective validation of a patient-reported nasal quality-of-life tool for endonasal skull base surgery: The Anterior Skull Base Nasal Inventory-12. J Neurosurg. 2013;119(4):1068–74. https://doi.org/10.3171/2013.3.jns122032. Original description of the ASK Nasal-12, a rhinologic-specific skull base QOL instrument.

- 9.•• Bhenswala PN, Schlosser RJ, Nguyen SA, Munawar S, Rowan NR. Sinonasal quality-of-life outcomes after endoscopic endonasal skull base surgery. Int Forum Allergy Rhinol. 2019;9(10):1105–18. https://doi.org/10.1002/alr.22398. Comprehensive review and meta-analysis of SNOT-22 outcomes in EESBS, demonstrating transient worsening and then sustained improvement in post-operative sinonasal QOL.
- Shah JP. Quality of life after skull base surgery: the patient's predicament. Skull Base. 2010;20(1):3–4. https://doi.org/10.1055/s-0029-1242977.
- Cavel O, Abergel A, Margalit N, Fliss DM, Gil Z. Quality of life following endoscopic resection of skull base tumors. J Neurol Surg B Skull Base. 2012;73(2):112–6. https://doi.org/10.1055/s-0032-1301392.
- Amit M, Abergel A, Fliss DM, Gil Z. The clinical importance of quality-of-life scores in patients with skull base tumors: a metaanalysis and review of the literature. Curr Oncol Rep. 2012;14(2): 175–81. https://doi.org/10.1007/s11912-012-0222-3.
- Larjani S, Monteiro E, Witterick I, Vescan A, Zadeh G, Gentili F, et al. Preliminary cross-sectional reliability and validity of the Skull Base Inventory (SBI) quality of life questionnaire. J Otolaryngol Head Neck Surg. 2016;45(1):45. https://doi.org/10.1186/s40463-016-0158-y.
- 14. Ten Dam E, Korsten-Meijer AGW, Hoving EW, Kuijlen JM, van der Laan B, Feijen RA, et al. Evaluation of the psychometric properties of the endoscopic endonasal sinus and skull base surgery questionnaire (EES-Q) in a prospective cohort study. Clin Otolaryngol. 2019;44(4):565–71. https://doi.org/10.1111/coa. 13334.
- Pant H, Bhatki AM, Snyderman CH, Vescan AD, Carrau RL, Gardner P, et al. Quality of life following endonasal skull base surgery. Skull Base. 2010;20(1):35–40. https://doi.org/10.1055/s-0029-1242983.
- de Almeida JR, Witterick IJ, Vescan AD. Functional outcomes for endoscopic and open skull base surgery: an evidence-based review. Otolaryngol Clin N Am. 2011;44(5):1185–200. https://doi.org/10. 1016/j.otc.2011.06.017.
- de Almeida JR, Snyderman CH, Gardner PA, Carrau RL, Vescan AD. Nasal morbidity following endoscopic skull base surgery: a prospective cohort study. Head Neck. 2011;33(4):547–51. https:// doi.org/10.1002/hed.21483.
- Schreiber A, Bertazzoni G, Ferrari M, Rampinelli V, Verri P, Mattavelli D, et al. Nasal morbidity and quality of life after endoscopic transsphenoidal surgery: a single-center prospective study. World Neurosurg. 2019;123:e557–e65. https://doi.org/10.1016/j. wneu.2018.11.212.
- Yin LX, Low CM, Puccinelli CL, O'Brien EK, Stokken JK, Van Abel KM, et al. Olfactory outcomes after endoscopic skull base surgery: a systematic review and meta-analysis. Laryngoscope. 2019;129(9):1998–2007. https://doi.org/10.1002/lary.28003. Meta-analysis of olfactory outcomes following EESBS, demonstrates need for further investigation of olfaction given heterogeneity of results.
- 20. Griffiths CF, Barkhoudarian G, Cutler A, Duong HT, Karimi K, Doyle O, et al. Analysis of olfaction after bilateral nasoseptal rescue flap transsphenoidal approach with olfactory mucosal preservation. Otolaryngol Head Neck Surg. 2019;161(5):881–9. https://doi.org/10.1177/0194599819861340. Robust review of olfactory outcomes using the Brief Smell Identification Test (B-SIT) following EESBS, demonstrating minimal postoperative changes in olfaction in the setting of olfactory strip preservation.
- Jang MK, Oh EG, Lee H, Kim EH, Kim S. Postoperative symptoms and quality of life in pituitary macroadenomas patients. J Neurosci Nurs. 2020;52(1):30–6. https://doi.org/10.1097/jnn. 000000000000483.

- Blomqvist EH, Bramerson A, Stjarne P, Nordin S. Consequences of olfactory loss and adopted coping strategies. Rhinology. 2004;42(4):189–94.
- Neuland C, Bitter T, Marschner H, Gudziol H, Guntinas-Lichius O. Health-related and specific olfaction-related quality of life in patients with chronic functional anosmia or severe hyposmia. Laryngoscope. 2011;121(4):867–72. https://doi.org/10.1002/lary. 21387.
- Smeets MAM, Veldhuizen MG, Galle S, Gouweloos J, de Haan AJA, Vernooij J, et al. Sense of smell disorder and health-related quality of life. Rehabil Psychol. 2009;54(4):404–12. https://doi.org/ 10.1037/a0017502.
- Hopkins C, Gillett S, Slack R, Lund VJ, Browne JP. Psychometric validity of the 22-item Sinonasal Outcome Test. Clin Otolaryngol. 2009;34(5):447–54. https://doi.org/10.1111/j.1749-4486.2009. 01995.x.
- Farhood Z, Schlosser RJ, Pearse ME, Storck KA, Nguyen SA, Soler ZM. Twenty-two-item Sino-Nasal Outcome Test in a control population: a cross-sectional study and systematic review. Int Forum Allergy Rhinol. 2016;6(3):271–7. https://doi.org/10.1002/ alr.21668.
- DeConde AS, Mace JC, Bodner T, Hwang PH, Rudmik L, Soler ZM, et al. SNOT-22 quality of life domains differentially predict treatment modality selection in chronic rhinosinusitis. Int Forum Allergy Rhinol. 2014;4(12):972–9. https://doi.org/10.1002/alr. 21408.
- Gravbrot N, Kelly DF, Milligan J, Griffiths CF, Barkhoudarian G, Jahnke H, et al. The minimal clinically important difference of the anterior skull base nasal Inventory-12. Neurosurgery. 2018;83(2): 277–80. https://doi.org/10.1093/neuros/nyx401.
- Castelnuovo P, Lepera D, Turri-Zanoni M, Battaglia P, Bolzoni Villaret A, Bignami M, et al. Quality of life following endoscopic endonasal resection of anterior skull base cancers. J Neurosurg. 2013;119(6):1401–9. https://doi.org/10.3171/2013.8.jns13296.
- Glicksman JT, Parasher AK, Brooks SG, Workman AD, Lambert JL, Bergman JE, et al. Sinonasal quality of life after endoscopic resection of malignant sinonasal and skull base tumors. Laryngoscope. 2018;128(4):789–93. https://doi.org/10.1002/lary. 26833.
- Harvey RJ, Winder M, Davidson A, Steel T, Nalavenkata S, Mrad N, et al. The olfactory strip and its preservation in endoscopic pituitary surgery maintains smell and sinonasal function. J Neurol Surg B Skull Base. 2015;76(6):464–70. https://doi.org/10.1055/s-0035-1554905.
- McCoul ED, Anand VK, Bedrosian JC, Schwartz TH. Endoscopic skull base surgery and its impact on sinonasal-related quality of life. Int Forum Allergy Rhinol. 2012;2(2):174–81. https://doi.org/10. 1002/alr.21008.
- 33.• McCoul ED, Bedrosian JC, Akselrod O, Anand VK, Schwartz TH. Preservation of multidimensional quality of life after endoscopic pituitary adenoma resection. J Neurosurg. 2015;123(3):813–20. https://doi.org/10.3171/2014.11.jns14559. One of the original studies demonstrating improved postoperative skull basespecific QOL and sustained sinonasal QOL in patients undergoing EESBS for pituitary adenoma.
- Patel KS, Raza SM, McCoul ED, Patrona A, Greenfield JP, Souweidane MM, et al. Long-term quality of life after endonasal endoscopic resection of adult craniopharyngiomas. J Neurosurg. 2015;123(3):571–80. https://doi.org/10.3171/2014.12.jps141591.
- Ransom ER, Doghramji L, Palmer JN, Chiu AG. Global and disease-specific health-related quality of life after complete endoscopic resection of anterior skull base neoplasms. Am J Rhinol Allergy. 2012;26(1):76–9. https://doi.org/10.2500/ajra.2012.26. 3713.
- Awad AJ, Mohyeldin A, El-Sayed IH, Aghi MK. Sinonasal morbidity following endoscopic endonasal skull base surgery. Clin

- clineuro.2015.01.004.
  37. Soudry E, Psaltis AJ, Lee KH, Vaezafshar R, Nayak JV, Hwang PH. Complications associated with the pedicled nasoseptal flap for skull base reconstruction. Laryngoscope. 2015;125(1):80–5. https://doi. org/10.1002/lary.24863.
- Thorp BD, Sreenath SB, Ebert CS, Zanation AM. Endoscopic skull base reconstruction: a review and clinical case series of 152 vascularized flaps used for surgical skull base defects in the setting of intraoperative cerebrospinal fluid leak. Neurosurg Focus. 2014;37(4):E4. https://doi.org/10.3171/2014.7.focus14350.
- Rowan NR, Wang EW, Gardner PA, Fernandez-Miranda JC, Snyderman CH. Nasal deformities following Nasoseptal flap reconstruction of Skull Base defects. J Neurol Surg B Skull Base. 2016;77(1):14–8. https://doi.org/10.1055/s-0035-1555136.
- Bedrosian JC, McCoul ED, Raithatha R, Akselrod OA, Anand VK, Schwartz TH. A prospective study of postoperative symptoms in sinonasal quality-of-life following endoscopic skull-base surgery: dissociations based on specific symptoms. Int Forum Allergy Rhinol. 2013;3(8):664–9. https://doi.org/10.1002/alr.21161.
- Gallagher MJ, Durnford AJ, Wahab SS, Nair S, Rokade A, Mathad N. Patient-reported nasal morbidity following endoscopic endonasal skull base surgery. Br J Neurosurg. 2014;28(5):622–5. https://doi.org/10.3109/02688697.2014.887656.
- Little AS, Kelly D, Milligan J, Griffiths C, Prevedello DM, Carrau RL, et al. Predictors of sinonasal quality of life and nasal morbidity after fully endoscopic transsphenoidal surgery. J Neurosurg. 2015;122(6):1458–65. https://doi.org/10.3171/2014.10.jns141624.
- Seo MY, Nam DH, Kong DS, Lee JJ, Ryu G, Kim HY, et al. Quality of life after extended versus transsellar endoscopic skull base surgery from 767 patients. Laryngoscope. 2019;129(6):1318–24. https://doi.org/10.1002/lary.27630.
- 44. Ahn JC, Cho SW, Kim DK, Han DH, Kim DY, Rhee CS, et al. Recovery period of sinonasal quality of life and its associated factors after endoscopic endonasal approach for anterior skull base tumors. Acta Otolaryngol. 2019;139(5):461–6. https://doi.org/10. 1080/00016489.2019.1574982.
- Lee DD, Peris-Celda M, Butrymowicz A, Kenning T, Pinheiro-Neto CD. Quality of life changes following concurrent septoplasty and/or inferior turbinoplasty during endoscopic pituitary surgery. World Neurosurg. 2017;98:303–7. https://doi.org/10.1016/j.wneu. 2016.10.114.
- 46.• Choi KJ, Ackall FY, Truong T, Cheng TZ, Kuchibhatla M, Zomorodi AR, et al. Sinonasal quality of life outcomes after extended endonasal approaches to the skull base. J Neurol Surg B Skull Base. 2019;80(4):416–23. https://doi.org/10.1055/s-0038-1675592. Retrospective series that demonstrates minimal postoperative QOL differences in patients undergoing a transsellar approach, and those with surgery beyond the sella.
- Rowan NR, Soler ZM, Storck KA, Othieno F, Ganjaei KG, Smith TL, et al. Impaired eating-related quality of life in chronic rhinosinusitis. Int Forum Allergy Rhinol. 2019;9(3):240–7. https://doi.org/10.1002/alr.22242.
- Keller A, Malaspina D. Hidden consequences of olfactory dysfunction: a patient report series. BMC Ear Nose Throat Disord. 2013;13(1):8. https://doi.org/10.1186/1472-6815-13-8.
- Krusemark EA, Novak LR, Gitelman DR, Li W. When the sense of smell meets emotion: anxiety-state-dependent olfactory processing and neural circuitry adaptation. J Neurosci. 2013;33(39):15324–32. https://doi.org/10.1523/jneurosci.1835-13.2013.
- Kohli P, Soler ZM, Nguyen SA, Muus JS, Schlosser RJ. The association between olfaction and depression: a systematic review. Chem Senses. 2016;41(6):479–86. https://doi.org/10.1093/ chemse/bjw061.
- Pinto JM, Wroblewski KE, Kern DW, Schumm LP, McClintock MK. Olfactory dysfunction predicts 5-year mortality in older adults.

PLoS One. 2014;9(10):e107541. https://doi.org/10.1371/journal. pone.0107541.

- Soler ZM, Smith TL, Alt JA, Ramakrishnan VR, Mace JC, Schlosser RJ. Olfactory-specific quality of life outcomes after endoscopic sinus surgery. Int Forum Allergy Rhinol. 2016;6(4):407– 13. https://doi.org/10.1002/alr.21679.
- Yoo F, Schlosser RJ, Storck KA, Ganjaei KG, Rowan NR, Soler ZM. Effects of endoscopic sinus surgery on objective and subjective measures of cognitive dysfunction in chronic rhinosinusitis. Int Forum Allergy Rhinol. 2019;9(10):1135–43. https://doi.org/10. 1002/alr.22406.
- Soler ZM, Eckert MA, Storck K, Schlosser RJ. Cognitive function in chronic rhinosinusitis: a controlled clinical study. Int Forum Allergy Rhinology. 2015;5(11):1010–7. https://doi.org/10.1002/ alr.21581.
- Purohit A, Jha R, Khalafallah AM, Price C, Rowan NR, Mukherjee D. Endoscopic endonasal versus transcranial approach to resection of olfactory groove meningiomas: a systematic review. Neurosurg Rev. 2019:1–7. https://doi.org/10.1007/s10143-019-01193-2.
- 56. Lu VM, Goyal A, Rovin RA. Olfactory groove and tuberculum sellae meningioma resection by endoscopic endonasal approach versus transcranial approach: a systematic review and metaanalysis of comparative studies. Clin Neurol Neurosurg. 2018;174:13–20. https://doi.org/10.1016/j.clineuro.2018.08.029.
- Gompel JJV, Janus JR, Hughes JD, Stokken JK, Moore EJ, Ryan T, et al. Esthesioneuroblastoma and olfactory preservation: is it reasonable to attempt smell preservation? J Neurol Surg B Skull Base. 2018;79(2):184–8. https://doi.org/10.1055/s-0037-1606307.
- 58.• Puccinelli CL, Yin LX, O'Brien EK, Van Gompel JJ, Choby GW, Van Abel KM, et al. Long-term olfaction outcomes in transnasal endoscopic skull-base surgery: a prospective cohort study comparing electrocautery and cold knife upper septal limb incision techniques. Int Forum Allergy Rhinol. 2019;9(5):493–500. https://doi. org/10.1002/alr.22291. Small prospective cohort study failing to demonstrate differences in olfactory outcomes when upper limb of nasoseptal flap incision is made with a cold knife as compared with incisions made with monopolar cautery.
- Suberman TA, Zanation AM, Ewend MG, Senior BA, Ebert CS Jr. Sinonasal quality-of-life before and after endoscopic, endonasal, minimally invasive pituitary surgery. Int Forum Allergy Rhinol. 2011;1(3):161–6. https://doi.org/10.1002/alr.20029.
- Jones SH, Iannone AF, Patel KS, Anchouche K, Raza SM, Anand VK, et al. The impact of age on long-term quality of life after Endonasal endoscopic resection of Skull Base Meningiomas. Neurosurgery. 2016;79(5):736–45. https://doi.org/10.1227/neu. 000000000001360.
- Borg A, Kirkman MA, Choi D. Endoscopic endonasal anterior skull base surgery: a systematic review of complications during the past 65 years. World Neurosurg. 2016;95:383–91. https://doi. org/10.1016/j.wneu.2015.12.105.
- Hadad G, Bassagasteguy L, Carrau RL, Mataza JC, Kassam A, Snyderman CH, et al. A novel reconstructive technique after endoscopic expanded endonasal approaches: vascular pedicle nasoseptal flap. Laryngoscope. 2006;116(10):1882–6. https://doi.org/10.1097/ 01.mlg.0000234933.37779.e4.
- Gardner PA, Kassam AB, Thomas A, Snyderman CH, Carrau RL, Mintz AH, et al. Endoscopic endonasal resection of anterior cranial base meningiomas. Neurosurgery. 2008;63(1):36–52; discussion -4. https://doi.org/10.1227/01.neu.0000335069.30319.1e.
- Manthuruthil C, Lewis J, McLean C, Batra PS, Barnett SL. Endoscopic endonasal management of olfactory neuroblastoma: a retrospective analysis of 10 patients with quality-of-life measures. World Neurosurg. 2016;90:1–5. https://doi.org/10.1016/j.wneu. 2016.02.035.
- 65. Tajudeen BA, Adappa ND, Kuan EC, Schwartz JS, Suh JD, Wang MB, et al. Smell preservation following endoscopic unilateral

resection of esthesioneuroblastoma: a multi-institutional experience. Int Forum Allergy Rhinol. 2016;6(10):1047–50. https://doi. org/10.1002/alr.21794.

- Chislett SP, Limjuco AP, Solyar AY, Lanza DC. Cranial nerve V2 and Vidian nerve trauma secondary to lateral pterygoid recess encephalocele repair. Int Forum Allergy Rhinol. 2020;10(1):81–8. https://doi.org/10.1002/alr.22448.
- Choi JE, Noh YS, Lee KE, Jung YG, Chung SK, Kim HY, et al. Morbidities associated with the endoscopic transnasal transpterygoid approach: focusing on postoperative Sequelae. World Neurosurg. 2019. https://doi.org/10.1016/j.wneu.2019.12. 023.
- Geltzeiler M, Turner M, Rimmer R, Zenonos G, Hebert A, Snyderman C, et al. Endoscopic nasopharyngectomy combined with a nerve-sparing transpterygoid approach. Laryngoscope. 2019. https://doi.org/10.1002/lary.28479.
- Alves-Belo JT, Mangussi-Gomes J, Truong HQ, Cohen S, Gardner PA, Snyderman CH, et al. Lateral transorbital versus endonasal transpterygoid approach to the lateral recess of the sphenoid sinus-a comparative anatomic study. Oper Neurosurg (Hagerstown). 2019;16(5):600–6. https://doi.org/10.1093/ons/ opy211.
- Zoli M, Milanese L, Bonfatti R, Faustini-Fustini M, Marucci G, Tallini G, et al. Clival chordomas: considerations after 16 years of endoscopic endonasal surgery. J Neurosurg. 2018;128(2):329–38. https://doi.org/10.3171/2016.11.jns162082.
- Koutourousiou M, Gardner PA, Tormenti MJ, Henry SL, Stefko ST, Kassam AB, et al. Endoscopic endonasal approach for resection of cranial base chordomas: outcomes and learning curve. Neurosurgery. 2012;71(3):614–24; discussion 24-5. https://doi. org/10.1227/NEU.0b013e31825ea3e0.
- Gardner PA, Tormenti MJ, Pant H, Fernandez-Miranda JC, Snyderman CH, Horowitz MB. Carotid artery injury during endoscopic endonasal skull base surgery: incidence and outcomes. Neurosurgery. 2013;73(2 Suppl Operative):ons261–9; discussion ons9–70. https://doi.org/10.1227/01.neu.0000430821.71267.f2.
- Kooshkabadi A, Choi PA, Koutourousiou M, Snyderman CH, Wang EW, Fernandez-Miranda JC, et al. Atlanto-occipital instability following endoscopic endonasal approach for lower Clival lesions: experience with 212 cases. Neurosurgery. 2015;77(6):888– 97; discussion 97. https://doi.org/10.1227/neu. 000000000000922.
- Fernandes Cabral DT, Zenonos GA, Fernandez-Miranda JC, Wang EW, Gardner PA. Iatrogenic seeding of skull base chordoma following endoscopic endonasal surgery. J Neurosurg. 2018;129(4): 947–53. https://doi.org/10.3171/2017.6.jns17111.
- Patel CR, Wang EW, Fernandez-Miranda JC, Gardner PA, Snyderman CH. Contralateral transmaxillary corridor: an augmented endoscopic approach to the petrous apex. J Neurosurg. 2018;129(1):211–9. https://doi.org/10.3171/2017.4.jns162483.
- Gode S, Lieber S, Nakassa ACI, Wang EW, Fernandez-Miranda JC, Gardner PA, et al. Clinical experience with secondary endoscopic reconstruction of clival defects with extracranial pericranial flaps. J

Neurol Surg B Skull Base. 2019;80(3):276–82. https://doi.org/10. 1055/s-0038-1668517.

- Greig SR, Cooper TJ, Sommer DD, Nair S, Wright ED. Objective sinonasal functional outcomes in endoscopic anterior skull-base surgery: an evidence-based review with recommendations. Int Forum Allergy Rhinol. 2016;6(10):1040–6. https://doi.org/10. 1002/alr.21760.
- Jalessi M, Jahanbakhshi A, Amini E, Kamrava SK, Farhadi M. Impact of nasoseptal flap elevation on sinonasal quality of life in endoscopic endonasal approach to pituitary adenomas. Eur Arch Otorhinolaryngol. 2016;273(5):1199–205. https://doi.org/10.1007/ s00405-015-3729-z.
- Harvey RJ, Malek J, Winder M, Davidson A, Steel T, Mrad N, et al. Sinonasal morbidity following tumour resection with and without nasoseptal flap reconstruction. Rhinology. 2015;53(2):122–8. https://doi.org/10.4193/Rhin14.247.
- Hanson M, Patel PM, Betz C, Olson S, Panizza B, Wallwork B. Sinonasal outcomes following endoscopic anterior skull base surgery with nasoseptal flap reconstruction: a prospective study. J Laryngol Otol. 2015;129(Suppl 3):S41–6. https://doi.org/10.1017/ s002221511500047x.
- 81.• Lavigne P, Faden DL, Wang EW, Snyderman CH. Complications of Nasoseptal flap reconstruction: a systematic review. J Neurol Surg B Skull Base. 2018;79(Suppl 4):S291–s9. https://doi.org/10. 1055/s-0038-1668158. Comprehensive review of complications associated with nasoseptal flap reconstruction.
- 82.• Rowan NR, Valappil B, Chen J, Wang EW, Gardner PA, Snyderman CH. Prospective characterization of postoperative nasal deformities in patients undergoing endoscopic endonasal skullbase surgery. Int Forum Allergy Rhinol. 2019. https://doi.org/10. 1002/alr.22466. Prospective study of external nasal deformities following EESBS, demonstrating clear association with nasoseptal flap reconstruction of the skull base.
- Chin D, Harvey RJ. Endoscopic reconstruction of frontal, cribiform and ethmoid skull base defects. Adv Otorhinolaryngol. 2013;74: 104–18. https://doi.org/10.1159/000342285.
- Kimple AJ, Leight WD, Wheless SA, Zanation AM. Reducing nasal morbidity after skull base reconstruction with the nasoseptal flap: free middle turbinate mucosal grafts. Laryngoscope. 2012;122(9):1920–4. https://doi.org/10.1002/lary.23325.
- Caicedo-Granados E, Carrau R, Snyderman CH, Prevedello D, Fernandez-Miranda J, Gardner P, et al. Reverse rotation flap for reconstruction of donor site after vascular pedicled nasoseptal flap in skull base surgery. Laryngoscope. 2010;120(8):1550–2. https:// doi.org/10.1002/lary.20975.
- Nayak JV, Rathor A, Grayson JW, Bravo DT, Velasquez N, Noel J, et al. Porcine small intestine submucosal grafts improve remucosalization and progenitor cell recruitment to sites of upper airway tissue remodeling. Int Forum Allergy Rhinol. 2018;8(10): 1162–8. https://doi.org/10.1002/alr.22156.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.