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

Reconstruction Following Endoscopic Endonasal Skull Base Surgery: Options and Technical Considerations

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Abstract

Purpose of Review To provide a brief overview of the options available for reconstruction of the skull base and to discuss their technical considerations. To review the contemporary literature surrounding adjunctive measures such as acetazolamide and perioperative cerebrospinal fluid (CSF) diversion.

Recent Findings A recent randomized, control trial examining perioperative lumbar drainage following endoscopic skull base surgery has demonstrated that perioperative lumbar drainage is significantly associated with decreased incidence of postoperative CSF leak in specific anatomical subsites.

Summary Many factors must be weighed when considering proper skull base reconstruction. For large defects, multilayered repair with vascularized tissue is the gold standard. Perioperative lumbar drainage is recommended for large anterior or posterior fossa defects. The effect of acetazolamide on postoperative CSF leak remains unclear. Indocyanine green angiography (ICG) is a promising innovation that can aid in assessment of vascularized flaps.

Keywords Cerebrospinal fluid rhinorrhea · Cerebrospinal fluid leak repair · Endoscopic skull base surgery · Skull base defect · Lumbar drain · Nasoseptal flap

Introduction

Reconstruction of skull base defects in endoscopic endonasal surgery is evolving alongside the expanse of extended endoscopic approaches to the skull base. The skull base surgeon has access to an array of techniques, tissues, and biomaterials to fashion a robust repair that recreates the barrier between the cranial vault and the sinonasal compartment. There is no consensus as to what constitutes proper reconstruction of any skull base defect; however, basic principles should be followed and will be discussed in this review.

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Several retrospective studies and case series have suggested that high rates of successful CSF leak repair (typically greater than 90%) [1–8] can be achieved for most small defects with a variety of techniques, materials, and grafts. Large skull base defects with resultant high-flow CSF leaks, however, require a more scrupulous repair in order to achieve acceptable rates of postoperative CSF leak. This typically entails a multiple layered repair that includes a vascularized flap. The layers can be comprised of autologous grafts (such as fascia lata, temporalis fascia, or fat) and engineered materials such as collagen matrices and irradiated cadaveric dermis. With multilayered, vascularized repair in the setting of large skull base defects, postoperative CSF leaks have been reported by many high-volume centers to be less than 5% [9–11]. In this article, we discuss repair considerations dealing with closure of large skull base defects following endoscopic skull base surgery.

Local and Regional Vascularized Flaps

Nasoseptal Flap

The advent of the nasoseptal flap has been the most substantial reconstructive advance to date [9, 12]. Owing to its hardiness, ability to be scaled to the size of the defect, and its excellent reach in covering nearly all sagittal plane skull base defects, it should be the primary reconstructive consideration when vascularized tissue repair is needed. The nasoseptal flap has revolutionized skull base repair across many centers. In a single institution review of 800 patients that had undergone endoscopic endonasal skull base surgery, the adoption of the nasoseptal flap led to a marked reduction in incidence of postoperative CSF leak from 15.9% to 5.4% [13]. The same institution saw an approximately 52% reduction in postoperative CSF leak incidence (58% vs 5.56%) in patients who had undergone endoscopic endonasal resection of craniopharyngioma after routine incorporation of the nasoseptal flap into their reconstruction [14, 15].

In cases where there is a large dural defect or high-flow cerebrospinal fluid leak, history of previous skull base irradiation, anticipated adjuvant irradiation, or a patient with multiple comorbidities that may preclude normal healing, a nasoseptal flap should be particularly considered. It is important to realize that it may not be available in the context of injury to the vascular pedicle during surgery, infiltration by tumor, previous surgery (septoplasty or other endoscopic endonasal surgeries), or septal necrosis from granulomatous diseases or intranasal drug use. The skull base surgeon should attempt to discern this preoperatively during an endoscopic examination or can consider intraoperative evaluation with indocyanine green (ICG) angiography, a recent innovation which is later discussed.

While the standard nasoseptal flap is sufficient in most skull base cases, the width of the flap can be tailored to the defect by harvesting varying degrees of the nasal floor and inferior meatus if necessary ("extended nasoseptal flap"), thereby increasing the surface area of the flap by 774 mm^2 and craniocaudal length by 21 mm on average [12]. The nasoseptal flap covers virtually all types of sagittal plane defects including transcribriform approach defects (from posterior wall of the frontal sinus to the anterior wall of the sphenoid sinus), transsellar and/or transplanum defects, and panclival defects (from the level of the dorsum sella to foramen magnum) (Table 1) [16–20].

It is important to note that there are instances where the nasoseptal flap may only marginally cover the defect or possibly be inadequate to do so. In a radiologic study examining the ability of the nasoseptal flap to cover an anterior skull base resection defect in 30 cases, it was found that a standard nasoseptal flap adequately covered the defect in all cases (average reconstruction area of flap 17.12 cm^2, average defect area 8.64 cm^2) [16]. However, in 26.7% of cases, the anteroposterior extent of the defect and length of nasoseptal flap differed by ≤ 5 mm, and in 33% of cases, the width of the flap and the interorbital distance differed by ≤ 5 mm. Also important to note is that while a single nasoseptal flap can cover each of these defect types (i.e., transcribriform, transsellar, transclival, etc.) separately, it is not sufficient to repair a very large defect resulting from multiple approaches (i.e., transcribriform in addition to transsellar) [19]. However, in these instances, the repair can be augmented with additional reconstructive tissue such as free tissue grafts (fat or fascia) or other local and regional vascularized flaps.

The use of the nasoseptal flap to repair large skull base defects has been well demonstrated to significantly reduce the incidence of postoperative CSF leak following extended skull base approaches [13]. A systematic review of endoscopic skull base reconstruction of large skull base defects by Harvey et al. found that postoperative CSF leak rates occurred on average 6.7% with vascularized repair compared to 15.6% using only free grafts [20]. Additionally, multiple series from high-volume skull base centers examining only patients with large skull base defects that have undergone endoscopic endonasal surgery and repair with a nasoseptal flap have reported postoperative CSF leak rates of approximately 4–6% [9, 13, 21, 22].

It was once considered a drawback that the nasoseptal flap had to be raised prior to resection forcing the skull base surgeon to anticipate the defect and to potentially raise a larger flap than what was necessary. However, with the recent introduction of the "rescue" flap, this dilemma has been ameliorated as the flap is only raised enough to protect the vascular pedicle prior to sphenoidotomy and posterior septectomy [23].

There are a few negative aspects to consider related to harvest and use of the nasoseptal flap. A recent systematic review by Lavigne et al. examining the morbidity and complications related to use of nasoseptal flaps found that across the included studies, incidence of flap necrosis ranged from 0 to 1.3%,

Table 1 Local and regional vascularized flaps: blood supply and most suitable anatomic subsites for use

Flap	Blood supply	Anatomic areas for use
Nasoseptal flap	Posterior septal artery (from sphenopalatine artery)	Cribriform*, planum, parasellar, clival
Inferior turbinate flap	Inferior turbinate artery (from posterior lateral nasal artery)	Clival > parasellar**
Pericranial flap	Supraorbital and supratrochlear arteries	Cribriform, planum, parasellar, clival

*Consider raising an extended nasoseptal flap as width of defect may be close to width of standard nasoseptal flap

**Inferior turbinate flap should be used primarily for small clival defects but if an extended inferior turbinate flap is used, can be considered for parasellar defects mucocele formation 0 to 3.6%, septal perforation 0 to 14.4%, and nasal dorsum collapse 0.7 to 5.8% [24]. With respect to effect on olfaction, most studies appear to be in concordance that olfaction is not significantly affected when comparing long-term postoperative olfactory function to preoperative baseline olfaction in the majority of patients [24, 25].

Inferior Turbinate and Lateral Nasal Wall Flap

The inferior turbinate flap is based on the inferior turbinate artery, a terminal branch of the posterior lateral nasal artery which in turn arises from the sphenopalatine artery just after it exits the sphenopalatine foramen. The inferior turbinate artery enters the superolateral aspect of the posterior portion of the inferior turbinate and gives rise to at least two small terminal branches that course along the superior and inferior aspects of the turbinate [26–28].

This vascularized pedicled flap should be considered when the nasoseptal flap is not available. It is a less desirable option than the nasoseptal flap because its arc of rotation and reach is significantly less [28]. It also has significantly less surface area for coverage (only approximately 5 cm^2 compared to 25 cm^2 of a standard nasoseptal flap) [26, 28], is much narrower in width (2.2 cm) [29], and is technically more difficult to harvest. Furthermore, the flap segment harvested around the inferior aspect of conchal bone typically does not relax making it difficult to have the flap in full apposition to the margins of the skull base defect [28].

To increase the surface area for defect coverage, an extended inferior turbinate flap has been described [28]. This extended approach involves extending the inferior cut to capture the mucoperiosteum of the nasal floor. The extended flap increases the width of the flap 250% to approximately $5.46 \text{ cm} \pm 0.58 \text{ cm}$ and the surface area 500% to approximately $27.26 \pm 3.65 \text{ cm}^2$. Septal mucosa and mucoperiosteum along the superior aspect of the lateral nasal wall can also be incorporated to further enlarge the surface area. The inferior turbinate flap is an effective repair primarily only for sellar or clival defects [28–31]. In a study of 5 patients that underwent revision CSF leak repair with an extended inferior turbinate flap as a nasoseptal flap was not available, 80% had successful repair [28]. In another series, three CSF leak defects were repaired with an inferior turbinate flap without any failures [31].

Extracranial Pericranial Flap

The pericranial flap is based on the deep branches of the supraorbital and supratrochlear vessels and is the extranasal, pedicled flap of choice in endoscopic skull base surgery [32]. This flap not only includes the calvarial periosteum but also the overlying associated areolar tissue (also called subgaleal fascia). This flap can be raised via a traditional bicoronal approach or in an endoscopic-assisted, minimally invasive manner using three small incisions described by Zanation et al. [33] This flap is usually utilized to cover anterior skull base defects but can also cover sagittal plane defects caudal to this extending to the clivus [34]. The pericranial flap has the relative advantages of being technically easy to dissect and raise, reliable, and having minimal cosmetic consequence and morbidity [32–34].

The adequate length for pericranial flaps to cover defects along the sagittal plane has been determined by a radioanatomic study to be 11.31 to 12.44 cm for anterior skull base defects, 14.31 to 15.57 cm for sellar defects, and 18.50 to 20.42 cm for clival defects [35]. In this same study, outcomes for 10 patients who had underwent endoscopic skull base resection of tumors were examined. There were no reported postoperative CSF leaks. Patel et al. had 16 endoscopic-assisted pericranial flaps in their retrospective series examining outcomes following endoscopic skull base surgery [31]. There were no reported postoperative CSF leaks. Another study examined seven patients with large clival defects who had undergone previous primary CSF leak repair [34]. Neither nasoseptal nor inferior turbinate flaps were available options for repair. This study is of interest because pericranial flaps are typically thought to have inadequate reach to cover clival defects. Success of secondary repair with a pericranial flap in this series was reported to be 58% suggesting that it may be a viable option in patients with clival defects who have had local flap failure.

Autologous Free Tissue Grafts

Free Mucosal Grafts

These are typically used to patch small dural defects (< 1 cm) without CSF leak or with a low-flow CSF leak [36, 37]. Most sellar defects resulting from endoscopic endonasal resection of pituitary adenoma are particularly suitable. A recent study of 122 patients that had undergone endoscopic endonasal pituitary adenoma resection and repair with an overlay free mucosal graft demonstrated a 0.82% postoperative CSF leak rate [38]. 39% of these cases had an intraoperative CSF leak. The use of free mucosal grafts to repair larger defects has been shown to lead to an unacceptably high incidence (15.6%) of postoperative CSF leak according to a recent systematic review [20]. Free mucosal grafts can be harvested from the middle turbinate or nasal floor. A mucosal graft taken from the septum is discouraged as it may compromise future use of a nasoseptal flap.

Fascia Lata

Fascia lata is the deep fascia that envelops the three fascial compartments of the thigh [39]. It is robust and has good tensile strength. The harvested graft should be fashioned larger than the estimated dural defect, as it is typically used as an inlay or overlay graft. It can also be used as a dural patch in duraplasty where it is sutured to the edges of the dural defect. Its use has been described in different multilayer reconstruction techniques [40, 41].

Fat Graft

Fat can be used to obliterate dead spaces to prevent against pooling of CSF or a hanging cistern such as in sellar defects where the arachnoid has herniated [42]. Fat can also be used to bolster repairs and act as a biological dressing that promotes early vascularization [43]. Additionally, fat may be placed between layers of a reconstruction to provide a more favorable surface and thus better apposition, for the graft or flap that overlies it [44]. In a recent large series examining outcomes of endonasal transsphenoidal surgery, autologous fat was used to repair or fill the sellar defect in 380 patients. Of these, 14 (3.7%) developed postoperative CSF leak [45].

Biomaterials

Using biomaterials rather than autologous grafts can circumvent donor-site morbidity and decrease operative time. However, there is the disadvantage of added costs [42]. An array of biomaterials exist that can be used such as allografts, xenografts, and synthetic materials.

Acellular Cadaveric Dermis

AlloDerm (LifeCell, Branchburg, New Jersey, USA) is an acellular dermal matrix created from cadaveric human skin that has been processed to remove all cellular elements and immunogenic components [46, 47]. Its pliability, tensile strength, and availability in different thicknesses make it a suitable graft option. Revascularization of the graft has been shown at about 7 days after placement in animal models [48]. Histologically, the graft has also been shown to eventually resemble the tissue surrounding the graft [47]. Retrospective review by Germani et al. ($n = 56$) examined the repair of anterior skull base defects with AlloDerm. All large defects (> 2.0 cm) were repaired using acellular dermal allograft alone resulting in 97% (29/30 cases) of cases without postoperative CSF leak [49]. Successful use of AlloDerm requires maximal apposition to vascularized bone if used as an overlay or adequate dural and bony ledges to seat as an inlay graft. Most skull base defects (i.e., parasellar and clival) resulting from endoscopic tumor resections, however, are limited in these regards [22].

Dural Collagen Grafts

Collagen matrices such as DuraMatrix (Stryker, Kalamazoo, Michigan) and DuraGen (Integra Neurosciences, Plainsboro, NJ, USA) are commonly utilized in skull base repair as intradural inlay grafts. DuraMatrix is derived from purified bovine Achilles tendon and DuraGen is a synthetic material. These materials provide a scaffold for collagen synthesis and do not require dural sutures. When collagen matrices are used as an intradural inlay graft and as part of a multilayer reconstruction that includes a vascularized nasoseptal flap, postoperative CSF leak rates have been reported to be ≤ 5% [9, 46, 50].

Perioperative Cerebrospinal Fluid Diversion

Lumbar drainage is a frequent consideration following skull base surgery. Two randomized control trials (RCTs) have been performed to date investigating the difference in CSF leak resolution following lumbar drain placement [51, 52•]. Albu et al. examined patients with traumatic CSF leaks and randomized these patients to either conservative management (bed rest, head elevation, and Valsalva avoidance) or lumbar drainage. Both of these treatment arms ($n = 30$ in each arm) were allowed to continue for a maximum of 10 days after which endoscopic closure was attempted if CSF rhinorrhea persisted. CSF leaks resolved significantly earlier with lumbar drainage, with resolution reached on average at 4.83 days (± 1.88) compared to 7.03 days (± 2.02) in the conservatively managed cohort ($p < .0001$). There was no difference in CSF leak recurrence or meningitis between the treatment arms; however, in the lumbar drainage arm, 40% of patients had reported headache.

Zwagerman et al. examined 170 patients who underwent endoscopic endonasal skull base surgery [52•]. Subjects were randomly assigned to undergo perioperative lumbar drainage or not, in a double-blinded fashion. Inclusion criteria required subjects to have a high-flow CSF leak with a dural defect greater than 1 cm^2. The postoperative leak rate of the lumbar-drained cohort was 8.2%, compared to 21.2% of subjects who did not undergo lumbar drainage ($p = 0.017$). Defect size had a significant impact on postoperative CSF leak rate ($p = 0.03$), while body mass index (BMI) had no significant bearing ($p = 0.79$). Post hoc analysis of defect location on postoperative CSF leak incidence demonstrated that lumbar drainage led to a marked reduction in CSF leak rates that approached significance in posterior (30.8% vs 12.5%; $p = 0.12$) and anterior cranial fossa defects (35.3% vs 11.1%; $p = 0.12$). Lumbar drainage for suprasellar defects had an equivocal effect on CSF leak rate (9.5% vs 4.7%; $p = 0.43$).

Acetazolamide

Acetazolamide is a carbonic anhydrase inhibitor that decreases CSF production. Its primary use in endoscopic skull base surgery lies in the adjunctive management of patients with idiopathic, spontaneous CSF rhinorrhea related to intracranial hypertension. A 2013 prospective study measured the change in intracranial pressure after oral acetazolamide and CSF leak repair with either ventriculostomy or lumbar drain placement in 36 patients. After clamping of drains and prior to oral acetazolamide administration, intracranial pressure (cm H_2O) was 32.0 ± 7.4 without acetazolamide compared to 21.9 ± 7.5 4–6 h following 500 mg of oral acetazolamide [53]. Despite the findings of this study and others [54, 55] in support of acetazolamide, recent systematic reviews have concluded that there is insufficient evidence to neither support nor reject use of acetazolamide as an adjunctive treatment in spontaneous CSF rhinorrhea management [56, 57••]. The potential adverse side effects of acetazolamide use include taste disturbance, metabolic acidosis, and hypokalemia. These must be weighed against the potential benefit when considering use [57••].

Intraoperative Indocyanine Green Fluorescence Angiography

A recent innovation has been the use of indocyanine green (ICG) intraoperative angiography for real-time assessment of tissue perfusion. One application of ICG angiography is intraoperative examination of pedicled flap vascularity. Flaps are typically raised prior to tumor extirpation, and as such, the vascular pedicle can be inadvertently damaged during the approach to tumor resection. The vascular pedicle can also be tenuous or indeterminate from previous surgery. While uncommon, postoperative flap necrosis can occur and lead to CSF leak and meningitis [58]. ICG has been used in neurosurgery and plastic surgery to assess tissue viability and only recently has been introduced into endonasal endoscopic skull base surgery. ICG angiography requires an endoscope that emits near-infrared light and intravenous administration of ICG. A recent study by Geltzeiler et al. qualitatively examined 38 flaps after they were raised intraoperatively with ICG fluorescence angiography [59]. This assessment was juxtaposed with postoperative contrast-enhanced MRI assessment of the flap, the gold standard for evaluation of flap vascularity. When both the body and pedicle enhanced with ICG, there was enhancement of the flap on postoperative MRI with contrast in 100% of cases and no incidence of flap necrosis. Two of three patients without ICG enhancement developed flap necrosis. In patients with a history of prior surgery, ICG fluoroscopy can also be used in conjunction with Doppler ultrasonography to assess the vascular pedicles and aid in choosing the optimal side for elevation.

Conclusion

Several reconstructive options and concepts in contemporary endoscopic skull base surgery are reviewed. As is evident, there is great variability in the approaches and materials that can be used for skull base repair. The judgment of the skull base surgeon is critical in order to synthesize and execute an effective repair on a case-by-case basis. An evidence-based approach guides the use of vascularized tissue and CSF diversion.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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