Complications in Skull Base Surgery and Subsequent Repair

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Historically, malignant tumor involvement of skull base precluded surgical intervention. Advances over the past several decades have allowed surgeons to resect malignancies involving skull base, pushing the limits of traditional resection limits. Skull base surgery has evolved over several past decades with shift toward endoscopic surgery. Open surgery remains as important approach for various pathologies. With more aggressive approaches, including combined anterior cranial fossa, temporal, frontotemporal craniotomy, as well as orbitozygomatic and orbitocranial approaches, advances in reconstructive techniques have allowed for acceptable complication rates, which were previously a source for significant morbidity and mortality.

Complications following skull base surgery can include intracranial bleeding, blindness, cerebrospinal fluid (CSF) leak, osteonecrosis, cerebral abscess, meningitis, cranial nerve neuropathies, and cosmetic deformity. O’Malley and Janecka reviewed a 40-year evolution of skull base surgery and described initial complication rates of CSF leak at 31% and overall infection to be 54%. The following decade experienced increased procedures pushing the limits of surgical resection with variable infection rates up to 48% but improved CSF leak rates from 3 to 19%. From the 1980s to 1990s, a multidisciplinary team approach to cranial base surgery was introduced and led to significant decreases in complications rates, with infectious rates dropping to 0 to 28% in some studies, and CSF leak rates down to 2 to 4% in some studies with improvement in local disease control and overall 5-year survival rates.1 Multidisciplinary team approach to skull base (including neurosurgeons, otolaryngologists, plastic surgeons, ophthalmologists, radiation and medical oncologists, anesthesiologists, and rehabilitation specialists) has been important in minimizing mortality and complications. Endoscopic nasal approaches in the recent decades have allowed for shorter hospital stays, decreased major complications, and decreased mortality. Overall complications rates are quoted to be between 10 and 20%. Herein, we discuss the complications of skull base surgery and approaches to management.

Complications

Vascular

Vascular complications are potentially the most serious complications following skull base surgery. This can be related to tumor infiltration to circle of Willis, technical error, and inadequate preparation. Cerebral angiography when clinical suspicion exists for large vessel involvement is warranted. Occlusion studies can be utilized and preparations made for bypass where possible. Carotid rupture can occur from infection or pseudoaneurysm from excessive adventitial dissection. While often sudden and fatal, these events may be preceded by a sentinel bleed, in which case angiography and possible stenting can be used for definitive management. Furthermore, cerebral edema, acute brain dysfunction, long-term encephalomalacia, and neurocognitive deficits can occur with...
Prolonged brain retraction for various approaches and patients should be cautioned on this. Embolic stroke can be secondary to excessive adventitial dissection and manipulation of the carotid arteries leading to dislodgment of plaque. One study reports a stroke in a patient deemed to be from secondary vasospasm after developing postoperative aseptic meningitis. While rare, the sequelae can be devastating for the patient. Poststroke management includes tight control of hemodynamic factors to prevent extension of infarct, control of airway, maintenance of oxygenation, fluid and electrolyte balance, and optimizing nutrition.

Compromise of the sagittal sinus beyond the distal one-third can produce venous infarction with attendant cascading ischemia of brain tissue. This is important in surgery of the frontal sinus and especially where there is a highly developed pneumatized frontal sinus. In the transtemporal approaches and especially where there is a planned sigmoid sinus removal or risk of injury and occlusion of the sigmoid sinus the contralateral sigmoid for flow needs to be evaluated. In 1% of individuals the contralateral sinus will be either severely hypoplastic or absent. In these patients sacrifice of the sigmoid sinus should be avoided. Similarly, in the transtemporal approaches occlusion of the sigmoid sinus or the superior petrosal vein can lead to compromise of the anastomotic vein of Labbe with serious consequences to the ipsilateral temporoparietal lobe. The region of outflow of the vein of Labbe is variable and should be assessed preoperatively with magnetic resonance venography.

**Pneumocephalus**

Intracranial air accumulation can be described as acute or delayed with various definitions of cutoff between 72 hours to 7 days. Two mechanisms are thought to result in pneumocephalus. One is a one-way valve type scenario where air can enter from extracranial space through CSF drainage, that is, nose blowing insufflation of air after dural closure. In a similar fashion, pneumocephalus after transtemporal approaches is usually the result of air entering the splanchnocranium from insufficiently sealed air cell tracts in the temporal bone. The other mechanism is air entering and displacing removed CSF creating negative intracranial pressure, that is, overdraining of CSF from lumbar spine drain. In rare instances, gas-producing infection can cause spontaneous development of gas intracranially. Prevention includes proper patient instruction on nose blowing precautions, judicious spinal drainage at a conservative rate with drain removed after 24 to 72 hours.

While often asymptomatic and resolves without clinical manifestations, clinical presentation of pneumocephalus can include headache, nausea, vomiting, irritability, dizziness, and seizures. When intracranial hypertension results from large pneumocephalus, it is tension pneumocephalus and can often be fatal. Immediate decompression is necessary to relieve pressure on brain parenchyma. This can be via burr holes, needle aspiration, and closure of intracranial communication leading to the pneumocephalus.

**Cerebrospinal Fluid Leak**

Recent reported rates of CSF leak can be high, such as following endoscopic skull base procedures at 13.8% and 8.2% in open anterior cranial fossa approaches. Suspicion is confirmed on B2 transferrin testing. Small volume leaks can be managed with observation, with conservative bed rest. Lumbar drain can be placed to reduce intracranial pressure and resolve leaks. High volume leaks generally do not respond to conservative treatment. Nasal endoscopy can be an invaluable tool for identification of the location of the CSF leak, particularly when intrathecal fluorescein is utilized. Computed tomography cisternography can also be used to localize leak. CSF leak rates can be reduced if the original repair is performed with vascularized local tissue particularly in patients with history of prior irradiation.

Management strategies vary significantly depending on the location of the posttraumatic CSF leak. For lateral skull base defects, conservative management can be used for the first 7 to 10 days with a high rate of spontaneous closure, reserving more invasive measures for higher risk of ascending infection. Operative interventions in posttraumatic CSF leak are generally reserved for recalcitrant leak despite conservative measures, loss of facial nerve function, and evidence of brain herniation. The majority of operative interventions for lateral skull base repair involve transmastoid, retrosigmoid, or middle fossa approaches. In the instance of a persistent leak in the face of a transverse temporal bone fracture, where there is complete ipsilateral sensorineural hearing loss, a transpetrosal approach including the labyrinth and cochlea for resection, facial nerve mobilization and repair if this is indicated, and sealing of the cavity by free fat grafting and closure of the external auditory canal is the preferred method for managing this situation. By contrast, CSF leak of the anterior cranial fossa have been increasingly managed via transnasal endoscopic techniques. The nasoseptal flap is commonly utilized via endonasal skull base approaches, whereas pericranial flaps, temporalis muscle, galeofrontalis flap, or intracranial free tissue transfer can be utilized for open approaches.

**Infection**

Infections of the meninges and brain parenchyma can be a source of significant morbidity and mortality following skull base surgery. Key prevention practice guidelines include perioperative antibiotics, sterile technique, minimizing dural exposure to aerodigestive tract, and attention to detail during reconstruction. When the barrier between the intranasal and intracranial cavities is disrupted, it is imperative to recreate a water-tight seal to prevent ascending infection. Patient demographics play a significant role as patients with multiple comorbidities such as diabetes mellitus tend to be more susceptible to postoperative infection. History of radiation therapy leads to poorly vascularized tissue of the skull base and increased infection risk if reconstruction is performed without using vascularized nonirradiated tissue. Management of postoperative infection includes antibiotics. Surgical exploration is indicated for abscess drainage and removal of contaminated sources.
Due to the proximity of the sinonasal cavities to the anterior skull base, specifically the frontal and ethmoid sinuses, open surgical approaches through sinuses cavities require proper management of sinonasal drainage pathways to avoid frontoethmoidal mucoceles. Endoscopic ethmoidectomy with marsupialization can address ethmoid mucoceles. Frontal sinus mucoceles can occur when the frontal sinus outflow tract becomes obstructed. Maximizing medical management is important in the treatment of chronic rhinosinusitis.

Orbital
Visual disturbance can have significant impact on patient quality of life postsurgery. In anterior skull base defects involving the orbit, injury to or paresis of the optic, oculomotor, trochlear, and abducens nerves can result in diplopia or even loss of vision. Additionally, injury to the trigeminal branches can lead to loss of corneal sensation, increasing the risk for corneal injury. Facial nerve paralytic can lead to exposure keratitis secondary to lagophthalmos. Epiphora was noted to be the most common delayed orbital complication following resection of malignant skull base tumors. Pulsatile exophthalmos can occur secondary to intraorbital meningoencephalocele where the arterial pulsations are transmitted from the vessels in the brain and passed through the CSF and blood–brain barrier directly to the orbit. Additionally, pulsating exophthalmos can occur following surgery or trauma in the region of the orbit by a delayed arteriovenous malformation (AVM). These AVMs are difficult to manage as they invariably involve the cavernous sinus and require extensive angiographic investigation and management. Orbitozygomatic osteotomies in open skull base approaches thus require two-thirds of orbital roof to prevent pulsation transmission to orbit or enophthalmos. In cases where significant orbital defects are present following ablation, reconstruction with titanium mesh, custom implant, or bone grafting is recommended.

Cosmetic Deficits
While not a direct complication following many open approach craniotomies, well-planned incisions can avoid obvious scarring and deformity for patients, leading to improved patient satisfaction and self-image. Cranial incisions are placed ideally behind the hairline and in natural skin creases. Designing of scalp flaps must take into account the regional blood supply to avoid flap necrosis and potential subsequent implant or calvarial exposure. Bony defects are reconstructed with either alloplasts or autograft to recreate calvarium contour. Complications of scalp skin thinning over titanium mesh cranioplasty has been described by Yoshioka and Tominaga and hypothesized to be secondary to pressure differential between the intracranial cavity and atmosphere. The senior author’s (Y.D.) preferred cranioplasty approach includes initial titanium mesh reconstruction followed by replacement with polyether ether ketone patient-specific implant to optimize aesthetic contours and avoid thinning of skin overlying the mesh cranioplasty.

Management of Complications
The objectives of surgical correction of skull base complications include (1) separation of the intracranial cavity from the upper aerodigestive tract, (2) obliteration of intracranial dead space, (3) replacement of nonviable areas with vascularized tissue, and (4) restoration of facial cosmesis. Initial skull base reconstruction inevitably fails when one or more of these objectives is not met. The described complications indeed can present simultaneously as CSF leak, infection, and pneumocephalus. Often, when less invasive approaches fail, there is need to go further down the reconstructive ladder. – Fig. 1 is an algorithm taking into account prior radiation and limitations of endoscopic repair.

Endoscopic Repair
With advances in endoscopic techniques and technology, the role of endoscopic repair of anterior cranial fossa complications has expanded considerably and is now the standard for repair of many traumatic CSF leak of the anterior cranial fossa. The success of endoscopic repair is dependent on the ability to identify the location of the leak in addition to proper characterization of the defect size. Intrathecal fluorescein has been advocated by some groups to help localize the leak. Multilayered closure using free grafts of muscle, cartilage, bone, fat, or fascia have been described as superior to single layer. Intradural underlay techniques are advocated by some. In the setting of high flow CSF leak, vascularized pedicled flaps including the nasoseptal flap and pericranial flaps are more robust than nonvascularized free grafts with closure rates of 90 and 82%, respectively.

Open Anterior Approach, Locoregional Flaps
Transcranial and transfacial approaches are generally reserved for large skull base defects and CSF leaks, complications that have failed endoscopic management, or where intracranial complications may concurrently arise such as epidural hema-tomas. The access granted from various anterior craniofacial approaches allows addressing skull base defects beyond the scope of endoscopic approaches and enables multilayered reconstruction with vascularized tissue in many cases. Skull base reconstruction studies are largely of heterogeneous pathology and relatively small sample sizes. This in addition to surgeon preference limits the ability to compare objectively different reconstructive approaches to elucidate the ideal method. In complex skull base defects, rarely is there a single method that is optimal in every patient.

Nonvascular, free graft material utilized in skull base reconstruction include perichondrium, periosteum, tensor fascia lata, temporoparietal fascia, bone grafts from calvaria and other sources, and abdominal free fat grafts. Allograft and alloplastic material is available as well in various forms but have a theoretical increased risk of infection compared with autografts. In the 1960s, Ketcham et al described unacceptably high CSF leak rates following skin graft duraplasties that has led to a shift to vascularized tissue reconstruction. While no longer the workhorse reconstruction for skull base defects, these remain viable options particularly when regional flaps
are not available or patients are unsuitable candidates for free tissue transfer. ►Fig. 2 demonstrates a case of recurrent sinonasal malignancy presenting as a brain abscess. A large tensor fascia lata graft was needed for separation of the sinonasal cavity from the intracranial space as prior pericranial flap was harvested and patient was not an ideal free flap candidate given multiple comorbidities and medical deterioration. Free calvarial bone grafts can be augmented with vascularized regional flaps for reliable reconstruction of mid-face and orbit defects to restore cosmesis and function.

While the nasoseptal flap has revolutionized endoscopic skull base reconstruction, it has limited use in open anterior approaches as often the septum is resected due to the advanced nature of such tumors. The pericranial flap has been the workhorse of anterior open skull base reconstruction. Based off the supratrochlear and supraorbital vessels, the flap can offer a large surface area of coverage with significantly long reach and reliable vascularity. Smith and Ducic describes an extended pericranial flap technique by modifying the flap elevation in a suprapercranial plane posteriorly along the occiput allowing an extra 10 to 14 cm of length on the flap.

The temporalis muscle and temporoparietal fascia flaps are excellent laterally based vascularized flap options. The temporalis muscle has the added benefit of tissue bulk, allowing it to fill dead space. It is an excellent option for combined orbital and anterior skull base defects as the soft tissue bulk allows filling of the orbital cavity, but the muscle is limited in reach due to arc of rotation and muscle length, making it not ideal for any contralateral reconstruction. Sokoya et al describe a modification by making a sphenoid keyhole and tunneling the temporalis muscle flap through for orbital skull base reconstruction. The advantages of this approach include reducing the arc of rotation and providing a tension-free reconstruction with vascularized muscle.

The temporoparietal fascia flap is based off the superficial temporal artery and has similar properties to the pericranial flap. It can similarly be tunneled via keyhole approaches for skull base reconstruction and thus can be utilized for both lateral and anterior skull base defects. Patel et al describes the use of temporoparietal fascia flaps in lateral skull base tumor reconstruction and noted decreased incidence of CSF leak rates compared with those who underwent free fat graft.

Other regional flap options are limited for the anterior skull base due to limitations of reach. The trapezius, latissimus, and pectoralis flaps are potential options for lateral skull base reconstruction with the added benefit of the option to bring large amounts of vascularized muscle, fascia, and skin. Supraclavicular artery island and submental island flaps are fasciocutaneous flaps that have been described to

Fig. 1 Algorithm for cerebrospinal fluid (CSF) leak repair.
Fig. 2  (A) Frank purulence within the frontal sinuses, (B) communication of anterior cranial fossa and frontal sinus with nasal cavity in the setting of nasopharyngeal carcinoma recurrence after prior resection and chemoradiation, (C) cranialization with free fat graft obliteration of the frontal outflow tract, (D) harvest of large tensor fascia lata graft, (E) application of tensor fascia lata graft along anterior skull base to separate intranasal and intracranial cavities, and (F) titanium mesh cranioplasty.

Fig. 3  Left, harvest of extended pericranial flap through coronal approach left attached to the anterior scalp until needed to prevent desiccation. Right, frontal sinus obliteration with temporalis muscle plug to be followed by pericranial flap.
reconstruct lateral temporal bone defects. These are based off the transverse cervical vessels and submental pedicle, respectively, and use is limited in patients with prior neck dissection where the vascular supply may be potentially injured.

**Free Tissue Transfer**

Microvascular reconstruction allows added flexibility in flap design not limited by the pedicled nature of regional flaps. Additionally, composite vascularized tissue of skin, fascia, and muscle can be introduced to accomplish multiple objectives of skull base reconstruction, including obliteration of dead space and sealing off the intracranial cavity from the upper aerodigestive tract. Neligan et al reported decreased complication rates with microvascular free tissue transfer compared with regional flaps in skull base reconstruction.\(^\text{12}\) Califano et al reported no difference in major complication rates between regional flaps and free tissue transfer.\(^\text{11}\) Inman and Ducic reported the use of intracranial free flap with keyhole craniotomy for pedicle in the setting of massive CSF leak of the anterior cranial fossa.\(^\text{25}\)

Rectus abdominis free flaps have been the workhorse of skull base reconstruction given reliable anatomy from the deep inferior epigastric artery, adequate bulk to obliterate large complex dead space, and ability to harvest as both muscle only or with skin paddle.\(^\text{26}\) The anterolateral thigh flap has been recently popularized as a good alternative for skull base reconstruction with less donor site morbidity.\(^\text{27}\) Based off the lateral femoral circumflex artery, a primary disadvantage is variability and lack of length of the pedicle. The radial forearm free flap is a reliable flap for head and neck reconstruction. Based off the radial artery, its advantages include a long pedicle, pliable nature allowing it to fold and conform to complex defects ideal for orbital skull base reconstruction, and ability to harvest as fascial only flap for vascularized intracranial coverage of the anterior skull base when other regional options have failed (►Fig. 4). Various other soft tissue flaps have been described for skull base reconstruction, including the latissimus dorsi, lateral arm fasciocutaneous flap, and omental flap. The ultimate decision on which type of flap to utilize lies with the reconstructive surgeon’s experience and preference.

Bony flap reconstruction of the skull base is controversial. Studies report use of fibula, scapula, and iliac crest osseous free flaps for reconstruction of the orbital rim and mid-face in the setting of skull base defects.\(^\text{28-32}\) Alloplastic material such as titanium mesh and patient-specific implants have made it possible for aesthetic restoration of calvarial and orbital defects. Bony free flaps have the advantage of lower resorption rates compared with free bone grafts, but added operative times and technical difficulty in mid-face reconstruction have limited their role in skull base reconstruction.

**Conclusion**

Reconstruction of skull base defects remains a challenging endeavor given the complex spatial anatomy. Complication rates have improved with advances in transnasal endoscopic techniques and technology as well as free tissue transfer. Successful management of skull base complications requires surgical separation of intracranial and aerodigestive tract, obliteration of intracranial dead space, reinforcement of repair with vascularized tissue when possible, and restoration of aesthetic and function. Accomplishment of these objectives requires an individualized approach that may range from endoscopic transnasal repair to open transfacial, transcral approaches with free tissue transfer.

**Conflict of Interest**

None declared.
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