Endoscopic trans-nasal craniotomy

Author:
Harvey, Richard

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Endoscopic trans-nasal craniotomy

Richard J Harvey

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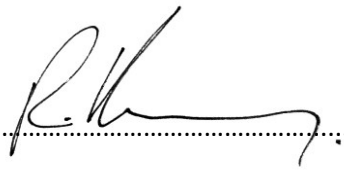
Signed 

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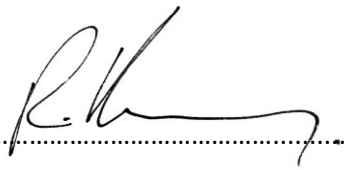
Signed ……  ……

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NSF – Nasoseptal Flap, ITF – Inferior Turbinate Flap, MTF – Middle Turbinate Flap, PCF – Pericranial Flap, TPFF – Temporoparietal Fascia Flap, PF- Palatal Flap

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Publications arising from thesis

1. Harvey RJ, Shelton W, Timperley D, et al. Using fixed anatomical landmarks in endoscopic skull base surgery. *Am J Rhinol Allergy.* Jul-Aug 2010;24(4):301-305.

2. Harvey RJ, Parmar P, Sacks R, Zanation AM. Endoscopic skull base reconstruction of large dural defects: A Systematic Review of Published Evidence. *Laryngoscope.* Feb 2012;122(2):452-459.

3. Harvey RJ, Malek J, Winder M, et al. Sinonasal morbidity following tumour resection with and without nasoseptal flap reconstruction. *Rhinology.* accepted November 12th 2014 2014;accepted November 12th 2014.

4. Jo HW, Dalgorf DM, Snidvongs K, Sacks R, Harvey RJ. Postoperative irrigation therapy after sinonasal tumor surgery. *Am J Rhinol Allergy.* Mar-Apr 2014;28(2):169-171.

5. Harvey RJ, Winder M, Davidson A, et al. The olfactory strip and its preservation with a modified nasoseptal flap in endoscopic pituitary surgery maintains smell and sinonasal function. *Journal of neurological surgery. Part B, Skull base.* 2015; in press

6. Harvey RJ, Nalavenkata S, Sacks R, et al. Survival outcomes for stage-matched endoscopic and open resection of olfactory neuroblastoma. *Head & Neck.* 2015;under review.

Declaration

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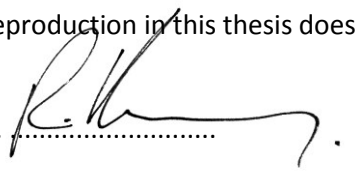

... .

Richard Harvey

Supervisor statement

I herby certify that all co-authors of the published or submitted papers agree to Richard John Harvey submitting those papers as part of his Doctoral Thesis.

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Date 13/1/15

Chapter 1

Introduction

Over the past 10 years, advancements in anatomic understanding and technical developments coupled with improvements in instrumentation have facilitated the exposure and resection of intra-dural lesions via fully endoscopic endonasal approaches [(1)] . While endonasal skull base surgery encompasses a wide range of surgical pathology including everything from extradural benign tumors to sinonasal cancers to intra-dural primary brain tumors, the endoscopic trans-nasal craniotomy very much defines the surgical intervention of an intracranial intra-dural procedure. It is this approach that has led to a fundamental shift in the way skull base pathologies are now managed. There is evidence that both neurological[(2)], visual[(3)] and functional[(4)] outcomes are superior with an endoscopic endonasal approach[(5)]. Additionally, patients have a faster recovery and less in-hospital time post-surgery [(6)].

When the initial outcomes of successful endonasal resection were first reported, the primary disadvantage documented was postoperative cerebrospinal fluid (CSF) leak from where the dura was violated during surgery[(7)]. A significant shift has occurred in the techniques now employed to reconstruct this barrier. Collagen grafts and dural substitutes along with vascularized mucosal flaps have dramatically improved the reliability of skull base reconstruction [(8, 9)]. The traditional "Achilles' heel" of trans-nasal craniotomy appears to have had an answer. However, the use extensive vascularized mucosal flaps, their associated donor site morbidity and impact on subsequent nasal function has raised debate [(10, 11)].

In managing skull base pathology, the surgeon comfort should never dictate the surgery performed. The anatomical location and areas involved by pathology should always be the determining factor. Similarly, pathology such as inverted papilloma, should never imply a particular surgery; 'endoscopic medial maxillectomy' or 'lateral rhinotomy'. While endoscopic resection has replaced many open approaches, a combination of techniques is still used to remove extensive disease. The endoscopic surgeon performing extended procedures should be equally comfortable performing a similar open procedure. Endoscopic surgery should not imply conservative surgery and the concept of curative intent for malignancy is paramount. Ensuring the resection is complete for malignancy is critical and an oncologic principal [12]. If pathology is considered non-resectable via open approaches then it is axiomatic that this is true for the endoscopic option.

Endoscopic removal of benign neoplastic disease of the anterior skull base and paranasal sinuses is now widely practiced[13]. Selected malignancies can also be successfully managed by an endoscopic approach [1, 14, 15]. Unfortunately, the evolution of adapting such techniques is slow. Training and development of skilled surgeons is hampered by the low incidence of skull base pathology and the significant morbidity that can be associated with complications. In a survey of surgeons from the North American Skull Base Society the proportion utilizing endosopic techniques in trans-cribriform operations was 70.5%, trans-planum 66%, and in trans-clival, only 66%[16]. Less than 17% of practising Rhinologic surgeons have experience in >50 cases per year [17]. Although both virtual[18] and animal models are available to assist with training[19, 20], real-life experience is still required with a minimum case volume of 20-30 procedures estimated to overcome the learning curve[21] along with a progression through complexity[22]. Contemporary skull base surgeons are keen to avoid the orbital and cranial

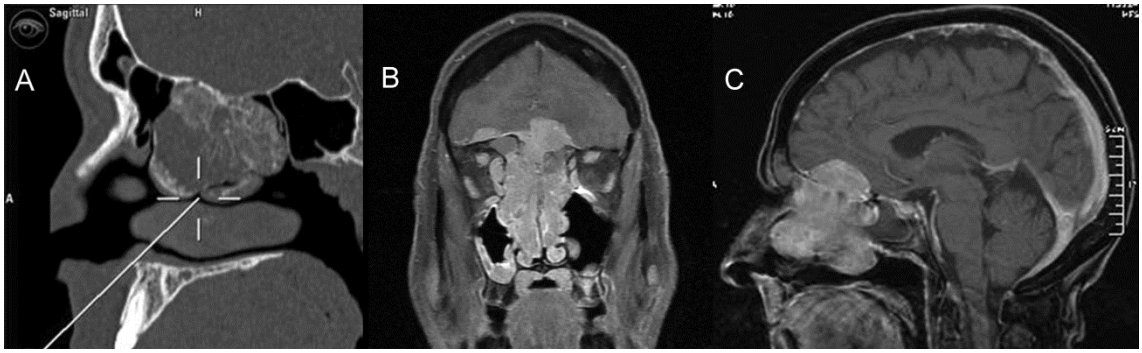
complications that were associated with the introduction of endoscopic techniques to managing inflammatory sinus disease in the 1980s and 90s.

This thesis represents a collection of work that was designed to address several key evolutionary steps in the progression of the endoscopic trans-nasal craniotomy. Firstly, the ability of the surgeon to define the skull base even in the presence of extensive disease is critical. It can appear daunting to locate key landmarks via an endoscope in such a surgical field (figure 1). However, simple anatomical rules can be followed to achieve this. The ability to close the skull base and separate the intra-cranial cavity is paramount. This prevents subsequent intracranial infective episodes and avoids some of the severe sequelae of skull base complications [(23)]. Although, vascularized flaps have improved perioperative outcomes, the data to demonstrate that this was possible beyond a few large institutions was lacking. Collation of research efforts is essential to provide a path forward for further development. The impact of endonasal tumour surgery on the nose and sinonasal function is an important secondary endpoint in malignancy and an even more important outcome in managing benign disease via an endoscopic endonasal route. Ensuring that the impact of new techniques is known is essential for decision making. Different post-operative regimes exist to assist with this recovery. Defining the optimal post-operative care to achieve sinonasal recovery is explored. Finally, the application of these techniques to the sinonasal and olfactory outcomes in the management of benign pituitary adenoma surgery is assessed. In malignant disease, the impact of the endoscopic trans-nasal craniotomy on the survival and oncologic outcomes in the management of olfactory neuroblastoma reflects the direct application of the evolution of the endoscopic trans-nasal craniotomy.

Figures

Figure 1.1

Large skull tumours obscure the common landmarks used during endoscopic sinus surgery for inflammatory disease. (A: Chondrosarcoma, B: Atypical meningioma, C: Olfactory neuroblastoma)



Chapter 2

Using fixed anatomical landmarks in endoscopic skull base surgery

Abstract

Objective

The identification of anatomical landmarks in endoscopic skull base or revision sinus surgery can be challenging. Normal anatomy is significantly altered with many paranasal tumors. Traditional endoscopic surgical landmarks extrapolated from inflammatory disease, such as the superior turbinate, may have been previously removed or involved in pathology. A frequently used rule to enter the sphenoid ; 'Stay below or at the level of the orbital floor as dissection proceeds posterior and one will avoid the skull base' is assessed anatomically.

Methods

The maxillary sinus roof height, relative to the nasal floor, was assessed as an operative landmark. Computed tomography (CT) performed on paranasal sinuses were studied. The relative height, ratio and proportions of the maxillary sinus, ethmoid roof, cribriform fossa and sphenoid planum were measured using computerized assessments.

Results

Three hundred paranasal sinus systems were evaluated. The roof of the maxillary sinus was below the level of the skull base in 100% relative to the cribriform and 100% to the sphenoid planum. The mean distance of the maxillary roof below the skull base was 10.1$\pm$2.7mm for the cribriform and 11.0$\pm$2.9mm for the sphenoid.

Conclusion

The maxillary sinus roof can be used as a robust landmark to allow safe dissection and de-bulking of pathology. Pathology removal can proceed posterior with this landmark to enable a safe entry to the sphenoid sinus, and thus the true skull base, when normal structures such as the superior turbinate and ostium are not available.

Introduction

Endoscopic resections of benign neoplastic disease of the anterior skull base and paranasal sinuses is now widely practiced[13]. Selected malignancies can also be successfully managed by an endoscopic approach[14, 15]. However, anatomy for endoscopic surgeons has its foundations in functional endoscopic techniques[24]. Uncinectomy and 'removal of the bulla' have little meaning to those removing large bulky pathology from the para-nasal sinuses. Large tumors, such as inverted papilloma or malignancy, may have significantly distorted or destroyed these functional anatomic features. While it is important to include the natural ostia into any final endoscopic resection cavity, the steps to gain orientation for tumor resection differs from surgery for inflammatory disease. Similar challenges may be faced in revision endoscopic surgery for inflammatory disease where the usual landmarks have been removed or altered by the previous surgery. In this situation, the uncinate process, turbinates and ethmoids may be absent and the use of fixed anatomic landmarks is required.

Discovering fixed anatomy allows safe dissection and completeness of tissue removal. The nasal floor, posterior choana, Eustachian tube opening, skull base, sella, and orbital wall are the fixed anatomical features that we seek out during endoscopic surgery. Finding traditional anatomic landmarks around the periphery of tumor will always be the mainstay of endoscopic orientation. Similarly, the contra-lateral paranasal sinus anatomy can be used to find key landmarks, such as the sphenoid roof, for small lesions. However, for bulky tumors that span nearly orbit to orbit, these techniques may not be practical. Discovery of the maxillary sinus will lead to location of the orbital floor (maxillary sinus roof) and the sphenoid sinus allows identification of the skull base (sphenoid sinus roof). However, significant tumor bulk can sit between these two key landmarks and prevent quick progress (Figure 1). Image guidance

surgery (IGS) can greatly enhance our confidence and orientation in this situation[25]. But IGS is an accessory not always available, accurate or reliable.

The use of the orbital floor and orbital axis is commonly taught at tertiary rhinologic and skull base units[26]. However, this teaching was a law learnt from experience rather than data driven. 'Stay below or at the level of the orbital floor as dissection proceeds posteriorly and one will avoid the skull base' (Figure 1); this rule of orientation is founded in experience and wisdom rather than data driven. The reference point is the nasal floor to ensure that a parallel line extending from the maxillary sinus roof (orbital floor) will allow safe entry to the sphenoid sinus. This study aims to evaluate the utility of this rule as it applies to providing a safe route of entry into the sphenoid when all other anatomical features have been distorted. Once the sphenoid roof is located, the remainder of the skull base can be identified by working from posterior to anterior.

Methods

A cross-sectional study of previously performed computed tomography (CT) scans undertaken for paranasal sinus imaging at St Vincent's Hospital, Sydney Australia, University of Utah Hospital, Salt Lake Salt Lake City, UT, and the Medical University of South Carolina, Charleston SC was performed. A measurement protocol was followed to ensure consistency of measurements between sites. Pilot data was presented from each site, prior to study commencement, to ensure standardization of assessors. Institutional research and ethics review approval was obtained at each site

Radiological Measurements

The maxillary sinus roof was taken at the maximal height within any area of the maxillary sinus. This was usually posterior. The nasal floor is the reference point as this landmark is available to the endoscopic surgeon. The measurements were taken in two anatomical planes. Coronal and sagittal reconstructions were modified so that the nasal floor was horizontal (Figure 2). Sagittally, the right plane centred on the superior turbinate (or close to) was used to: a) Measure nasal floor to height of skull base at the anterior sphenoid wall, b) Measure nasal floor to lowest point of the sphenoid floor (Figure 3). This was repeated on the left. The measurements were made sagittally at the level of the superior turbinate for consistency and are likely to represent a common plane of entry to the sphenoid sinus.

In the coronal view, a single view at the maximum height to the right maxillary sinus was used to: a) measure nasal floor to right maxillary sinus roof, b) measure nasal floor to right ethmoid roof and c) measure nasal floor to right cribriform (Figure 4). If there was a lower cribriform height at another point anterior to sphenoid (based on sagittal review as well) then this was used for the cribriform roof height. The measurements were repeated on the left.

Statistical Analysis

The majority of the study results are descriptive data only. Statistical assessments were performed as parametric data after normality was confirmed from histogram. ANOVA analysis was used to compare the three institution groups. The measurements were assessed with unpaired t-test analysis. Pearsons correlation coefficient was used to relate maxillary to ethmoid height as an influence on distance to skull base. Calculations were performed with SPSS Version 15 (Statistical software for social sciences, SPSS Inc. Chicago, IL).

Results

One hundred and fifty CT scans were reviewed at three institutions. In total, 300 sinus systems were assessed. There was excellent correlation between each institution's reporting. Similar maxillary roof to sphenoid roof measurements were reported from Charleston, Sydney and Salt Lake (10.5±2.8mm, 11.5±3.3mm and 11.1±2.4mm, ANOVA $p>0.05$).

In 300 measurements, no maxillary sinus roof (orbital floor) was higher than the sphenoid roof or lowest cribriform height. The minimum distance between maxillary sinus roof and sphenoid planum was 3.9mm and to the cribriform 4.0mm. The mean distances were 11.0±2.9mm and 10.1±2.7mm for these two landmarks (Table 1).

Some patients have a very high and well pneumatized maxillary sinus (Figure 5). The distances to critical anatomy were reduced but the rule held true even for those with ethmoids accounting for less than 20% of the total height (Figure 6). There was a close correlation between a well pneumatized maxillary sinus and tighter, narrower corridor to the sphenoid and cribriform (Pearsons $r=0.57$ and $r=0.70$ $p<0.001$ for both). The mean distance between the maxillary roof and the roof of the ethmoid at that point was 14.5±3.5mm. The mean sphenoid depth was 23.1±3.8mm. The maxillary roof line intersects the anterior sphenoid face at 52±13% of the height of the sphenoid. This entry point was higher with increasing maxillary sinus pneumatization but the correlation was not as strong ($r=0.40$, $p<0.001$) and might reflect greater sphenoid pneumatization in these patients as well.

Discussion

During endoscopic surgery, we follow a structured approach to the identification of fixed landmarks to allow quick and easy orientation in relation to the skull base. The nasal floor is an essential landmark and is always considered the reference plane when discussing other landmarks, The stepwise approach is followed: floor of nose and inferior turbinate, posterior choana and Eustachian tube orifice, maxillary sinus roof (orbital floor) and posterior wall and then the medial orbital wall. The next group of landmarks are in the posterior skull base, superior turbinate (defining the lateral boundary of the olfactory cleft), skull base (sphenoid roof to posterior frontal table) and finally a clear view of the orbital axis (optic nerve to lamina papyracea). The superior turbinate serves as a key landmark in ESS[27, 28]. However, when the superior turbinate is not available, previously resected or replaced by pathology, transitioning from the anterior group to the posterior group of landmarks can be challenging. Superior dissection will potentially damage the olfactory fossa or posterior ethmoid roof.

Although it may appear obvious that the maxillary sinus roof is below the skull base, the distances are within one or two instrument depths. The maxillary sinus roof represents an excellent landamark for entry to the sphenoid sinus. The study presents a reliable orientation rule for the endoscopic surgeon, that can be used both during surgery for neoplastic or inflammatory disease. ‘Stay below or at the level of the orbital floor as dissection proceeds posterior and one will avoid the skull base’. The level of dissection is always relative and parallel to the nasal floor. The anatomic and surgical rule represents a reliable evidence based approach (Figure 1). It is not in substitution of careful discovery of normal anatomy around the tumor to ensure good orientation. However, with bulky disease that fills the operative area, it can assist debulking of tumor and further posterior discovery of a safe entry to the sphenoid and thus allowing identification of the skull base.

Casiano published on the use of the medial orbital floor as a key landmark[29]. He recognized that the medial orbital floor was a safe distance from the carotid, optic nerve and orbital roof. Distance down to the sphenoid floor and the roof of the ethmoid sinus was also recorded. Direct distances were used rather than a vertical height relative to a fixed anatomic landmark (the nasal floor) as described in this study. The medial orbital floor was also noted to approximate to 40% of the sphenoid height. There was approximately 14mm and no less than 10mm between this landmark and carotid, optic nerve, ethmoid roof and anterior ethmoidal artery. The current study compliments this data to support both vertical location as well as direct proximity of the orbital floor as a useful surgical landmark in the skull base. Orlandi et al. acknowledged that perforation of the basal lamella at the level of the maxillary sinus roof will be a safe maneuver in proceeding to posterior ethmoidectomy[28]. This is supported by the Casiano study. However, the remaining technique described relies on discovery of the superior turbinate, sphenoid ostium and posterior ethmoid cells that may not be available with neoplastic pathology.

Large well developed maxillary sinuses will shorten the height of the posterior ethmoid cavity and is recognized as a feature that may lead to poor surgical trajectory and potential skull base injury . Using the nasal floor and the height of the maxillary sinus roof, even in this situation, still allow a good margin of safety in approach to the sphenoid sinus (Figure 6)

Deep, Keros grade 3, cribriform fossae and the lateral lamella can be a hazard during ESS[30]. The rule of the maxillary sinus roof also maintains a good safety margin. Additionally, the few

patients with very asymmetrical nasal floors, still had a maxillary sinus roof below the skull base in posterior extension.

Experienced surgeons reporting on safe approaches to posterior dissection recommend proceeding low in the ethmoid from anterior ethmoid to the sphenoid sinuses. By the term ''low'' is referred to as parallel to the maxillary ostium, junction of the horizontal and vertical basal lamella, or lower one third of the middle turbinate[30]. This may be too conservative as the maxillary sinus roof may lie superior to the natural ostium. If dissection through the basal lamella is too low, destabilization of the middle turbinate can occur. Attempts to enter the sphenoid low on the anterior face can be difficult due to thicker bone. Additionally, defining the highest maxillary sinus roof point allows easier identification of the transition to the medial orbital wall. Discovery anterior and low can occasionally lead to a row of periorbital anterior ethmoid cells that remain unopended. The authors' alternative guides to the skull base, medial orbital wall and sphenoid sinus are described in Table 2.

There are appears to be a mean vertical distance of 10mm, from this study and direct distance of at least 10mm from the orbital floor[29] to critical anatomy. This distance encompasses the bite size of many commonly used surgical instruments (Table 3).

Conclusion

The maxillary sinus roof, or orbital floor, represents a reliable landmark based on fixed anatomy during endoscopic dissection. It represents an excellent landmark for the height of entry to the sphenoid sinus. The surgeons rule of :'Stay below or at the level of the orbital floor

as dissection proceeds posterior and one will avoid the skull base' should assist endoscopic surgeons to de-bulk tumor and locate the sphenoid at an appropriate height when other landmarks are not available.

Figures

Figure 2.1

'Stay below or at the level of the orbital floor as dissection proceeds posterior and one will avoid the skull base': Sagittal computed tomography of the skull base. The maxillary roof line, parallel to the nasal floor, can direct orientation to the sphenoid and avoid the skull base. The distance from this study, represented by the arrow, is 11.0±2.9mm.

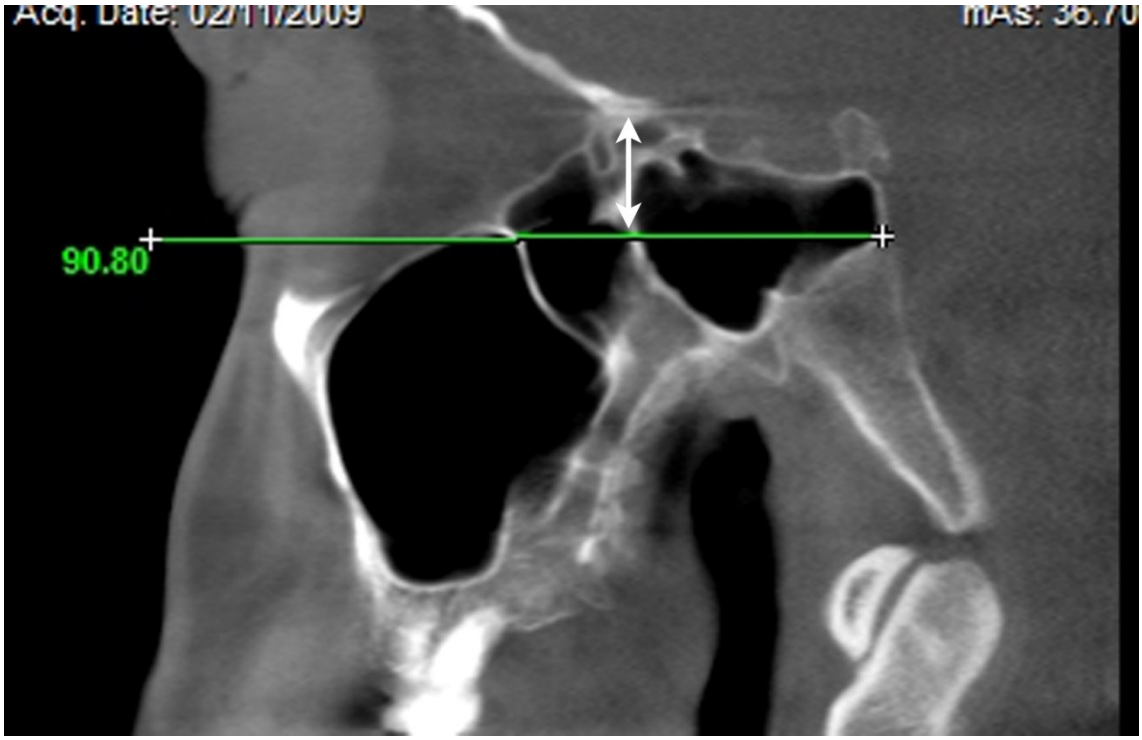


Figure 2.2

The multiplane reconstructions were reconstituted so that the nasal floor was horizontal for sagittal and coronal measurements.

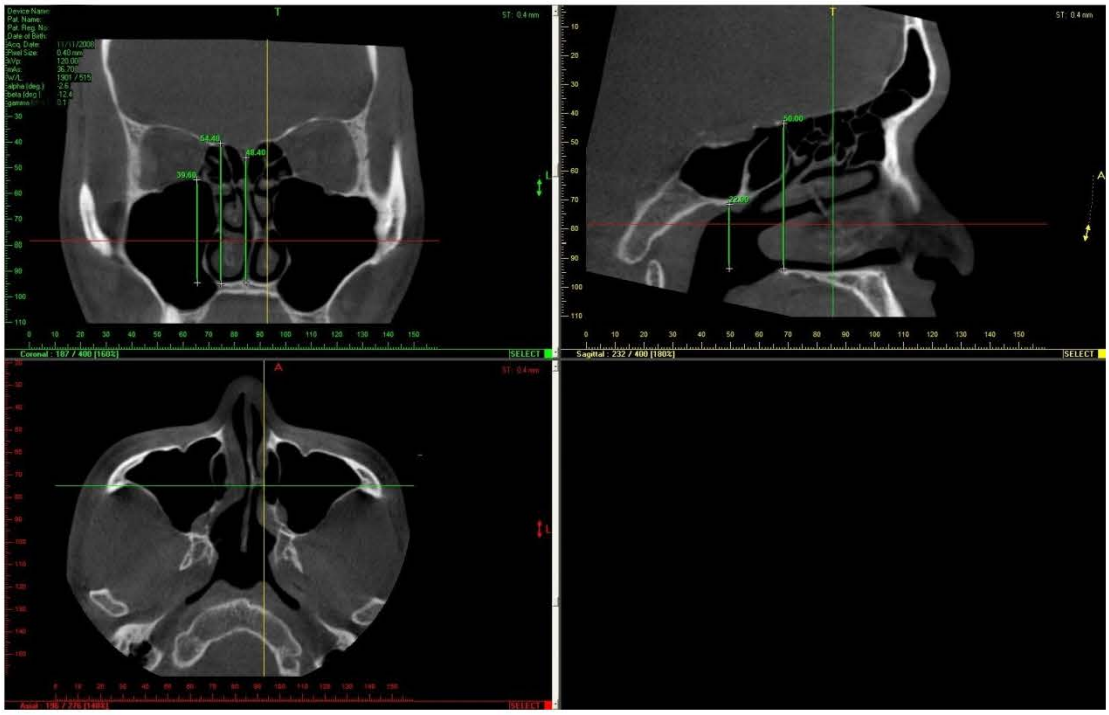


Figure 2.3

The measurements from the nasal floor to define the coronal relationships. A: The lowest height of the cribriform to the nasal floor, B: The ethmoid roof height from the nasal floor and C: The Roof of the maxillary sinus (or orbital floor). The reference point is always the nasal floor as this is available during surgery.

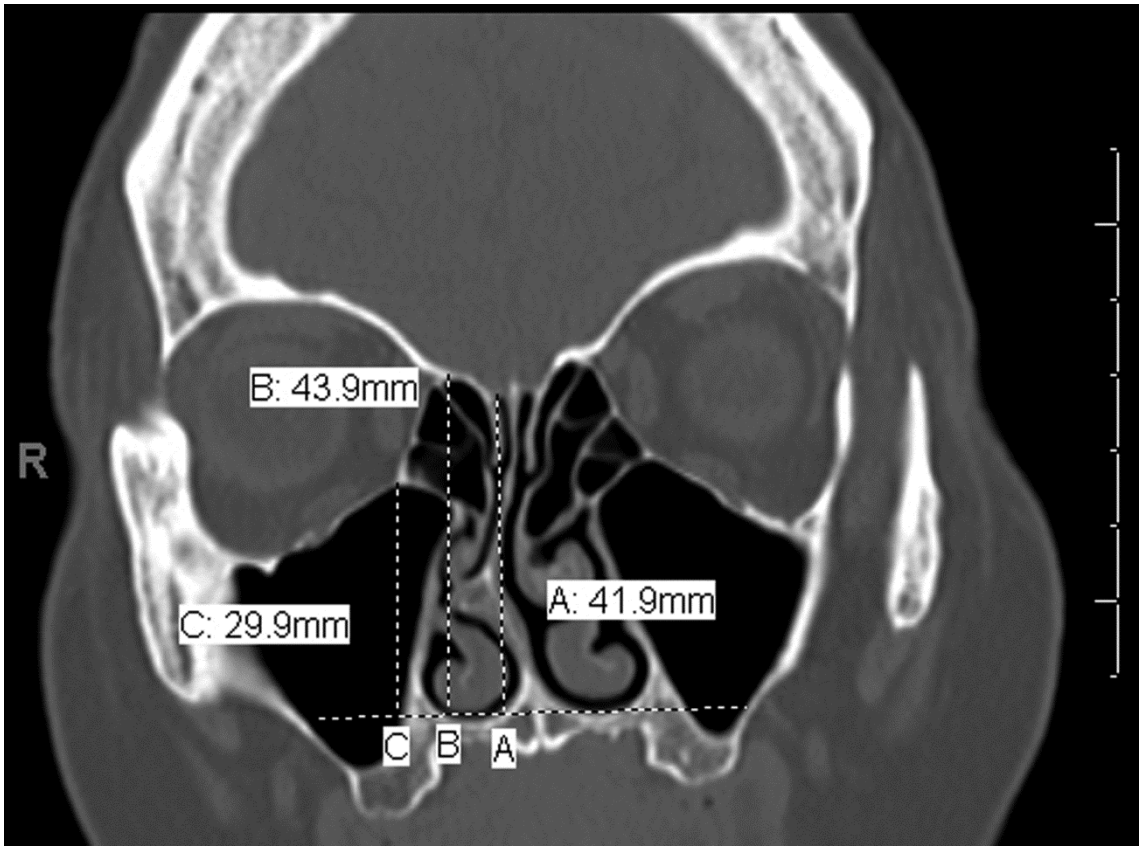


Figure 2.4

The measurements from the nasal floor to define the sagittal relationships.

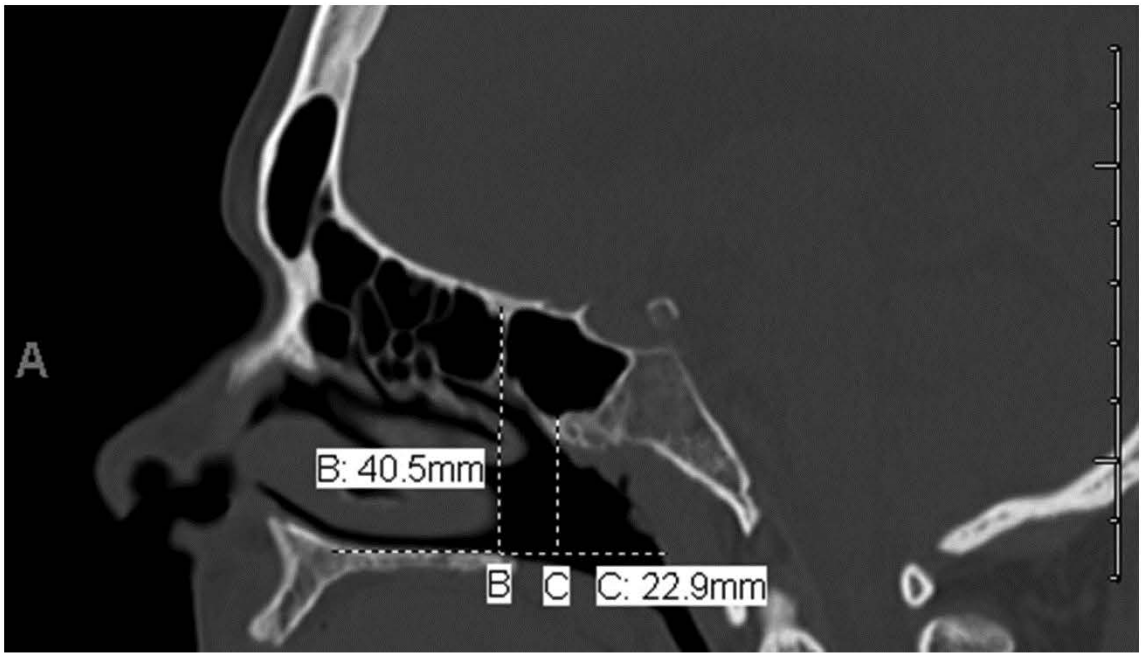


Figure 2.5

A patient with a high maxillary to ethmoid pneumatization. The distance was still 4mm between maxillary roof and cribriform on the left side in this coronal computed tomography.

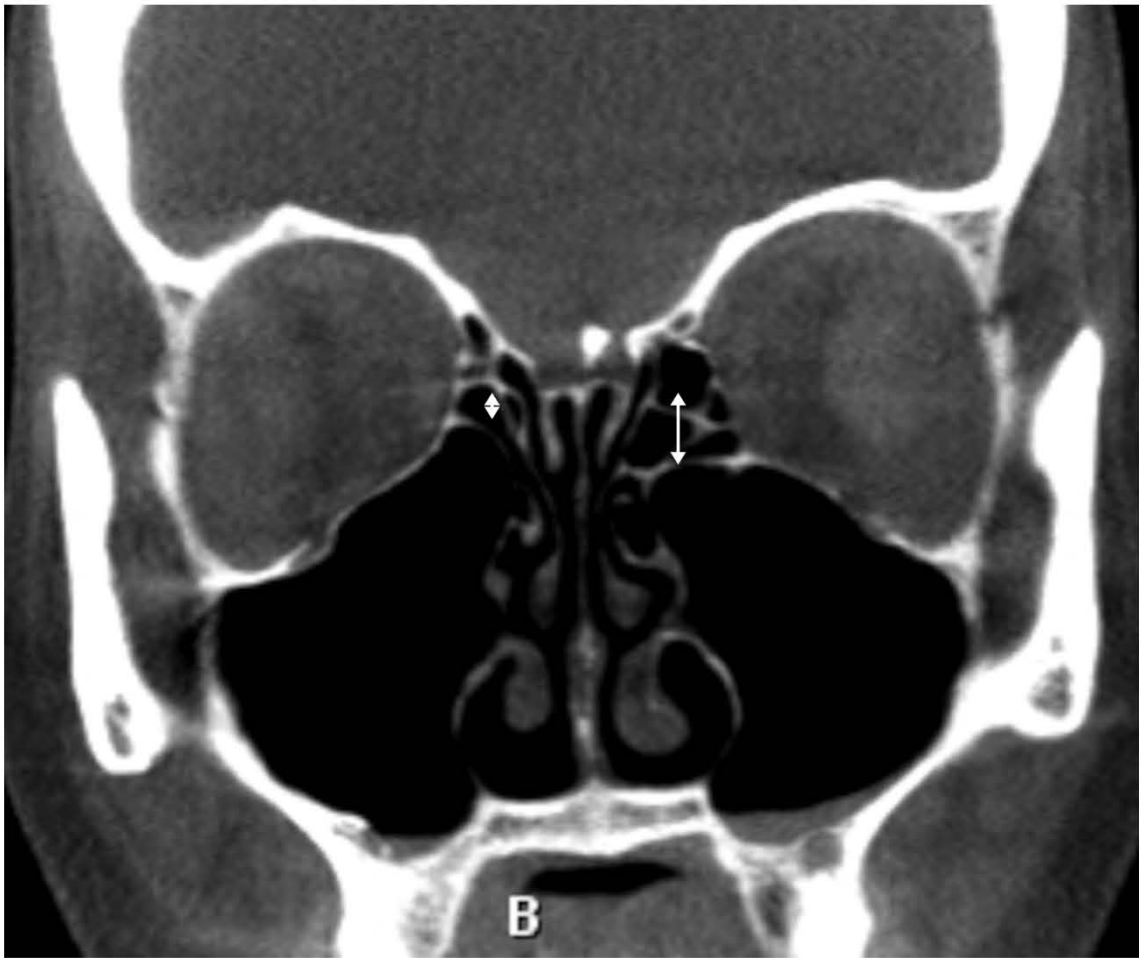
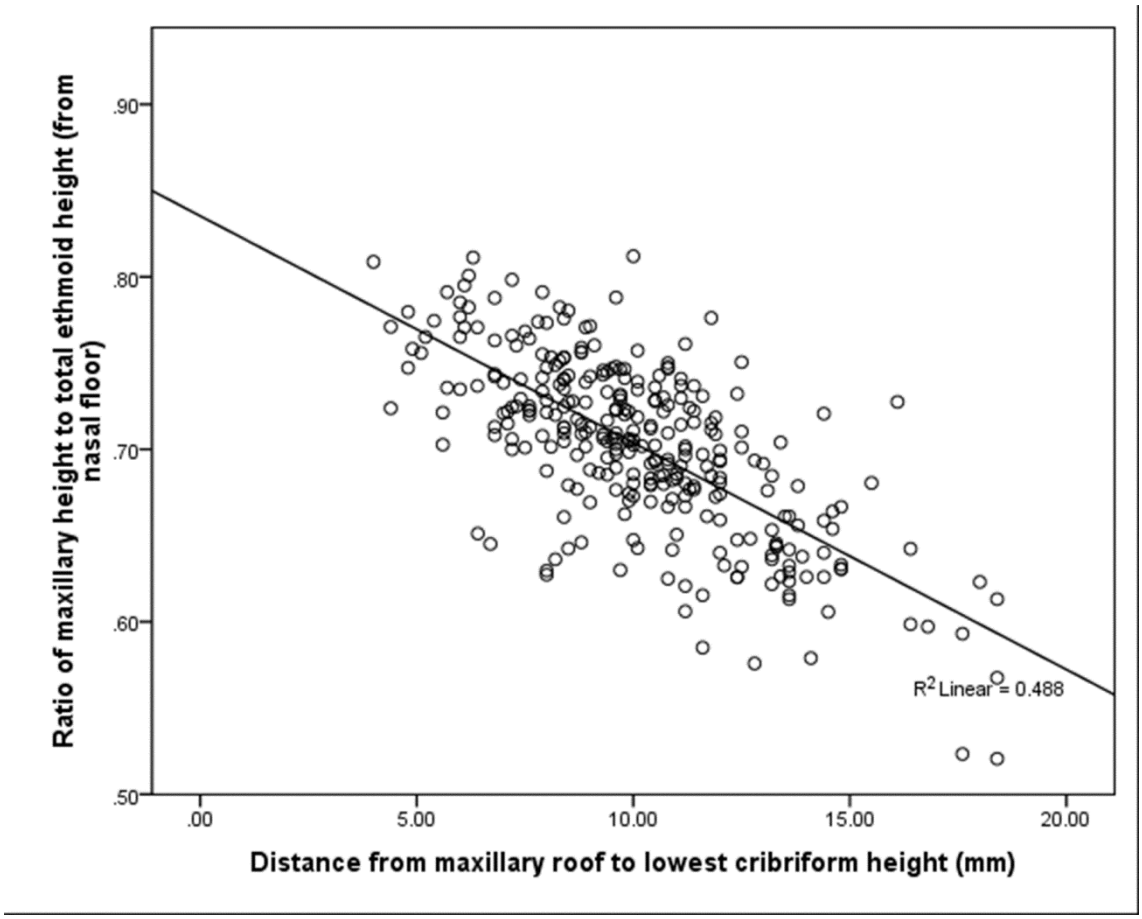


Figure 2.6

Distance to the sphenoid roof based on the extent of the maxillary sinus development to posterior ethmoid. Even for those patients with short ethmoid sinuses (<20% total height) there is still a reasonable dissection zone between the landmarks.



Tables

Table 2.1

Summary of relationship distances between nasal floor, maxillary roof and the skull base. Although it may appear a given that the maxillary sinus roof is below the skull base the distances are within one or two instrument depths.

	N	Minimum	Maximum	Mean	Std. Deviation
Maxillary Sinus Roof (Orbital Floor) from nasal floor	300	27.2	44.2	33.9	3.0
Sphenoid Roof from nasal floor	300	36.2	56.1	44.9	3.7
Lowest cribriform from nasal floor	300	34.8	53.5	44.0	3.7
Maxillary Roof to Sphenoid Roof	300	3.9	19.6	11.0	2.9
Maxillary Roof to Cribriform	300	4.0	18.4	10.1	2.7

Chapter 3

Endoscopic skull base reconstruction of large dural defects: A Systematic Review of Published Evidence

Abstract

Objective

Systematically review of the outcomes of endoscopic endonasal techniques to reconstruct large skull base defects(ESBR). Such surgical innovation is likely to be reported in case series, retrospective cohorts or case-control studies rather than higher level evidence.

Design: Systematic review

Methods

EMBASE (1980-December 7, 2010) and Medline (1950 – November 14, 2010) were searched using a search strategy designed to include any endoscopic endonasal reconstruction of the skull base. A title search selected those relevant to clinical or basic science of an endoscopic approach. A subsequent abstract search selected manuscripts of any defect other than simple CSF fistula, sella only, meningoecoele or simple case reports. The manuscripts selected were subject to full text review to extract data on perioperative outcomes for ESBR. Surgical technique was used for sub-group analysis.

Results

4770 manuscripts were selected initially and full text analysis produced 38 studies with extractable data regarding ESBR. Of these manuscripts, 12 described a vascularized reconstruction, 17 described free graft and 9 were mixed reconstructions. Three had mixed data in clearly defined patient groups that could be analyzed for meta-analysis. The overall CSF leak rate was 11.5% (70/609). This was represented as 15.6% leak rate (51/326) for free grafts and 6.7% leak rate (19/283) for the vascularized reconstructions (X^2 =11.88, p=0.001).

Conclusion

Current evidence suggests that ESBR with vascularised tissue is associated with a lower rate of CSF leak compared to free tissue graft and is similar to reported closure rates in open surgical repair .

Level of evidence: 3a

Introduction

There has been a rapid evolution of the approach to many ventral skull base pathologies in the last decade. The endoscopic route is now a preferred option for many surgical centres when managing both benign and malignant disease. Endoscopic transnasal transcranial surgery now performed was considered highly risky only 10 years ago. Much of the morbidity was associated with the inability to provide a consistent and robust separation of the cranial cavity from the paranasal sinus cavity after the endonasal resection. The reported rates of CSF leaks were as high as 30-40%[7] and with significant complications such as meningitis, abscess formation and ventriculitis; this was seen as an achilles heal for endoscopic skull base surgery with dural resections[31].

The majority of small defects (<1cm) in the skull base (most commonly encountered during CSF fistula closure, post trauma and after iatrogenic injury) are reliably repaired endoscopically using multilayered free grafts[32], with rates of success greater than 90% with minimal difference between methods or material used[32, 33]. This provides a good long term prevention of further CSF leak and intra-cranial infection [23].

For larger skull base defects (>3cm), materials used for free graft repairs have included turbinate mucosa[34], cadaveric pericardium, acellular dermis[35], fascia lata[36], and titanium mesh[37]. In general, repair of larger defects with free grafting, gives a higher rate of cerebro-spinal fluid (CSF) leak than smaller defects[38], and surgery with free graft repairs of larger defects gave unacceptably high leak rates (>30%)[35, 39].

In response to these reconstructive failures, the use of local and regional vascularised flaps in the reconstruction of large skull base defects has provided a dramatic shift in our ability to manage such large defects between the cranial and sino-nasal cavities. Local vascularised flaps have been developed that can be harvested, tailored, and used in endoscopic endonasal skull base surgery[9, 14, 40], and increasingly these vascularised flaps are becoming the repair method of choice for endoscopic skull base defect repair due to their ease of use, low donor site morbidity and low complication rates[41, 42]

The aim of this study is to critically and systematically review the data available on the perioperative outcomes of published case series, cohorts and case-control studies on endoscopic endonasal reconstruction of large dural skull base defects. The primary outcome is overall CSF leak rates in the postoperative period and a secondary data stratification withcomparison based on avascular grafting versus vascularize tissue reconstructions are described.

Methods

A systematic review of published literature was performed for the primary outcome of CSF leak rates during endoscopic skull base surgery.

Eligibility criteria

Published manuscripts in English were eligible. All manuscripts reporting original data on patients undergoing endoscopic skull base reconstruction were eligible, including those with any intervention for the treatment of specific pathologies such as meningioma and craniopharyngioma, where a large defect would be anticipated. Since this review is of large skull base defects, outcomes of patients undergoing simple closure of CSF fistulae or

encephalocoeles were excluded since the vast majority of these defects are relatively small. Only studies where an endonasal craniotomy was created as part of a procedure were included. Trials included subjects of any age, with any co-morbidity, and with varied duration of follow-up were included. Local and regional flap reconstructions of endonasal skull base surgery series were included. Case series, case-control studies, cohort studies and randomized controlled trials were included.

Search criteria

The Medline database was searched from 1950 to November 14, 2010, and the EMBASE database was searched from 1990 to December 7, 2010. The Cochrane Collaboration database and the NHS Evidence Health Information Resources website were also searched. The bibliographies of identified manuscripts were also reviewed and used as an additional data source. No unpublished trials were included. We designed a search strategy to include manuscripts relevant to any aspect of endoscopic surgery and skull base reconstruction. The search strategy used for EMBASE and MEDLINE databases is shown in Table 1.

Once the searches were completed, study selection was performed by two authors (PP and RJH) in an un-blinded standardized manner. The publications extracted were grouped by title and obvious duplicates were excluded. The abstracts were then reviewed to ascertain whether the met inclusion and exclusion criteria described above.

Data extraction

Standardized data sheets were used for each study. Some studies included more than one patient reconstructive group(vascular versus grafted repair). The primary outcomes were recorded as post operative CSF leak closure. Secondary analysis of this outcome by

reconstruction type was recorded. For each group, the type of reconstruction, pathology addressed, number of patients, success of closure as defined by need for re-operation and perioperative morbidity relevant to the reconstruction was recorded. The complications recorded included bleeding (epistaxis or intracranial), infectious complications (meningitis, subdural or intracranial abscess and ventriculitis), persistent pneumocephalus, and any mortality related to the skull base surgery.

Management of heterogeneity

The large range of methods, study aims and pathologies were reported qualitatively in the data Tables 2-4. Studies were deemed suitable for inclusion only if they described dural defect reconstructions or could provide enough information to separate extradural surgery from those that had obvious arachnoid to sinonasal communication. This ensured a study population that was not confounded by patients whom did not have a significant risk of postoperative CSF leak.

Statistical Assessment

Statistical assessments were performed primarily with descriptive data. Case by case analysis was performed for summary data. Assessment of different pathologies was performed as nominal data and analyzed using Chi-square and Fishers exact tests via SPSS software 17 (Statistical software for social sciences, SPSS Inc. Chicago, IL).

Results

The search of EMBASE and Medline produced a total of 4770 studies written in English. After exclusion of duplicates, 1088 studies remained. A title search found 416 manuscripts on skull base surgery. Of the 416 abstracts reviewed, 268 described endonasal skull base surgery. Of

these 40 (15%) were reviews of endoscopic or endonasal techniques and 38 (14%) were simple case reports. These studies were excluded from analysis. The selection process is outlined in Figure 1.

The abstract search found 190 manuscripts directly relating endoscopic skull base repair or the management of conditions in which reconstruction would be required. Those studies which described sella only reconstruction (n=34), encephalocoele management (n=9) and unique locations of simple fistula (n=9) were excluded. The full text analysis produced 38 studies with extractable data regarding endoscopic skull base reconstruction with large dural defects [7-9, 37, 41, 43-75]. 12 of these described a vascularized reconstruction[8, 9, 41, 55, 57, 58, 61, 64, 69-72], 17 manuscripts described free graft repairs[7, 37, 43, 44, 47-51, 54, 59, 64-67, 74, 75] and 9 were mixed reconstructions[8, 45, 46, 52, 53, 56, 60, 62, 68]. Three of these had mixed data levels in clearly defined patient groups that could be used for comparison in this systematic review [8, 62, 68].

The study characteristics of the 38 included manuscripts are described in Table 2-4. Perioperative outcomes were defined as CSF leak, revision surgery, infectous complications (meningitis, intracranial abscess, sinusitis), hemorrhagic complications (epistaxis, intracranial bleeding), thromboembolic events, respiratory events and mortality. Of all these, only CSF leaks were consistently reported among all 38 studies.

CSF Leak Outcomes Results

There were 609 patients with large dural defect reconstructions included in the meta-analysis from the 38 papers above. 326 (54%) underwent a free graft reconstruction and 283 (46%)

had a vascularized reconstruction. The overall rate of CSF leak was 11.5% (70/609). This was represented as 15.6% leak rate (51/326) for free grafts and 6.7% leak rate (19/283) for the vascularized reconstructions (X^2 =11.88, p=0.001). The included studies stratified by reconstruction type are listed in Table 4. The vascularized reconstruction group compare favorably to the published rates in International Collaborative Study on craniofacial surgery (6.5-25%) [76].

Other Complications

Only CSF was routinely reported from the included studies. The reported non-leak perioperative morbidity is described in Table 4. However, the lack of uniform reporting makes for an unreliable meta-analysis and is reported as descriptive only.

Discussion

Early reconstructive techniques evolved from experiences with the endoscopic repair of defects following spontaneous CSF leaks and accidental or iatrogenic trauma. Many manuscripts and a meta-analysis have validated that small CSF fistulas can be reconstructed with a wide variety of free grafting techniques achieving success in more than 95% of patients and can be successfully revised if needed[23, 32]. The application of such techniques to the larger defects as a result of surgical intra-dural approaches proved to be inadequate. Additional layering and collagen matrixes had reduced the CSF leak rate but failure remained unacceptably high[35, 39, 77].

Larger defects pose additional challenges of a wide dural resection, intra arachnoid dissection and exposure to high flow CSF with the cisterns. But perhaps the most significant influence is the larger non-vascularized reconstructive bed, CSF on one side and sinus cavity on the other. The posteriorly pedicled septal flap is the workhorse of most endoscopic intradural

skull base surgery [14, 78]. Other vascular pedicled flaps provide alternatives to address skull base defects of various sizes and locations when the posterior septal flap is unavailable. A summary of these vascularized local and regional flap options and limitations are summarized in Table 5.

The endonasal approach may appear attractive to many anteriorly based pathologies. However, there is associated sino-nasal morbidity associated with such an approach. Although endoscopic skull base surgery differs greatly from functional endoscopic sinus surgery, the final cavity left behind from the approach still needs to be functional. Crusting and short term nasal morbidity is likely to be under-reported in trials. De ameldia et al reported nasal crusting the most common (98%) symptom, followed by nasal discharge (46%), while loss of smell was reported by only 9.5% of patients[79] Crusting was short-lived with half of the patients achieving a crust-free nose by 101 days (95% CI, 87.8 – 114.2 days)[79]. Sinonasal function does appear to improve over time for these patients[80] Loss of smell is often permanent and although olfactory loss may be the consequence of an open approach its risk should be considered when choosing the endonasal route.

Advancements in endoscopic skull base reconstruction have evolved with the ever-increasing size and complexity of lesions that are approached and resected endoscopically. The principles of multilayer reconstructions and the routine use of vascularized flaps in expanded endonasal surgery have reduced post operative CSF leak rates to between 5 and 10% (6.7% in this meta-analysis). In this review, vascularized skull base reconstructions for large dural defects had a clear and significant ($p = 0.001$) advantage over free grafting in the prevention of post operative CSF leaks. Future advances will help us to understand and manage patients at high risk for a post-operative CSF leak, especially those who have been previously irradiated and/or require revision surgery. Additionally, our knowledge of reconstruction donor site morbidity,

sino-nasal quality of life and methods to reduce patient post operative healing time will continue to advance.

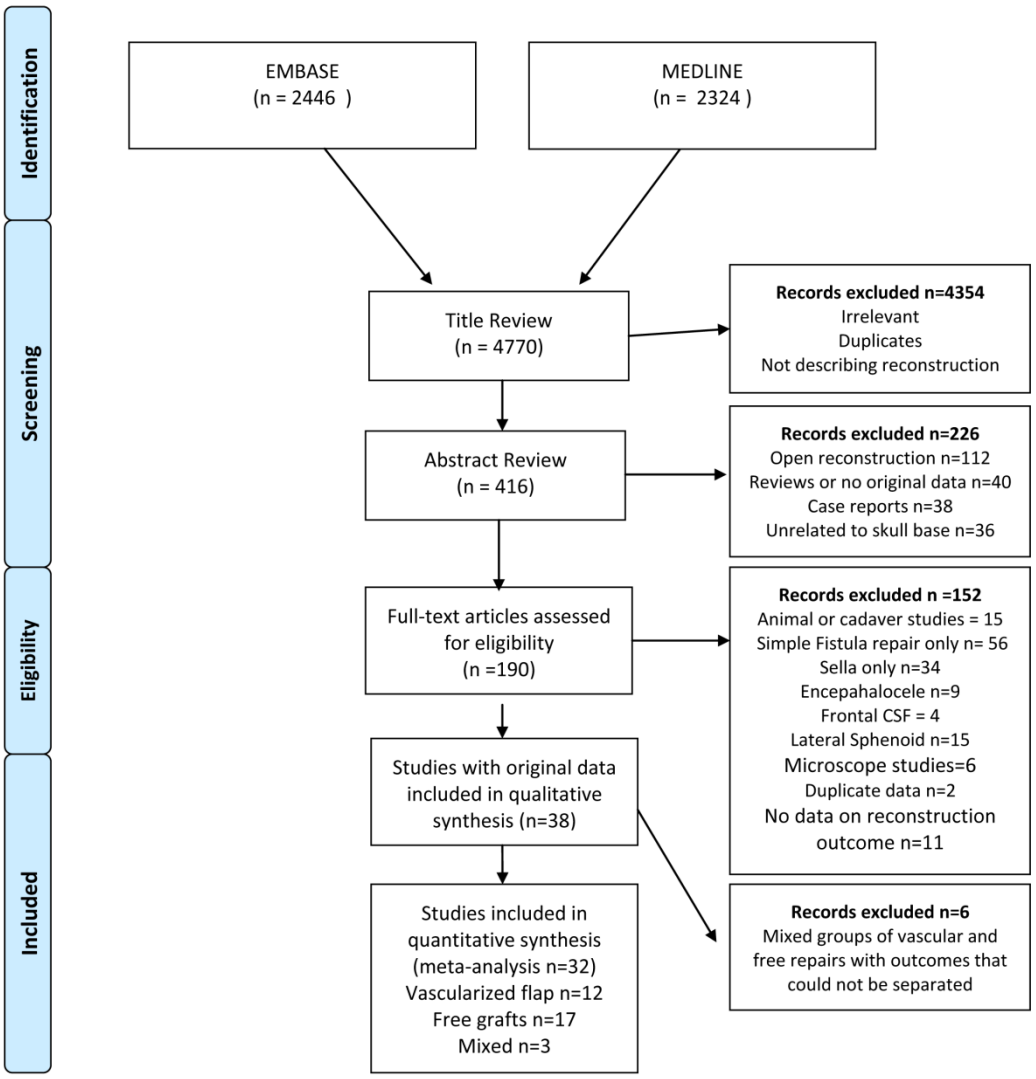
Conclusion

Current evidence in this systematic review suggests that skull base repair with vascularised tissue is associated with a lower rate of CSF leak compared to free tissue graft (Level 3b) and is similar to reported closure rates in open surgical repair (Grade C Recommendation).

Figures

Figure 3.1

PRISMA flow chart demonstrating the literature review and selection process with final included studies.



Tables

Table 3.1

Medline Search Strategy (similar modified version used in Embase)

1	Nasal.mp. or Nasal Cavity/
2	nose.mp. or Nose/
3	paranasal sinus.mp. or Paranasal Sinuses/
4	(transnas$ or trans-nas$).mp.
5	(sinonasal or sino-nasal).mp.
6	endoscop$.mp.
7	Endoscopes/
8	Endoscopy/
9	(endonas$ or endosin$).mp.
10	or/1-9
11	Surgical Flaps/ or Reconstructive Surgical Procedures/ or Suture Techniques/
12	reconstruct$.mp.
13	defect.mp.
14	repair.mp.
15	closure.mp.
16	sealing.mp.
17	Cerebrospinal Fluid/su [Surgery]
18	Dura Mater/su [Surgery]
19	or/11-18
20	Ethmoid Sinus/ or Ethmoid Bone/ or ethmoid.mp.
21	Sphenoid Sinus/ or Sphenoid Bone/ or sphenoid.mp.
22	(clivus or clival).mp.
23	anterior cranial fossa.mp. or Cranial Fossa, Anterior/
24	middle cranial fossa.mp. or Cranial Fossa, Middle/
25	posterior cranial fossa.mp. or Cranial Fossa, Posterior/
26	(transethm$ or transsphen$ or transcliv$ or transplan$).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
27	(trans-ethm$ or trans-sphen$ or trans-cliv$ or trans-plan$).mp. [mp=title, original title, abstract, name of substance word, subject heading word, unique identifier]
28	Craniotomy/ or craniotomy.mp.
29	craniectomy.mp.
30	Skull Base/ or skull base.mp. or skullbase.mp.
31	Brain Neoplasms/ or Pituitary Neoplasms/ or Skull Neoplasms/
32	Sella Turcica/ or Sella Turcica.mp.
33	or/20-32
34	10 and 19 and 33
35	limit 34 to english language

Table 3.2 Characteristics of included studies by endoscopic reconstruction type (vascular flap or mixed). (Men = meningioma, CP = craniopharyngioma, AD = adenoma, RC = Rathke's Cyst, Ch = Chordoma, CSF = cerebrospinal fluid, ITF = inferior turbinate flap, TPF = temporparietal flap, F = transfrontal, E = trans-ethmoid/cribriform, P = transplanum, C = transclival, ITF = transpetrous, ptyergoid or infratemporal fossa)

Characteristics of Included Studies by Endoscopic Reconstruction Type (Vascular Flap or Mixed).

Study	Year	Study Focus, Flap or Pathology	No.	No. With Defect	Repair Type	Age, yr (SD or Range)	% Female	Defect Size, Longest Axis	Defect Location	Lumbar Drain Use, % (Days)	Prior Radiotherapy
El-Sayed	2008	Local flap, posterior septal	30	20	Vascular flap	52 (18–86)	50	1.86 cm^2	E, P, C, ITF	55 (4)	20%
Fortes	2007	Local flap, ITF	4	4	Vascular flap	52.8 (4)	50	NR	C, P	NR	NR
Fortes	2007	Regional flap, TPF	2	2	Vascular flap	NR	NR	NR	C	NR	100%
Hackman	2009	Regional flap, palatal	1	1	Vascular flap	70	100	NR	C	NR	100%
Hadad	2006	Local flap, posterior septal	43	43	Vascular flap	NR (22–74)	28	NR	F, E, P, C	NR	NR
Harvey	2009	Local flap, septal and ITF	30	30	Vascular flap	45.5 (20.2)	43	24.9 mm	E, P, C, O	0	NR
Horiguchi	2010	Local flap, posterior septal	21	14	Vascular flap	58 (20–78)	43	NR	P, C	7	NR
Kassam	2008	Local flap, posterior septal	75	55	Vascular flap	47 (4–80)	37	NR	E, P, C, ITF, O	100 (4)	NR
Luginbuhl	2010	Mixed benign and malignant neoplasms, CSF leak	16	16	Vascular flap	NR	NR	NR	E, P, C	25–50 (7)	NR
Madhok	2010	Rathke cysts	35	3	Vascular flap	34 (12–67)	NR	NR	P	NR	NR
Nyquist	2010	Mixed benign neoplasms	5	5	Vascular flap	56.4 (31–72)	60	NR	P, C	20 (1)	NR
Patel	2010	Regional flap, pericranial	10	10	Vascular flap	NR	NR	NR	E, P	NR	30%
Shah	2009	Local flap, posterior septal pediatric	6	6	Vascular flap	13 (2.5)	NR	NR	E, P	NR	NR
Stamm	2008	Craniopharyngioma	4	4	Vascular flap	23.4 (16.3)	25	NR	E, P,C	0%	NR
Zanation	2009	Local flap, posterior septal	70	70	Vascular flap	NR	NR	>20 mm in 60%	E, P, C	93 (3)	23%
Greenfield	2010	Mixed benign and malignant neoplasms, CSF leak	44	33	Mixed	55.4 (17-85)	61	NR	F, E, P	NR	NR
Ceylan	2009	Mixed benign and malignant neoplasms	13	13	Mixed	47 (12.3)	62	NR	E, P, C	31	NR
Cavallo	2009	Craniopharyngioma	22	22	Mixed	49.4 (18–80)	32	NR	P	61	27%
Folbe	2009	Olfactory neuroblastoma	23	19	Mixed: 1 flap, 18 free	56.6 (15–79)	30	NR	E, P	NR	NR
de Divitiis	2008	Meningioma	11	11	Mixed: 3 flap, 8 free	56.1 (44–80	64	29.8 mm	E, P	NR	NR
Dehdashti	2008	Chordoma	12	9	Mixed: 5 flap, 7 free	49.4 (15.8)	33	40.3 mm	C	NR	25%

SD = standard deviation; E = transethmoid/cribriform; P = transplanum; C = transclival; ITF = transpetrous, ptyergoid or infratemporal fossa; NR = not reported; TPF = temporparietal flap; O = trans-odontoid; CSF = cerebrospinal fluid.

Table 3.3 Characteristics of included studies by endoscopic reconstruction type (free grafting). (Men = meningioma, CP = craniopharyngioma, AD = adenoma, RC = Rathke's Cyst, Ch = Chordoma, CSF = cerebrospinal fluid, ITF = inferior turbinate flap, TPF = temporparietal flap, F = transfrontal, E = trans-ethmoid/cribriform, P = transplanum, C = transclival, ITF = transpetrous, ptyergoid or infratemporal fossa)

Characteristics of Included Studies by Endoscopic Reconstruction Type (Free Grafting).

Study	Year	Study Focus, Flap or Pathology	No.	No. With Defect	Repair Type	Age (SD or Range)	% Female	Defect Size (Longest Axis)	Defect Location	Lumbar Drain Use, % (Days)	Prior Radiotherapy, %
Batra	2010	Mixed benign and malignant neoplasms	31	17	Free	57.5 (14–84)	42	16 mm	F, E, P	47	19
Cavallo	2007	Suprasellar: Men, CP, AD, RC, glioma	21	21	Free	NR	NR	NR	P	5 (7)	5
Chen	2006	Mixed malignant neoplasms	7	1	Free	52.7 (33–79)	29	NR	E, P	NR	NR
Church	2003	Iatrogenic post-ESS defects	3	3	Free	43.7 (10.6)	0	>20 mm	E, P	67	0
de Divitiis	2007	Suprasellar: Men, CP, AD, RC, AC	20	20	Free	49.5 (24–70)	55	NR	P	15	NR
de Divitiis	2007	Craniopharyngioma	10	10	Free	57.2 (26–70)	40	52.8 mm^2	P	NR	NR
de Divitiis	2007	Meningioma	6	6	Free	56.1 (44–70)	50	24.7 mm	P	0	0
El-Banhawy	2008	Meningioma (from mixed group)	3	3	Free	42.5 (40–45)	0	14 mm	E, P	NR	NR
Esposito	2007	Mixed: Men, CP, AD, Ch, RC, malignant neoplasms	620	58	Free	46 (5–86)	59	NR	P, C	100	NR
Gardner	2008	Meningioma	35	35	Free	55 (39–79)	83	NR	E, P	100	6
Germani	2007	Mixed benign and malignant neoplasms, CSF leak	56	55	Free	NR	NR	29% 4–20 mm, 29% >20 mm	E, P	20	NR
Horiguchi	2010	Control patients: free grafts	11	10	Free	52 (27–79)	27	NR	E, P, C	90	NR
Kassam	2007	Mixed benign and malignant neoplasms, CSF leak	25	11	Free	11.9 (5.3)	52	NR	E, P, C	NR	NR
Laufer	2007	Suprasellar: Men, CP, RC	10	10	Free	54 (12.4)	NR	26.5 mm	P	50	NR
Leng	2008	Mixed: Men, CP, Ch, CSF leak	10	10	Free	NR	NR	NR	E, P, C	50	10
Leong	2006	Mixed benign and malignant neoplasms	14	10	Free	57.4 (26–84)	43	4–40 mm	E, P	70 (5)	29
Luginbuhl	2010	Control patients: free grafts	24	24	Free	NR	NR	17 mm	E, P, C	33	NR
Stamm	2008	Craniopharyngioma: free grafts	3	3	Free	23.4 (16.3)	33	NR	P	0	NR
Vergez	2009	Adenocarcinoma	17	5	Free	68 (44–82)	0	NR	C, P	NR	NR
Villaret	2010	Mixed malignant neoplasms	62	14	Free	61.7 (25–84)	29	NR	E, P	47	19

F = transfrontal; E = transethmoid/cribriform; P = transplanum; CP = craniopharyngioma; AD = adenoma; RC = Rathke's cyst;, NR = not reported; ESS = endoscopic sinus surgery; AC = astrocytoma; Ch = chordoma; C = transclival; CSF = cerebrospinal fluid; Men = meningioma.

Table 3.4. Perioperative utcomes of included studies by endoscopic reconstruction type. (Men = meningioma, CP = craniopharyngioma, AD = adenoma, RC = Rathke's Cyst, Ch = Chordoma, CSF = cerebrospinal fluid, ITF = inferior turbinate flap, TPF = temporparietal flap, F = transfrontal, E = trans-ethmoid/cribriform, P = transplanum, C = transclival, ITF = transpetrous, ptyergoid or infratemporal fossa)

Perioperative Outcomes of Included Studies by Endoscopic Reconstruction Type.

Study	Year	No.	No. With Defect	CSF Leak	Pneumocephalus	Epistaxis	Intracranial Bleed	Meningitis	Other Intracranial Infective	Sinusitis	PE/DVT	Mortality
Vascular flap reconstructions												
El-Sayed	2008	30	20	0	0	0	1	0	0	0	0	0
Fortes	2007	4	4	0	0	0	0	0	0	0	0	0
Fortes	2007	2	2	0	0	0	0	0	0	0	0	0
Hackman	2009	1	1	0	NR	NR	NR	NR	NR	NR	NR	0
Hadad	2006	43	43	2	NR	1	0	0	0	0	NR	o
Harvey	2009	30	30	1	0	2	0	0	0	1	0	0
Horiguchi	2010	21	14	2	NR	NR	NR	NR	NR	NR	1	0
Kassam	2008	75	55	8	NR	1	NR	0	0	NR	NR	0
Luginbuhl	2010	16	16	1	NR	NR	NR	NR	NR	NR	NR	NR
Madhok	2010	35	3	0	NR	NR	NR	NR	NR	NR	NR	0
Nyquist	2010	5	5	0	NR	0	0	0	0	0	0	0
Patel	2010	10	10	0	NR	NR	NR	NR	NR	NR	NR	0
Shah	2009	6	6	1	NR	NR	NR	NR	NR	NR	NR	NR
Stamm	2008	4	4	0	NR	0	0	0	0	0	0	0
Zanation	2009	70	70	4	NR	NR	NR	NR	NR	NR	NR	0
Free graft reconstruction												
Batra	2010	31	17	2	1	1	0	1	0	1	1	0
Cavallo	2007	21	21	2	NR	NR	NR	0	NR	1	NR	0
Chen	2006	7	1	0	NR	NR	NR	NR	NR	NR	NR	0
Church	2003	3	3	0	0	0	0	0	0	0	0	0
de Divitiis	2007	20	20	1	1	NR	NR	NR	NR	1	NR	NR
de Divitiis	2007	10	10	2	0	0	2	0	0	1	NR	1
de Divitiis	2007	6	6	2	NR	0	1	NR	NR	NR	NR	1
El-Banhawy	2008	3	3	0	NR	NR	NR	NR	NR	NR	NR	0
Esposito	2007	620	58	7	NR	NR	NR	2	NR	NR	NR	0
Gardner	2008	35	35	14	1	NR	1	0	NR	1	3	0
Germani	2007	56	55	3	0	1	0	0	1	0	NR	0
Horiguchi	2010	11	10	3	NR	NR	NR	NR	NR	NR	NR	NR
Kassam	2007	25	11	2	NR	NR	NR	0	NR	NR	NR	0
Laufer	2007	10	10	1	NR	NR	NR	NR	NR	NR	NR	0
Leng	2008	10	10	0	NR	NR	NR	NR	NR	NR	NR	0
Leong	2006	14	10	0	NR	1	0	2	0	2	1	0
Luginbuhl	2010	24	24	10	NR	NR	NR	NR	NR	NR	NR	0
Stamm	2008	3	3	2	NR	0	0	0	0	0	0	0
Vergez	2009	17	5	0	0	0	0	1	0	NR	0	0
Villaret	2010	62	14	8	NR	NR	NR	1	0	NR	NR	0
Mixed reconstructions												
Greenfield	2010	44	33	4	NR	0	NR	0	2	5	NR	0
Ceylan	2009	13	13	5	NR	NR	1	NR	NR	NR	NR	1
Cavallo	2009	22	22	3	0	0	0	0	0	1	0	0
Folbe	2009	23	19	4	0	1	0	0	0	0	0	0
de Divitiis	2008	11	11	3	0	0	1	0	0	0	0	1
Dehdashti	2008	12	9	4	1	0	1	0	0	0	0	0

CSF = cerebrospinal fluid; PE/DVT = pulmonary embolus/deep vein thrombus; NR = not reported.

Table 3.5.Intranasal and Regional Vascular Flaps Available for Skull Base Reconstruction[ϕ]

terminal branch of posterior lateral nasal artery of the sphenopalatine artery

NSF – Nasoseptal Flap, ITF – Inferior Turbinate Flap, MTF – Middle Turbinate Flap, PCF – Pericranial Flap, TPFF – Temporoparietal Fascia Flap, PF- Palatal Flap

Intranasal and Regional Vascular Flaps Available for Skull Base Reconstruction.

Location	Vascular Tissue Flap	Pedicle	Comments/Limitations
Intranasal vascular tissue flap	NSF	Sphenopalatine artery	Ideal for all skull base reconstructions
	ITF	Inferior turbinate artery*	Good for small clival defects, cannot reach ACF or sella
	MTF	Middle turbinate artery*	Good for small ACF or transphenoidal defects, small in size, thin mucosa, difficult to elevate
Regional vascular tissue flap	PCF	Supraorbital and supratrochlear artery	Hearty flap with versatile dimensions, extends from ACF to sella but not to posterior skull base
	TPFF	Superficial temporal artery	Good for clival or parasellar defects, 90° pedicle rotation limits reconstruction of ACF
	PF	Greater palatine artery	Theoretical flap that reaches all areas of skull base, 3-cm pedicle but difficult to dissect, experience

*Terminal branch of posterior lateral nasal artery of the sphenopalatine artery.
NSF = nasoseptal flap; ITF = inferior turbinate flap; ACF = anterior cranial fossa; MTF = middle turbinate flap; PCF = pericranial flap; TPFF = temporoparietal fascia flap; PF = palatal flap.

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Chapter 4

Sinonasal morbidity following tumour resection with and without nasoseptal flap reconstruction

Abstract

Objective

Sinonasal function can be affected by multiple treatment modalities but surgical techniques, such as the nasoseptal flap or Draf 3 procedure, have been implicated in poor post-treatment function. Prior studies have rarely used comparable populations and this study aims to assess the impact of surgical technique, mainly the nasoseptal flap, on sinonasal function in a group of comparable patients.

Methods

A prospective cohort of patients undergoing endoscopic surgery for sinonasal and skull base tumours was studied. Patients were analysed according to whether a nasoseptal flap was used. Other treatment factors included; use of the Draf 3, radiotherapy, removal of olfactory apparatus and dural resection. The Sinonasal Outcome Test 22 (SNOT22), a nasal symptom score (NSS), global function score and nasal obstruction scores were recorded pre and post treatment.

Results

One hundred and eighteen **(**118) patients (39.8% female, age54.78$\pm$17.58 years) were assessed. Forty-two patients 36 % had a nasoseptal flap. Perioperative radiotherapy (40.5%v17.1%, p=0.01) was higher in the nasoseptal group, as was dural resection and the need to remove the olfactory apparatus. Despite this, there was no significant difference in SNOT22 scores (1.33±0.98v1.23±0.85, p=0.65) and NSS(1.71±1.15v1.48±1.11, p=0.36). Radiotherapy was detrimental to sinonasal function with SNOT22(1.73±0.96v1.15±0.84, p= 0.01) and NSS(1.71±1.15v1.48±1.11, p=0.36).

Conclusion

The use of a nasospetal flap in surgery does not affect patient quality of life and sinonasal function after endoscopic tumour resection. Pathology is a better predictor of morbidity, with

loss of function from radiotherapy or resection of functional areas such as the olfactory apparatus having a greater impact.

Introduction

The nasoseptal flap along with other local mucosal flaps, as part of skull base reconstruction, have dramatically changed the reconstructive outcomes for patients with endoscopic endonasal skull base surgery[81]. They provide a robust barrier when reconstructing dural defects [23] and are superior to free grafts[81]. There are other components of reconstruction, such as collagen inlays that have avoided the donor site morbidity associated with fat or fascia from areas such as abdomen or lateral thigh[82]. Although not necessarily the standard of care[83], the nasoseptal flap is incredibly valuable as an option for the skull base surgeon when performing endoscopic tumour resections. The nasoseptal flap is not exclusively used to repair dural defects. It can be used to cover important neurovascular structures, such as the internal carotid artery, or provide rapid mucosalization to large areas of exposed bone or when early radiotherapy is required[84]. However, concerns have been raised over the impact of the nasoseptal flap on sinonasal function[85, 86]. The published studies investigating the impact of the nasoseptal flap are inherently biased as many include pituitary patients having simple-transphenoidal operations together with patients having more invasive or expanded approaches. They are often not comparable groups. Such comparisons are inherently flawed, as intracranial pathologies are more likely to involve more extensive surgery with greater modification of normal sinuses than simple sellar or extracranial surgeries in these series.

Additionally, function, such as olfaction, may be electively sacrificed in certain intracranial pathologies if the posterior cribriform plate is being traversed but the decision to approach endonasally may represent a less morbid option given the alternative morbidity related to frontal lobe retraction [2]. This study aims to assess the symptoms and disease specific quality of life in patients undergoing endoscopic endonasal resection for sinonasal and skull base tumors, some, but not all of whom had a nasoseptal flap. The comparison of two groups, both

with large areas of exposed sinus and skull base achieves equipoise more effectively when assessing the potential functional and quality of life impact of the nasoseptal flap.

Methods

This study was approved by the Hospital Human Research Ethics Committee (SVH09/083). Written informed consent was obtained from all patients.

Population

Consecutive patients undergoing endoscopic endonasal surgery for tumours of the nose, sinus and skull base were selected, regardless of whether a nasoseptal flap was utilized or not. Patients with pituitary adenomas and simple sella based pathology were excluded. Patients with active chronic inflammatory rhinosinusitis, allergic rhinitis, recreational nasal drug use, any regular nasal medication or a prior history of an airway disorder were excluded. The intervention group was those who had a nasoseptal flap used (for any reason) as part of the tumour resection. The comparison group were those who had an endoscopic resection (intra or extradural) where no nasoseptal flap was harvested. The rationale for nasoseptal flap use was heterogeneous and thus potential bias between the two groups was explored via the confounding factors below. A study period from 2009-2012 was taken to ensure adequate time to last follow-up.

Confounding factors

Five factors were recorded to assess whether the two groups were comparable. The extent of sinus modification was defined by those patients who had a Draf3 or modified endoscopic Lothrop as part of their surgery (yes/no)[87] and the impact of a true skull base reconstruction where intradural surgery was defined by the resection of dura (yes/no) The influence of the intentional resection of key functional areas was defined as whether the olfactory apparatus was intentionally removed as part of the tumour surgery (yes/no). The impact of adjuvant therapies was defined by having had post-operative radiotherapy as this factor has been

associated with worsening of sinonasal function[88, 89]. Finally, the nature of the pathology (benign/malignant) was used as an overall indicator of therapy as this takes into account several of the above mentioned factors (extent of resection, sacrifice of normal structures, removal of dura and radiotherapy).

Patient reported outcome measures

Four different constructs of patient reported outcome measures (PROMs) were reported. The sino-nasal outcome 22 test (SNOT22) was used to assess overall disease specific quality of life. This is a validated 22 question survey with four domains: psychological function, sleep function, rhinological symptoms, and ear and/or facial symptoms[90].The SNOT22 is reported as mean of the 22 questions with a score of 0 to 5. A global rating of sinonasal function on a ordinal scale from -6 (terrible) to 0 (neither good or bad) to +6 (excellent) was also obtained. Nasal symptoms were recorded via a 5 questionnaire Nasal Symptoms score (NSS) from 'nasal obstruction', 'thick nasal discharge', 'facial pain/pressure', 'smell disturbance' and 'need to blow nose'. This was reported as a mean score from 0 to 5. Nasal obstruction was recorded as a 6 point Likert score from 0 (no problem) to 5 (problem as bad as it could be)(5). All four PROMs were recorded at baseline and at last follow-up.

Surgical technique

A binostril approach with some form of posterior septal window was the standard approach for most cases in this study. To raise the nasoseptal flap, a medium length needle point monopolar diathermy (Megadyne E-Z Clean 0016AM, Draper, UH, USA) was used on settings of 12 cut and 12 coagulate power (ForceFX 8CS, Valleylab, Boulder, CO, USA) was used. A releasing back incision was made from the choana on the vertical palatine bone under the sphenopalatine artery (Figure 1a). The choana was outlined and the incision continued on the septum 2-3mm away from its posterior edge to ensure that the incision was down to bone at all times. The incision in the floor of the nose was brought forward at a variable distance

laterally on the floor to near the inferior turbinate (Figure 1b). Then the superior incision started at the superior limit of the sphenoid ostium and the striated 'thin' upper septal mucosa is preserved. The superior septal mucosa was thin, making it less effective for reconstructive purposes, contains the olfactory epithelium and avoided if preservation of olfaction was intended. The anterior limit was usually to the muco-squamous junction in the nasal vestibule (Figure 1c). The flap was mobilized everywhere but superiorly. The release from the superior edge was made last. The flap was stored in the nasopharynx or maxillary sinus for later use in reconstruction (Figure 1d)

Postoperative care

Silastic sheeting 0.51mm (Medtronic, Jacksonville, Fl,) was used to cover the septum bilaterally. Mupiricon 2% ointment and Amoxycillin 875mg/Clavulinic acid 125mg was used twice daily for 10 days. This was intended to reduce Staphylococcal colonization in the immediate post-surgical period. Large volume, positive pressure nasal irrigation with commercially prepared buffered isotonic saline was used via a 240ml squeeze bottle (Sinus Rinse, Neilmed, California). This was continued twice daily for 3 weeks, at which the first post-operative outpatient review occurred. The silastic sheets were removed and saline irrigation continued with instructions for daily use decreasing to 2-3 times weekly, but not stopped until 90 days post-op, when the majority of healing had occurred[(91)]. All sinonasal cavities were examined between 3 and 6 months to check for remucosalization, the absence of crusting, recovery of mucillary function, and the absence of chronic inflammation (apart from occasional small areas of granulation tissue). This process was mostly completed by 3 months[(91)] (Figure 2).

Statistical analysis

Statistical analyses were performed using SPSS v 20.0 (Statistical Package for the Social Sciences, Chicago, IL). Age, Nasal symptom scores and SNOT22 data were considered to be

parametric and the paired Student's t test was used to compare pre-op and post-op scores, and the independent samples t test was used for comparisons between study groups. Ordinal data from the nasal obstruction question and Global nasal function scores were assessed with a Kendal Tau-b for changes between study groups. Chi squared analysis of proportions was used for gender and all confounding factor assessment. All *p*-values were two-tailed and a value of $p<0.05$ was considered statistically significant.

RESULTS

One hundred and eighteen (118) patients (40% female, age 55 $\pm$ 18 years) were recruited. Patient baseline characteristics of the study groups are described in Table 1. As expected, the dural resection and olfactory apparatus removal were over represented in the nasoseptal flap group. Similarly, radiotherapy was more commonly given to the nasoseptal flap group. Mean follow-up was 13.00±10.1mths. The list of pathologies managed is presented in Table 2 with malignant tumours accounting for 33.8% of surgeries performed. The baseline SNOT22 and Nasal symptoms scores were 1.36±0.87 and 1.44±1.12 respectively and compared similarly at follow-up (1.28±0.90, p=0.93 and 1.59±1.12, p=0.41).

The impact of the nasoseptal flap

There was no statistically significant difference in sino-nasal function at follow-up between patients who had a nasoseptal flap versus those who did not based on either the SNOT22 (1.33±0.98 v 1.23±0.85, p=0.65) or the Nasal Symptom Score (1.71±1.15 v 1.48±1.11, p=0.36) (Figure 3). The overall rating of global nasal function was also similar between groups (nasoseptal flap group score 2.0(IQR4.0) v no nasoseptal flap group score 3.0(IQR5.0), p=0.30). There was an association between the use of nasospetal flap and sense of nasal obstruction, with less nasal obstruction reported in the nasoseptal flap group (1.0(IQR2.0) v 1.0(IQR3.0), p=0.01 Kendal's tau B).

The impact of radiotherapy

The most significant impact on post-operative nasal function was the adjuvant use of radiotherapy. The post-operative SNOT22 scores were higher (1.73±0.96 v 1.15±0.84, p= 0.01) and higher Nasal Symptom Scores (2.30±1.02 v 1.37±1.08, p=0.002) were reported in those with adjuvant radiotherapy versus those without. Global rating of nasal function was similar (2(IQR3.3) v 3(IQR4.0), p=0.83, Kendal's Tau b). The difference in nasal obstruction scores approached statistical significance (Radiotherapy 1.5(IQR2.0) v none 1.0(2.0), p=0.06, Kendal's tau b)

Impact of including a Draf 3 or modified Lothrop as part of the exposure

No negative influence could be seen from the inclusion of a Draf3 in the approach. . There was no statistically significant difference in SNOT22 scores in patients who had a Draf 3 approach (1.34±0.90 v 1.26±0.90, p=0.75), and Nasal Symptom Scores were not significantly different (1.76±1.01 v 1.52±1.16, p=0.44) (Figure 4). Both Global rating of nasal function and sense of nasal obstruction were unaffected (2.0(IQR4.0) v 3.0(IQR4.0), p=0.33 Kendals Tau b) and (1.0(IQR2.0) v 1.0(IQR 3.0), Kendals Tau b p=0.92).

The influence of olfactory apparatus removal

On initial analysis, the removal of the olfactory apparatus appeared to have a significant impact on SNOT22 scores (1.73 ± 0.98 v 1.10 ± 0.80, p=0.002) and Nasal Symptom Score (2.18 ± 0.98 v 1.33 ± 1.10, p=0.003). However, as "olfaction" makes up a component of these scores, a sensitivity analysis was performed with the 'olfaction' question removed from the nasal symptom score (1.74 ± 1.03 v 1.32 ± 1.16, p= 0.13), and with the psychosocial domain of the SNOT22 compared in isolation (1.49 ± 0.96 v 1.13 ± 0.83, p=0.08), revealing no significant difference in non-olfactory sinonasal symptoms. Global ratings of nasal function were (2.0(IQR4.0) v 3.0(IQR4.0), p=0.51).

Dural resection had little impact on postop function as assessed by SNOT22 (1.39 ± 0.98 v 1.17 ± 0.82, p=0.28), Nasal Symptoms Score (1.77 ± 1.12 v 1.39 ± 1.12, p=0.12), and global nasal

function score (2.0(IQR5.0) v 3.0(4.0), p=0.86 Kendal's Tau b). However, having a malignant tumour had a negative impact on aspects of postop function compared to benign neoplasia: SNOT22 (1.79±0.80 v 1.01±0.84, p<0.01), NSS (2.26±0.98 v 1.21±1.03, p<0.01) and Nasal Obstruction (2.0(IQR2.0) v 1.0(IQR2.0), p<0.01). However, Global function score was not significantly different (2.0(IQR3.5) v3.0(IQR4.0), p=0.56). This sub-analysis includes the influence of a range of surgical and treatment factors that results in this outcome (Figure 5).

Discussion

Comparing the sinonasal function of patients before and after their treatment has little external validity if the groups are fundamentally different, such as a comparison of paranasal sinus tumors with skull base tumors. Such a comparison fails to take into account the fact that some patients have extensive pre-treatment sinonasal dysfunction from pathology within the paranasal sinuses while others have near normal sinonasal tracts and their pathology primarily involves the skull base or intradural structures. However, assessing the impact of surgical technique and adjuvant therapies on the subsequent sinonasal cavity and function is of value. The data presented in this study suggests that most patients have good sinonasal function postoperatively with 71.1% of patients rating their function above the neutral (0) score. The post treatment sinonasal function was not influenced by surgical techniques, nasoseptal flap or use of the Draf 3, but was influenced by factors that contributed to loss of function (olfactory loss and post-operative radiotherapy).

Radiotherapy has only been recently reported as an important factor in determining outcome following endoscopic sinonasal tumour management [(88)]. There is, however, much literature on the influence of radiotherapy, with or without chemotherapy, in patients with nasopharyngeal tumours[(92)]. Castelnuovo et al demonstrated that QoL scores were worse in those >60yrs of age, who had radiotherapy or those needing craniectomy to remove extensive tumours[(88)]. Palme et al. also demonstrated that radiotherapy was the major factor influencing quality of

life for patients with anterior skull base neoplasms treated with both open and endoscopic approaches[89]. From the literature on the management of nasopharyngeal carcinoma, radiotherapy can have effects on both local function [93] and cognitive function [94]. Long term adverse effects of radiation to the skull base such as endocrinopathy[95], radionecrosis[96], cranial neuropathy[97] and hearing impairment[98] were not addressed here. With only 13mths follow-up, and from personal observation, it is conceivable that although some of the local mucosal post-radiation effects may have resolved, late radiation adverse effects can still occur. Late complications from radiotherapy are uncommon(6%)[98]. Lin et al showed that they mostly occur at a mean duration to event 5.4±4.4years with a latency range from 1-20years[97].

There have been several studies looking at the local sinonasal function and olfaction after endoscopic interventions uitlizing the nasoseptal flap[10, 85, 86]. However, many of these studies compare mismatched groups with disparate numbers of patients with more extensive skull base disease in the NSF group[10, 86]. The decision to take a more expanded approach through otherwise unaffected sinuses is balanced against the morbidity associated with brain retraction [2]. Also, with limited information about specific surgical technique in several studies, some of the olfactory consequences may have been related to unintentional damage to the 'olfactory strip' when creating the NSF or performing the septectomy[99, 100]. The data presented in this study demonstrates the influence of surgical technique on sinonasal function in comparable patient populations regardless of their degree of pre-operative sinonasal morbidity.

Despite more extensive resection of the dura, destruction of the olfactory bulb and post-operative radiotherapy in the nasoseptal flap group, the sinonasal performance was similar to the group without a nasoseptal flap. This favourable outcome in the NSF group is further strengthened when the baseline data potentially biases better function to the non-NSF group. This series suggests that the use of a NSF for extensive skull base resections has little negative

impact on the subsequent function of the sinonasal tract. Additionally, nasal obstruction scores were lower in the nasoseptal flap group. Nasal obstruction was uncommon in the population, as a whole, with only 14.1% of respondents noting it as a moderate problem or worse. In the senior authors' experience, when patients complain of nasal obstruction, there is usually a cause, such as local mucositis in the vestibule or post-operative formation of adhesions. Obstruction is not simply due to loss and then re-mucosalization of the septum although this process should not be under-estimated. There are techniques to reduce this time to remucosalization such as silastic covering[101], free grafting[102] or the "reverse flap" technique[103]. However, as with radiotherapy, the permanent impact of re-mucosalization of the septum is more reliably assessed after 3 months[91]..

Conclusion

The creation and utilization of a NSF after endonasal skull base resections does not appear to affect the quality of life and sinonasal function of patients when compared to a similar group of patients who did not have a NSF. Interestingly loss of function from adjuvant therapy or the need to resect functional areas, such as the olfactory apparatus did have a negative impact.

Figures

Figure 4.1

The standard approach to nasoseptal flap when performed as part of extensive tumour surgery. There are many reasons why it is used such as skull base reconstruction, or for coverage of exposed bone or neurovascular structures in paranasal sinus surgery. A flap is not utilised if none of these indications exists, or when the septum is involved by tumor. The pedicle is mobilised to the spehnopalatine foramen with a releasing incision on the medial pterygoid plate (a).The nasal floor is often a considerable part of the flap (b) and raising the flap to the squamo-mucosal junction gains maximum length. The final flap being mobilized to the nasopharynx with donor defect (d).

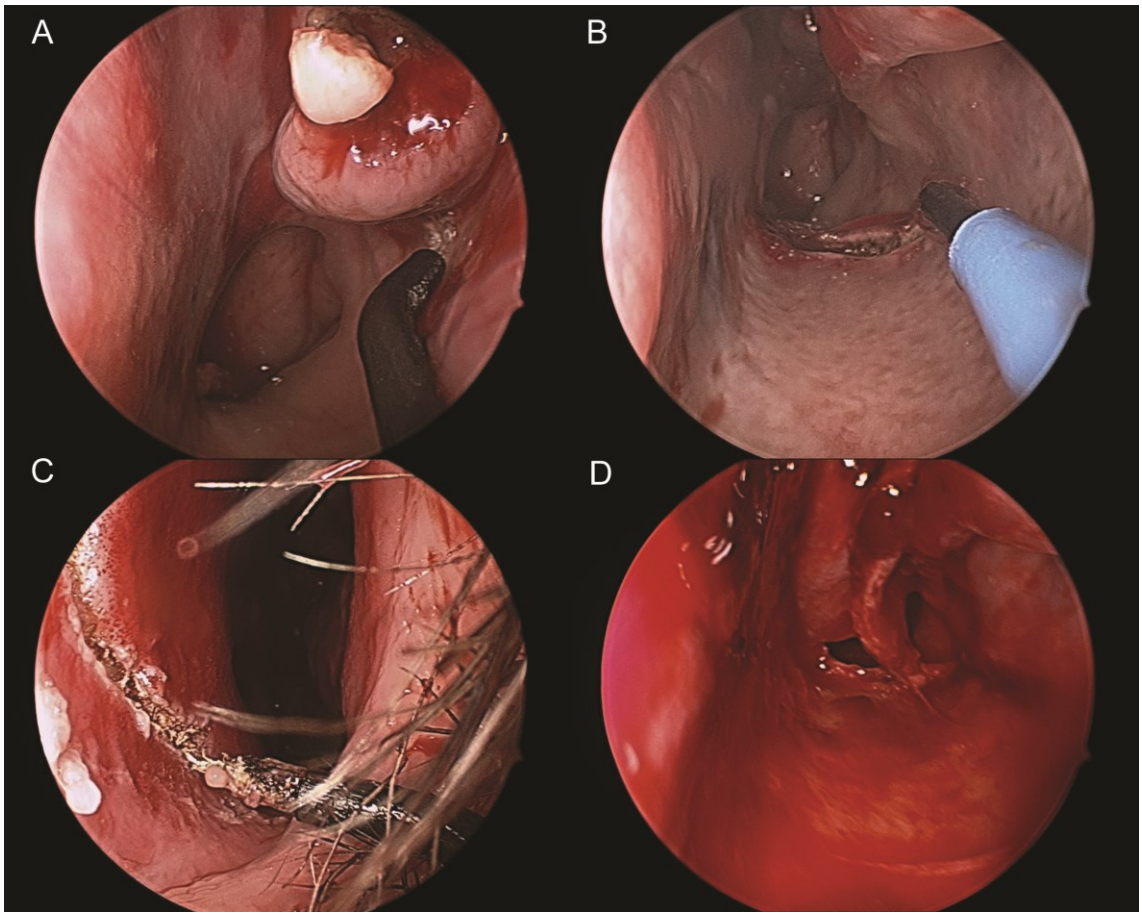


Figure 4.2

Examples of post radiation post-surgical cavities. A typical neuroblastoma post-surgery and radiotherapy (A and B) and a squamous cell carcinoma post-surgery and radiotherapy (C and D). Chronic sinonasal inflammation and crusting, regardless of nasoseptal flap use, are not expected longterm outcomes.

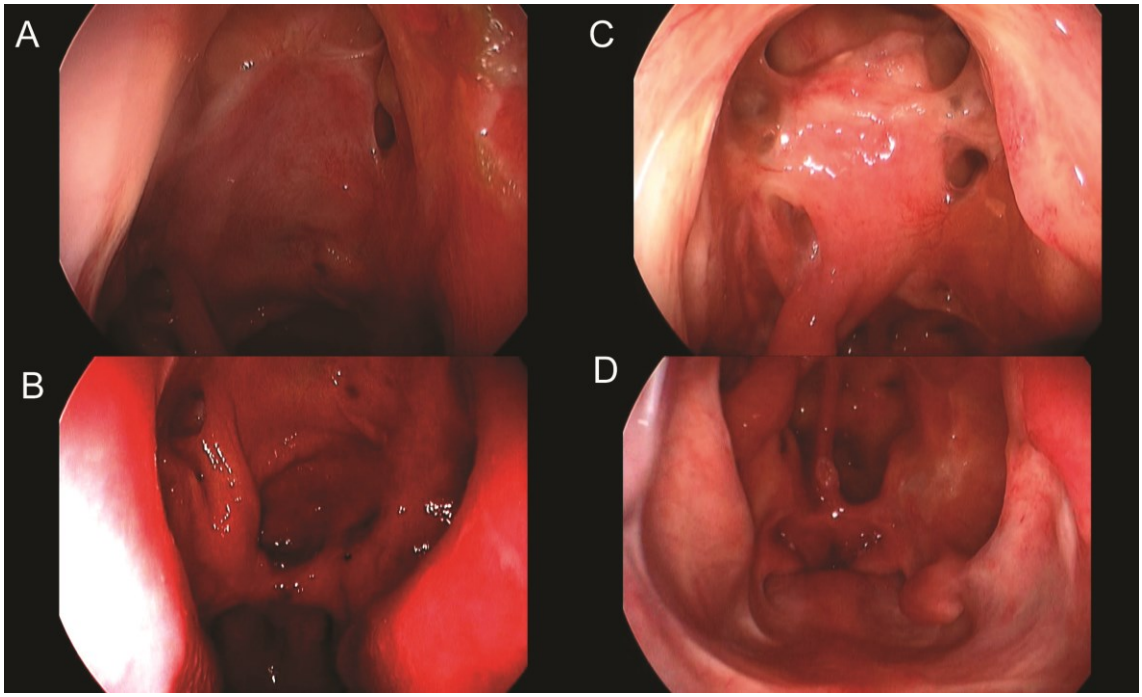


Figure 4.3

The impact of the nasoseptal flap on disease specific quality of life (a) and nasal symptom scores(b) in patients undergoing endoscopic resection of neoplasia.

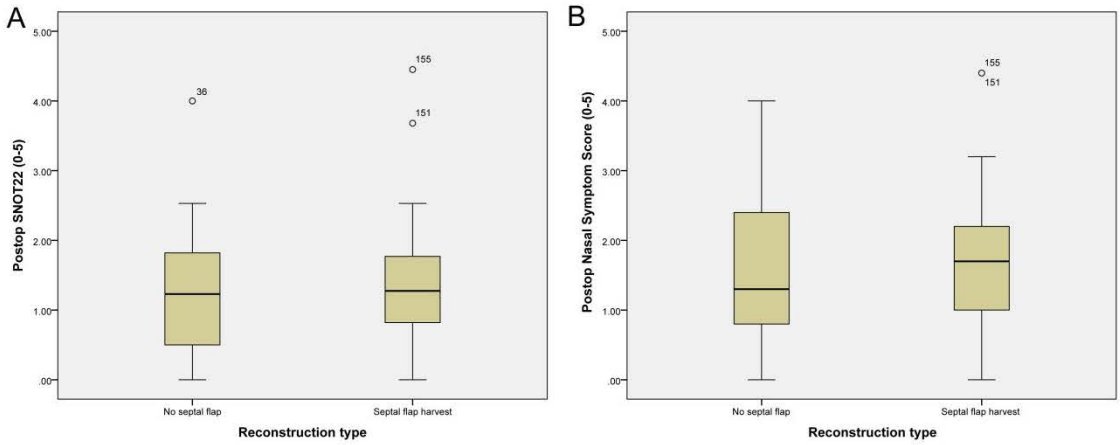


Figure 4.4 Radical sinus procedures that modify the normal anatomy to gain access such as the Draf 3 had no impact on disease specific quality of life (a) and nasal symptom scores(b) in patients undergoing endoscopic resection of neoplasia

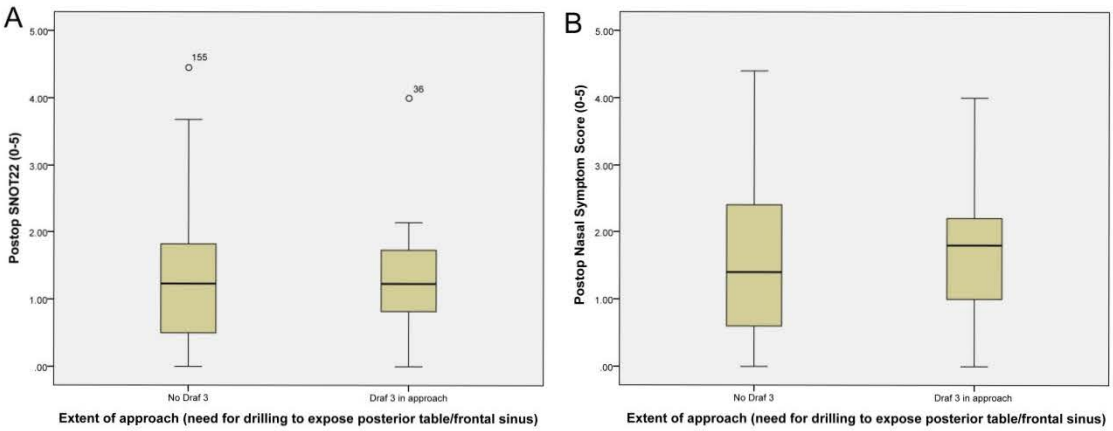
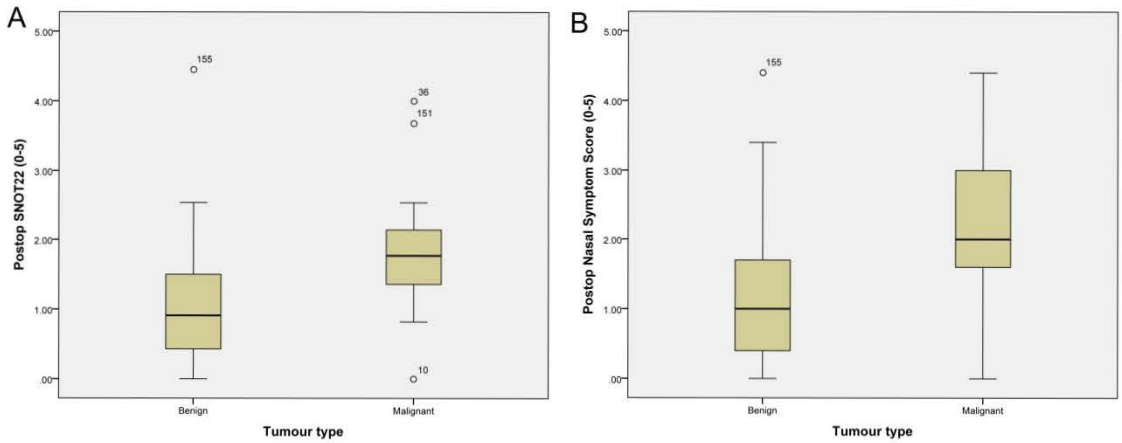


Figure 4.5 The presence of a malignant pathology was a predictor for poor performance specific quality of life (a) and nasal symptom scores(b) in patients undergoing endoscopic resection of neoplasia due to multiple factors



Tables

Table 4.1

Allocation table for baseline characteristics between groups.

	Nasoseptal flap	No flap	p value
n	42	76	
Age (yrs)	55.52±18.35	54.37±17.25	0.74
Gender (% female)	40.5%	39.5%	0.92
Draf 3 performed	23.8%	14.7%	0.22
Dura resection	88.1%	24.3%	<0.01*
Olfactory bulb and tract removed	40.5%	17.1%	<0.01*
Radiotherapy	33.3%	12.9%	0.01*
Neoplasm (%malignant)	38.1%	31.6%	0.47

Table 4.2

Pathology casemix for the cohort.

Pathology	**n**	**%**
Benign paranasal (other)	33	28.0
Meningioma	22	18.6
Papilloma	15	12.7
Minor Salivary Carcinoma	13	11.0
Craniopharyngioma/Cyst	10	8.5
Olfactory Neuroblastoma	8	6.8
SCC	7	5.9
Malignant paranasal (other)	5	4.2
Chordoma	3	2.5
Epidermoid	2	1.7
Total	118	100.0

Chapter 5

Postoperative irrigation therapy after sinonasal tumor surgery

Abstract

Objective

Sinonasal care after endoscopic tumour resection aims to manage crusting, oedema, mucus and a healing cavity. High volume irrigations have proved beneficial in this setting. The use of additives to the irrigation such as corticosteroid used in chronic rhinosinusitis (CRS) in modifying the postsurgical inflammatory response is unknown. Saline alone versus combination saline and corticosteroid irrigations in postoperative nasal care of sinonasal tumour patients was assessed.

Methods

A retrospective cohort of patients post endoscopic endonasal tumour resection was assessed. Patients used 240ml saline or 240ml saline with 1mg of betamethasone daily. Nasal symptom scores (NSS) and the Sino-Nasal Outcome Test 22 (SNOT 22) were recorded 3 months postoperatively. An endoscopic score was made of the area undergoing secondary healing at 3 months by two blinded assessors.

Results

59 patients were assessed (age 50.1±18.26yrs, 36% female). The groups were similar in number (saline n=31) and with regard to extent of surgery, pre or post radiation therapy, co-morbidities or the assessment site (mucosal flap donor site v tumour site). The endoscopic scores did not differ between the groups at 3 months. NSS was lower in the saline group [1.0 (IQR 3) v 7.0 (IQR 9) p=0.03] and similarly for SNOT 22 [0.24 (IQR 1) v 1.09 (IQR 1) p=0.01], compared to the saline + steroid group

Conclusion

Although corticosteroid irrigations have become routine for managing inflammatory sinus disease at our centre, their use post tumour surgery does not appear to be warranted. The

inflammatory healing process after tumour surgery differs from CRS inflammation and may explain the observed findings.

Introduction

Endoscopic endonasal surgery is used for the treatment of a wide range of both benign and malignant tumours with lower morbidity and faster recovery.[6, 104, 105] While an endoscopic skull base approach is generally regarded as minimally invasive, this is not the case. Expanded endoscopic surgery for sinonasal tumours can be very invasive to the nasal and sinus cavities resulting in significant nasal morbidity from a large resection area to heal by secondary intention.[102] Patients often experience transient but significant deteriorations in symptom scores such as the Sino-Nasal Outcome Test 22 (SNOT 22) postoperatively.[106] Saline irrigations are commonly used for postoperative nasal care after endoscopic endonasal tumour surgery.[102, 107, 108] The addition of topical corticosteroid to saline irrigation is effective in achieving symptom control and improving endoscopy scores amongst patients with chronic inflammatory sinus disease.[109] The current study aims to compare the use of saline alone versus combination of saline and corticosteroid irrigation for the management of postoperative nasal morbidity and symptoms following endoscopic endonasal tumour surgery.

Methods

A retrospective cohort of patients from an academic rhinology practice was reviewed. All patients underwent endoscopic endonasal tumour resection between November 2008 and June 2012 by a single surgeon. They were followed up at 3 months postoperatively for endoscopic assessment and patient completed symptom scores. Approval from the Human Research Ethics Committee of the St Vincent's Hospital was obtained.

Study Population

Consecutive patients undergoing endoscopic endonasal tumour resection were included. All patients had to have an area of mucosal loss that required healing by secondary intention. Patients in whom their primary area was the mucosal flap donor site were also included.

Postoperative management

Patients were treated either with 240ml saline nasal irrigation alone (the saline group) or 240ml saline nasal irrigation with 1mg of betamethasone (the saline + steroid group) once daily. All patients performed an additional 240ml saline only irrigation such that the topical care was twice daily but only with a medicated solution once daily for the saline + steroid group. Patients were assigned to the study groups by historical practice patterns as simple saline had been replaced by saline/steroid therapy in more recently treated patients.

Symptom assessment

Patient reported outcomes were assessed with the Nasal Symptom Score (NSS) and the SNOT 22 at the 3 month postoperative period. NSS is a mean summary score of 5 nasal symptoms recorded on a Likert scale from 0-5. These included questions on postnasal discharge, thick nasal discharge, facial pain and pressure, loss of smell and taste, and nasal obstruction. SNOT 22 was used as a validated disease-specific quality of life score and was reported as a summary score from 0 to 5.[90]

Endoscopic assessment

The area undergoing secondary healing (mucosal flap donor site or tumour site) was scored by two blinded assessors at 3 months. Endoscopic assessment was based on 9 outcomes collected from previously described publications on the evaluation of nasal mucosal morbidity following endoscopic endonasal surgery.[102, 110, 111] The outcomes assessed included exposure of raw bone (0 - absent, 1 - present), exposure of raw cartilage (0 - absent, 1 - present), degree of crusting (0 – no crusting, 1 – crusting over less than 25% of the area, 2 –25-50%, 3 – greater than 50%), granulation tissue (0 - absent, 1 - present), oedema (0 - absent, 1 – mild oedema, 2 – hyperplastic mucosa), bleeding (0 - absent, 1 – recent blood seen), blood crust (0 - absent, 1 - present), extent of healing (0 - complete healing, 1 – healing over 75-99% of the area, 2 – 50-75%, 3 – 25-50%, 4 – less than 25%) and presence of infection (0 – no purulence, 1 – purulent

secretions present). The sum of all individual outcome scores was also compared between the groups as a measure of total wound healing, although it is acknowledged that the clinical context of such a total measure is ambiguous.

Statistical analysis

All statistical analyses were performed using SPSS v 21.0 (Statistical Package for the Social Sciences, IBM, Chicago, IL). Parametric data was expressed using mean ± standard deviation and compared using the two-tailed student's t-test. Non-parametric data was presented as median (Interquartile Range, IQR), and the Mann-Whitney U test was used for comparison between the groups. Categorical data was compared using the Chi-Square analysis.

Results

Patient population

Fifty-nine patients with a mean age of 50.1 ± 18.26 years were assessed. Twenty-one (36%) patients were female. Thirty-one (53%) patients belonged to the saline group. Mucosal flap donor site was assessed in sixteen (52%) and thirteen (46%) patients in the saline and the saline + steroid group, respectively. The tumour resection bed was assessed in the remaining patients. A Draf 3 modified endoscopic lothrop procedure was performed in seven (23%) and five (18%) patients in the saline and the saline + steroid group, respectively. There was no statistically significant difference between the baseline characteristics of the groups (Table 1).

Endoscopic Assessment

No statistically significant differences were seen at 3 months between the groups in any of the individual endoscopic outcomes. There was also no significant difference between the groups for the sum of all outcome scores as a measure of total wound healing (Table 2).

Symptom Assessment

NSS was lower in the saline group [1.0 (IQR 3) vs. 7.0 (IQR 9) p=0.03] and similarly for SNOT 22 [0.24 (IQR 1) vs. 1.09 (IQR 1) p=0.01], compared to the saline + steroid group (Table 3).

Discussion

Nasal saline irrigation after endonasal surgery has been advocated for postoperative symptom management. The proposed mechanisms for this includes mechanical debridement of blood clots and crusts,[112] and removal of inflammatory mediators during recovery of sinonasal mucosa and mucociliary clearance.[113, 114] There is good evidence that the use of topical corticosteroid combined with high volume saline irrigation for patients with chronic inflammatory sinus disease is effective in controlling mucosal inflammation and symptoms in the post-surgical period.[109, 115, 116] Despite this evidence in chronic inflammatory sinus disease, the impact of this treatment approach on sinonasal tumour postoperative care, in which significant inflammatory response is present, remains unclear. The results of this study demonstrate significantly lower patient reported symptom scores among patients in the saline only group reflected in the NSS and SNOT 22 at 3 months postoperatively. These results potentially do not support the routine use of corticosteroid in nasal irrigations for sinonasal tumour patients. This is contrary to findings among CRS patients.

The lack of steroid irrigation efficacy in the current study may be attributed to differences in the mucosal recovery process that occurs during CRS and tumour patients. CRS is predominantly an inflammatory condition while mucosal recovery for tumour patients follows a wound healing model. While the anti-inflammatory effects of corticosteroid are a key factor in the efficacy of treating CRS through its ability to dampen T-cell production of inflammatory cytokines,[117] corticosteroid also is known to have detrimental effects on mucosal wound healing.[118-120]

Both mucosal healing and patient symptoms can be affected by confounding factors such as extent of surgery, previous or adjuvant radiotherapy, and co-morbidities such as diabetes. It was anticipated that 'larger' or more extensive resections may have been offered to the steroid irrigation group preferentially over the saline only patients and a potential bias of the retrospective structure of this study. However, these factors were evenly distributed between the two groups, suggesting that the results are due to the choice of the irrigation alone (Table 1).

One limitation of this study is the lack of a validated outcome tool to measure nasal mucosal healing after endoscopic tumour surgery. The endoscopic scoring system applied to this investigation was developed based on previous studies examining sinonasal morbidity following endonasal surgery.[102, 110, 111] Another limitation is that only the site undergoing secondary healing was scored. It is possible that the overall extent of mucosal healing for the entire operative field may more closely reflect patient symptom scores. Moreover, this study reflects the changes in patient reported symptom scores at the 3 month postoperative follow-up period. No conclusions can be drawn about long-term differences in patient symptom scores between the two groups or whether steroid irrigations introduced at a later stage may be beneficial if there is prolonged inflammation. Lastly, the data is historical, and the practice had changed from prescribing saline irrigation alone to the combined saline/corticosteroid. Similar aggressive pathology or extensive surgery appears to be distributed between the groups but bias might exist.

Conclusion

Despite the widespread use of corticosteroid irrigations after endoscopic sinus surgery for CRS, routine use of corticosteroid irrigations does not appear warranted after endoscopic endonasal surgery for sinonasal tumours. The inflammatory healing process after tumour

surgery is likely to differ from the chronic inflammation of CRS patients and may explain the observed findings. Further research is required to determine the optimal management strategy for postoperative nasal morbidity and symptoms in this patient population.

Tables

Table 5.1

Baseline characteristics of the patients

	Saline group (n = 31)	Saline + Steroid group (n = 28)	*p*-value
Gender (% female)	45%	25%	0.11
Age (years)	51.1 ± 18.7	49.1 ± 18.0	0.68
Smoker	7%	0%	0.16
Diabetes	7%	11%	0.61
Prior radiotherapy	7%	11%	0.58
Adjuvant radiotherapy	17%	18%	0.91
Malignancy (% of malignant tumour pathology)	26%	29%	0.81
Assessment site (% mucosal flap donor site)	52%	46%	0.69
Modified Lothrop Procedure	23%	18%	0.65
Endoscopy assessment (Days post-surgery)	95.9 ± 30.4	94.5 ± 21.6	0.84
Symptom assessment (Days post-surgery)	92.3 ± 19.6	96.9 ± 20.6	0.47

Table 5.2

Comparison of individual endoscopic outcomes between the groups at 3 months

Endoscopic Assessment	Saline group	Saline + steroid group	*p*-value
Exposed Bone			
Raw bone exposed	6.5%	4%	0.64
Exposed Cartilage			
Raw cartilage exposed	0%	12.5%	0.16
Crusting			
No crusting	45%	32%	0.14
<25% of area	23%	46%	
25-50% of area	32%	18%	
>50% of area	0%	4%	
Granulation Tissue			
Granulation tissue present	71%	64%	0.58
Mucosal Oedema			
Normal mucosa	48%	39%	0.54
Mild oedema	29%	43%	
Hyperplastic mucosa	23%	18%	
Bleeding			
Recent blood seen	35.5%	21%	0.23
Blood Crusts			
Blood crusts present	6.5%	4%	0.62
Extent of Mucosal Healing			
Complete mucosal coverage	77%	75%	0.06
75-99% of area healed	23%	11%	
50-75% of area healed	0%	14%	
25-50% of area healed	0%	0%	
<25% of area healed	0%	0%	
Presence of infection			
Purulent secretions present	19%	14%	0.60
Total wound healing			
Total endoscopic outcome score	3.2±2.53	3.2±1.93	0.94

Table 5.3

Comparison of symptom scores at 3 months

	Saline group	Saline + steroid group	*p*-value
NSS	1.0 (IQR 3)	7.0 (IQR 9)	0.03
SNOT 22	0.24 (IQR 1)	1.09 (IQR 1)	0.01

Chapter 6

The olfactory strip and its preservation with a modified nasoseptal flap in endoscopic pituitary surgery maintains smell and sinonasal function

Abstract

Objective

Return of olfaction and sinonasal function are important endpoints after pituitary surgery. Differing opinions exist on the impact of surgery as techniques vary greatly. A modified 'olfactory strip' preserving approach is described that utilises a small nasoseptal flap and wide exposure.

Methods

A cohort of patients undergoing pituitary surgery and endoscopic sinonasal tumour surgery were assessed. Patient reported outcomes (Sinonasal Outcome Test22(SNOT22) and a Nasal symptom score (NSS)) were recorded. A global score of sino-nasal function and the impact on smell and taste were obtained. Objective smell discrimination testing were performed in the pituitary group with a Smell Identification Test 40 (SIT40). Outcomes were assessed at baseline and 6 months

Results

Ninety-eight patients, n=40 pituitary (50.95±15.31yrs, 47.5% female) and n=58 tumour (52.35±18.51yrs, 52.5% female) were assessed. For pituitary patients, NSS were not significantly different pre and post-surgery (2.75±3.40 v 3.05±3.03, p=0.53). SNOT22 scores improved post-surgery (1.02±0.80 v 0.83±0.70, p=0.046). Objective smell discrimination scores between baseline and 6 months were similar (31.63±3.49 v 31.35±4.61, p=0.68). No difference in change of olfaction was seen compared to controls (Kendall tau-b p=0.46).

Conclusion

Preservation of the 'olfactory strip' can provide a low morbidity approach, without adversely affecting olfaction, while maintaining reconstruction options.

Introduction

Differing outcomes on olfaction have been reported from trans-sphenoid approaches [121-124]. In general, patients prefer the endoscopic approach [125] and olfactory scores are better after the endoscopic route [126]. The nasoseptal flap, in particular, to reconstruct the skull base as part of the overall process has been implicated in smell dysfunction. However, much of the literature on the impact of the nasoseptal flap comes from extended skull base surgery. In our institution, utilising a small modified nasoseptal flap during simple pituitary surgery has greatly improved our reconstructive options and access. However, controversy exists as to the additionally morbidity of utilizing such an approach. The existing studies on patients with large skull base tumours are not an appropriate population to discuss the impact of surgery or reconstruction as pathology has already dictated much of the morbidity There is no doubt that resecting large skull base tumours will leave the patient with a new remodelled neo-sinus cavity that is unlikely to compare with the function of a healthy un-operated un-irradiated sinonasal system.. Likewise, utilising the endoscopic endonasal approach to access a giant olfactory groove meningioma or other intracranial tumour is not an appropriate population to assess sino-nasal function, as the approach results in extensive modification of an otherwise normal anatomy, but is done so to avoid the potential morbidity of frontal lobe retraction[2]. Additionally, smell loss is anticipated in such a patient as the surgical approach or pathology often involves the olfactory apparatus. An ideal study population is the patient undergoing simple trans-sphenoid sella based surgery. Each procedure is relatively comparable, a similar technique applied each time, and options exist to the approach via an endonasal endoscopic, trans-nasal/trans-septal/sub-labial microscopic and with or without the use of a naso-septal flap.

Controversy exists regarding the impact of the nasoseptal flap and middle turbinate resection [85, 123, 127]. Unfortunately, standardization of surgical technique does not exist and what is being described surgically in some series is not the same as others. In particular, the degree of tissue

resection and the location of nasoseptal flap differ greatly between those centres with fellowship trained rhinologists and those without. Such differences are often noted at scientific meetings when video presentations of techniques are displayed.

Rhinologists have been aware of the unique appearance of the upper septal mucosa for some time with the term “olfactory strip” often used to describe the area (Personal correspondence – Ricardo Carrau) and this has been noted in editor comments[99]. Recent study into nasoseptal flap impact on sinonasal quality of life has suggested that modifications need to be made to ensure maximum preservation of sino-nasal function, however, there is little doubt that the nasoseptal flap allows for a vascularized graft and enhanced reconstruction compared to free grafting[81].

This study presents the sinonasal, smell and objective olfactory outcomes on a standardized ‘olfactory-strip preserving’ nasoseptal flap technique utilised in the endoscopic endonasal trans-sphenoid approach to pituitary pathology.

Methods

A prospective study of olfaction and sinonasal function was undertaken in patients having a nasoseptal flap as part of pituitary surgery. A retrospective cohort with patients undergoing sinonasal tumour surgery was also included. This study was approved by the Hospital Human Research Ethics Committee (SVH09/083). Written informed consent was obtained from all patients.

Population

Consecutive patients undergoing surgery for pituitary adenomas or simple sella pathology were selected from a tertiary centre. Patients with active chronic rhinosinusitis, allergic rhinitis, recreational drug nasal drug use, any regular nasal medication or a prior history of an olfactory disorder were excluded.

A comparative sino-nasal surgery patient was sought. Any patient having a sino-nasal tumour removed in which no nasoseptal flap was utilized and where no olfactory apparatus was resected were included. This data was retrospective and part of a previous database on post-tumour sinonasal function[128].

Patient reported outcome measures

Four different constructs of patient reported outcome measures (PROMs) were reported. The sino-nasal outcome 22 test (SNOT22) was used to assess overall disease specific quality of life (0-5). This is a validated 22 question survey with four domains: psychological function, sleep function, rhinological symptoms, and ear and/or facial symptoms [90]. A global rating of sinonasal function on a Likert ordinal scale from -6 (terrible) to 0(neither good nor bad) to +6 (excellent) was also obtained. "Disturbance in smell or taste" was recorded as a 6 point Likert score from 0 "no problem" to 5 "problem as bad as it could be". Nasal symptom scores (NSS) were recorded via a 5 questionnaire score from 'nasal obstruction', 'thick nasal discharge', 'facial pain/pressure', 'smell disturbance' and 'need to blow nose'. This was reported as a summary score from 0 -25. All four PROMs were recorded at baseline and 6mth post-surgery.

Olfactory testing

The Smell Identification Test 40 was utilised. This is a validated 'scratch and sniff' olfactory odorant discrimination test reported as dichotomous correct or incorrect smell identification[129, 130]. It was reported as a score from 0-40. The diskettes were scratched and held 2 inches from the nose. There were a closed set of four responses. The test was performed with the patient at rest with no prior food or flavoured drink for 30min prior to testing. No prior nasal spray or examination was performed. The test was performed at baseline and 6 months post-surgery in the pituitary patients only.

Surgical technique

A binostril approach with a contralateral port was the author's standard approach for pituitary work. With this approach the contralateral septal mucosa was nearly completely preserved. No middle turbinate is resected in this approach. After creating the naso-septal flap (see below), the bone of the septum was removed 2cm anterior to the face of the sphenoid or where the posterior septal bone becomes thin. The contralateral mucosa was preserved. The contralateral mucosa was swept laterally from the contralateral face of the sphenoid. The ostium was entered as described above but in the submucosal plane. An inferior vertical channel of sphenoid bone was removed on either side of the midline. A large straight Mayo scissor, double action or through-cutting instrument was used to separate the inter-sinus septum from the roof of the sphenoid. A large grasping forceps was used to remove the sphenoid rostrum. This often came out en-bloc but if not, a drill was used. The remaining face of the sphenoid was removed laterally and superiorly to expose the roof and lateral optico-carotid recess (OCR) (Figure 1A). A small opening was made in the elevated mucosa on the contralateral side, incorporating the natural ostium, to allow an instrument to pass through and make binasal surgery possible (Figure 1B).

Modified nasoseptal flap

A medium length needle point monopolar diathermy (Megadyne E-Z Clean 0016AM, Draper, UH, USA) is used on settings of 12 cut and 12 coagulate power (ForceFX 8CS, Valleylab, Boulder, CO, USA) to define the flap (Figure 2). A releasing back incision was made from the choana on the vertical palatine bone (or medial pterygoid) under the sphenopalatine artery (Figure 3b). The posterior choana was outlined and the incision continued on the septum 2-3mm away from its posterior edge to ensure that the incision was down to bone at all times. The incision in the floor of the nose was brought forward at a variable distance laterally on the

floor near to the inferior turbinate (Figure 3c). Then the superior incision starts at the superior limit of the sphenoid ostium and the striated 'thin' upper septal mucosa was preserved (Figure 3d). The superior septal mucosa is thin; making it less effective for reconstructive purposes and contains the olfactory epithelium. The flap was mobilized everywhere but superiorly. The release from the superior edge was made last. The flap was stored in the nasopharynx for later use in reconstruction.

Postoperative care

Silastic sheeting 0.51mm (Medtronic, Jacksonville, Fl,) was used to cover the septum bilaterally. A Nasopore (Polyganics, Groningen,The Netherlands) dressing was utilised within the sphenoid. The patient was allowed to breathe through their nose immediately postop. Mupiricon 2% ointment and Amoxicillin 875mg/Clavullinic acid 125mg was used twice a day for 10 days. This was intended to reduce Staphylococcal co-colonization in the immediate post-surgical period. Large volume, positive pressure nasal irrigation with commercially prepared buffered isotonic saline was used via a 240ml squeeze bottle (Sinus Rinse, Neilmed, California). This was continued twice daily for 3 weeks at which the first outpatient review occurred. The silastic sheets were removed, any residual Nasopore (Polyganics, Groningen,The Netherlands) suctioned and saline irrigation continued with instructions for daily use decreasing to 2-3 times weekly, but not to stop, until 90 days post-op when the majority of healing as occurred[(91)]. All sinonasal cavities were examined between 3 and 6mths to check for remucosalization, the absence of crusting, recovery of mucocillary function and the absence of chronic inflammation (apart from occasional small area of granulation tissue).

Statistical analysis

Statistical analyses were performed using SPSS v 20.0 (Statistical Package for the Social Sciences, Chicago, IL).Olfactory, Nasal symptom scores and SNOT22 data were considered to

be parametric and the paired Student's t test was used to compare pre-op and post-op scores. Comparisons between response groups were assessed with ANOVA and a Bonferroni post-hoc analysis for subgroup comparisons. Ordinal data from the smell question and Global nasal function scores were assessed with a Kendal Tau-b for changes. All *p*-values were two-tailed and a value of $p<0.05$ was considered statistically significant.

Results

Forty patients (age 50.95±15.31yrs, 47.5% female) under going pituitary surgery were assessed. Baseline nasal function and olfactory data is presented in Table 1. Approach related morbidity was minimal with one patient suffering a self-resolving epistaxis (2.5%) and one patient experiencing a CSF leak (2.5%) requiring exploration and revision of reconstruction. No cases of intracranial bleeding, infection or new onset neurological deficit occurred. All patients were available for their 6month assessment.

Sino-nasal function and quality of life

For the pituitary patients, the Nasal Symptom Scores were not significantly different following pituitary surgery with a non-significant lower score at 6mths (2.75±3.40 v 3.05±3.03, p=0.53). Similarly, the SNOT22 scores improved post-surgery (1.02±0.80 v 0.83±0.70, p=0.046). The patients global assessment of overall nasal function (-6 to +6) was statistically better after surgery at 6months (Kendall Tau-b for ordinal scales p=0.019)

Olfactory testing in pituitary patients

There was no significant difference in objective smell discrimination scores between baseline and 6mths (31.63±3.49 v 31.35±4.61, p=0.68). The subjective olfactory scores at baseline (Table1) did change following surgery (Kendal Tau B p=0.033) but the spread went in both directions, favouring improvement (Figure 4a).

To assess this further, the SIT40 scores of the patients based on a grouping of the change in "Disturbance in smell/taste" question at 6 months compared to baseline was undertaken. Patients were classified as having a subjective score lower, unchanged or improved. There was no difference in SIT40 scores between those who subjectively rate their smell lower or higher at 6months a (ANOVA F0.44, p=0.65) with a post-hoc Bonferroni analysis showing no difference on multiple two analysis (Figure 4b).

There was one patient that reported a 4+ decline in function subjectively (figure 5a). This was 39yro acromegalic male who had a suprasella CSF leak during surgery. He had a clear fluid discharge with a suspected low pressure headache without meningism at day2 and was re-explored. There was clot and Surgicel(Johnson & Johnson medical, Norderstedt, Germany) between the planum bone and the nasoseptal flap. The reconstruction was revised with Duragen (Integra LifeSCiences, NJ, USA) underlay and flap reposition. Surgicel and other material removed so that the flap made direct contact with the skull base. The sphenoid was packed with iodoform gauze to ensure that reconstruction layers did not separate again. The recovery was uneventful apart from poor smell at 6months. On endoscopy, there were only small amounts of granulation at 6months with a visible olfactory cleft and no adhesions to account for poor smell recovery. Local inflammation is thought to be the cause and a SIT score of 29/40 (original baseline 31/40) suggests recovery may occur with time.

Subjective olfaction compared to nasal tumour surgery patients

There were fifty eight control patients with paranasal tumours (age 52.35±18.51yrs, 52.5% female). There was no difference in age (50.95±15.31yrs v 52.35±18.51yrs,p=0.70) nor gender proportions (47.5% v 52.5%, p=0.29) between pituitary and paranasal sinus tumour patients (Table 1). No tumour patient had a septal flap raised. No tumour patient had there olfactory apparatus intentionally resected as part of their procedure. No statistical difference was seen

between the pituitary and paranasal sinus tumour scores for change in baseline to 6mths olfactory loss (Kendall tau-b p=0.46).

Discussion

Rhinologists regularly perform surgery to remove sino-nasal tumours, alter paranasal anatomy to access the skull base and treat inflammatory disease. It is the expectation that when mucosa regenerates and mucocillary function returns, normal sinonasal function will recover. Persistent sinonasal symptoms almost always have a cause, and do not occur simply because the anatomy was altered. Adhesions can cause mucus trapping if not divided in postop care, chronic inflammation can develop, 'sumps' of non-function mucosa can be created and temporary mucus clearance may not be well managed by nasal irrigations. These are common causes of post-surgical sinonasal dysfunction.

There has been some controversy regarding the morbidity of nasoseptal flaps, with some groups reporting significant disturbance in smell[86, 123]. The techniques employed, in these studies, may not have preserved the olfactory area in a manner as described in this study. Comparison with studies reporting expanded techniques that intentionally transverse the posterior cribriform area do not allow a good comparison of olfactory disturbance, because the olfactory morbidity is anticipated as a result of this approach[10]. Kim et al described differing outcomes based on cold dissection v electrocautery[131], noting that olfactory impairment was uncommon and reported in only one patient with impairment in their series. The premise that thermal injury might contribute highlights the fact that a defined area of olfactory bearing septal mucosa exists. This is further supported by a repeat study from the Rottenburg group, who originally described significant olfactory disturbance[123], and their subsequent study of patients with and without a nasoseptal flap,demonstrated that a large

flap being raised by this group is a detrimental factor[85]. However, the flap described by Tam et al has little respect for the "olfactory strip" on the septum.

The olfactory bearing septal and turbinate area is potentially not as low as many surgeons believe with prior study demonstrating that only 16% of the lower third of superior turbinates containing any neuronal elements[132]. These authors also noted that in the 12% of patients that reported any subjective disturbance, none of them had neuronal tissue in their specimens to incriminate resection of olfactory mucosa as the cause. Likewise, well-trained rhinologists are able to resect parts of the middle turbinate without affecting olfaction[127] and noting that the impact of surgery on olfaction occurs in the first month but recovers well by 3months[124]. Mucosal inflammation does occur from surgical intervention and this can be seen on endoscopy[127]. Some areas that heal by secondary intention can take 3mths or more to fully recover[91]. This suggests that a combination of minimising mucosal trauma/inflammation and respecting the olfactory bearing areas of the nasal cavity is likely to ensure minimal impact on olfaction.

The overall impact of trans-sphenoid surgery on sinonasal function has been previously assessed. The General Nasal Patient Inventory (GNPI) demonstrated that 3 - 6month scores returned to baseline for the average patient but 8% required ongoing consultation regarding nasal symptoms[122]. In this study, the baseline nasal symptom scores were higher in the pituitary group despite patients rating their overall sinonasal function as better in the pituitary group. This is difficult to explain but the 30% (12/40) rate of acromegaly in our group might account for nasal symptoms at baseline. As expected, the final sinonasal function favours the pituitary group. (Figure 5)

Tissue manipulation and trauma can be minimal with an endoscopic approach compared to microscopic access and this is reflected in patient preference[125] and in recovery of function[121, 126]. Ultimately, this mucosal trauma is dictated by differences in surgical technique, even

amongst procedures described under the umbrella term of an 'endonasal endoscopic approach'. However, the design of the nasoseptal flap has not been well addressed and it is likely that heterogeneous practices exist. Authors have suggested modifications to technique be made[86, 121] and the data presented in this study provides evidence that preservation of the 'olfactory strip' as a discrete area can avoid significant impact of both olfaction and sinonasal function. Although, the concept of an 'olfactory strip' has been promoted by colleagues (Ric Carrau) for many years and alluded to in publications[133] , the focus was on usually on septal mucosal recovery. Since then, the observation that mucosal regeneration occurs much quicker under silastic sheeting[134] with or without free mucosa grafts[102] has shifted the focus away from debate over the donor site morbidity. Only one comment to the editor could be found in the literature that discussed this unique area in relation to pituitary surgery[99].

A modified nasoseptal flap with preservation of the 'olfactory strip' can provide a low morbidity approach while maintaining reconstruction options. Such a flap can provide better reconstruction than free grafts[81] and can be easily reused as part of future surgical interventions[135]. Such options are potentially more important in the management of pituitary adenomas if complete resection is not the intended goal from initial surgery and further surgical interventions are considered likely in the future.

Conclusion

Separating the effects of post-surgical inflammation from the impact of approach will always be difficult. Surgeons have differing approaches to mucosal preservation, surgical technique and postoperative care. However preserving the 'olfactory strip' of septal mucosa can provide a low morbidity approach while maintaining reconstruction options.

Figures

Figure 6.1

The author's standard exposure is to have one view of all limits of the sphenoid cavity on view. The technique being described is not a 'limited' access. The floor is exposed by removal of rostrum and drill to ensure that a straight suction can easily reach the lowest point (A) and this allows easy freedom of movement for the surgeon during bimanual dissection (B).

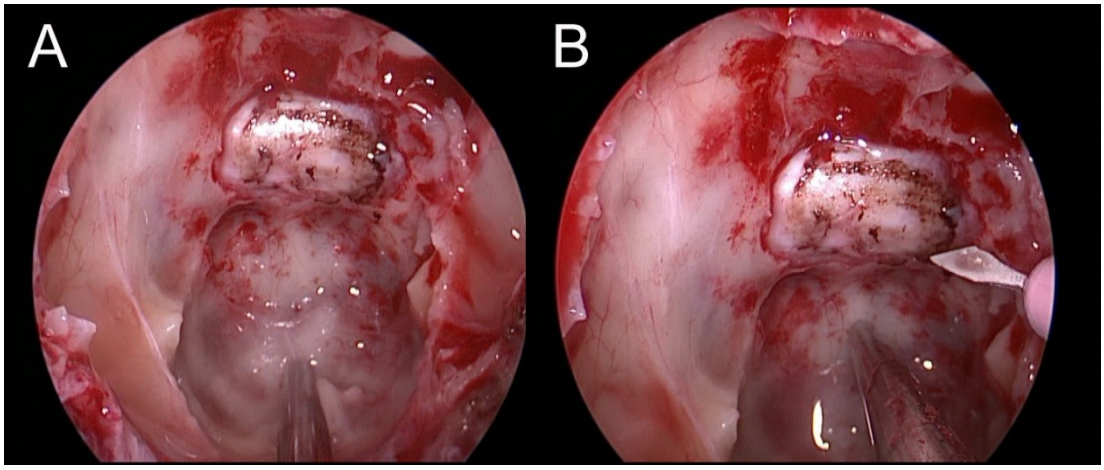


Figure 6.2

The design of the olfactory preserving nasoseptal flap is shown. The olfactory epithelium often has a distinct appearance compared to the mucosal in the lower septum. The mucosal in the lower septum and nasal floor is of better quality for reconstruction.

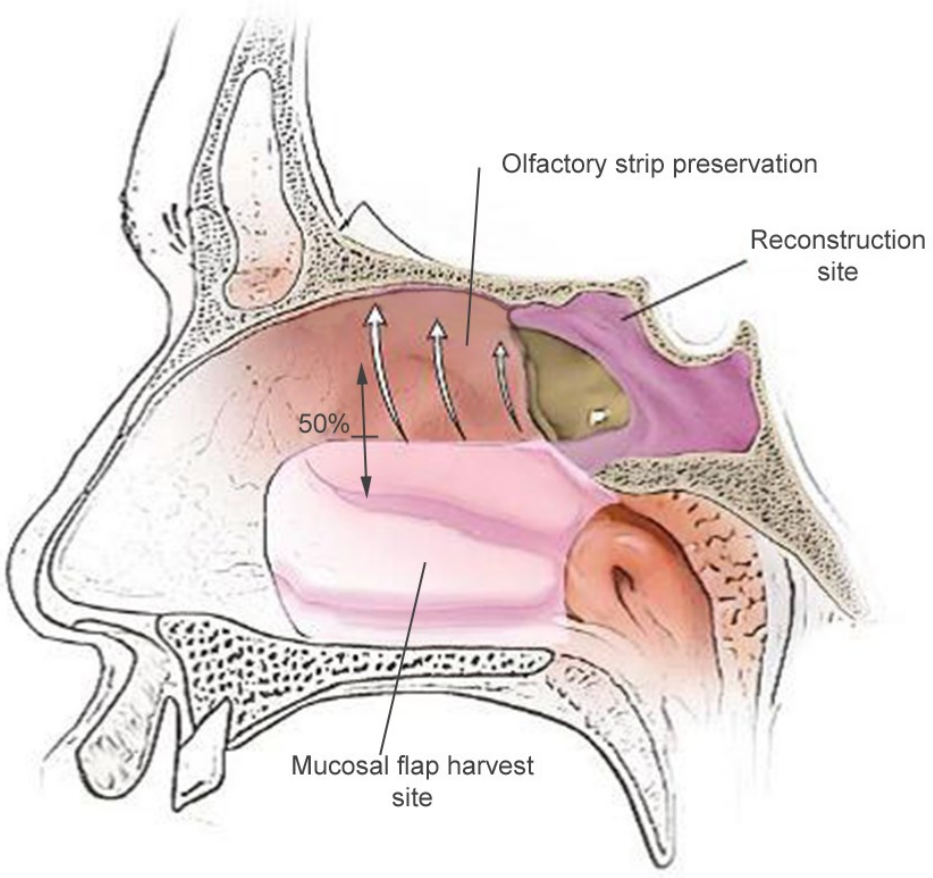


Figure 6.3

The approach for a right nasoseptal flap with the middle turbinate (#) seen in A. The incision starts on the medial pterygoid plate (B) and includes the floor (C). The olfactory epithelium (or strip) is often seen as distinct mucosa (arrow) with the superior turbinate (*) and middle turbinate (#) close (D). The incision runs below this area (E). The final donor site is only 50% the height of the middle turbinate (#) (F)

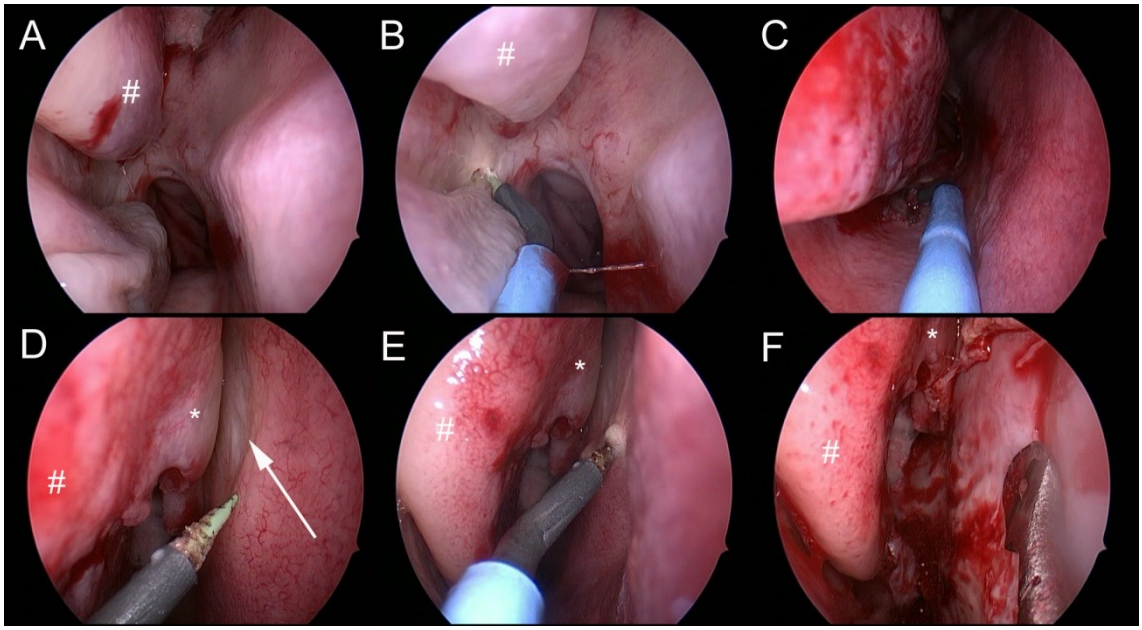


Figure 6.4

The frequency for patients and their subjective change in olfaction score (A) and the objective Smell Identification Scores based on the 3 subjective outcomes (B). There was no difference between groups on Bonferroni two-way post-hoc analysis.

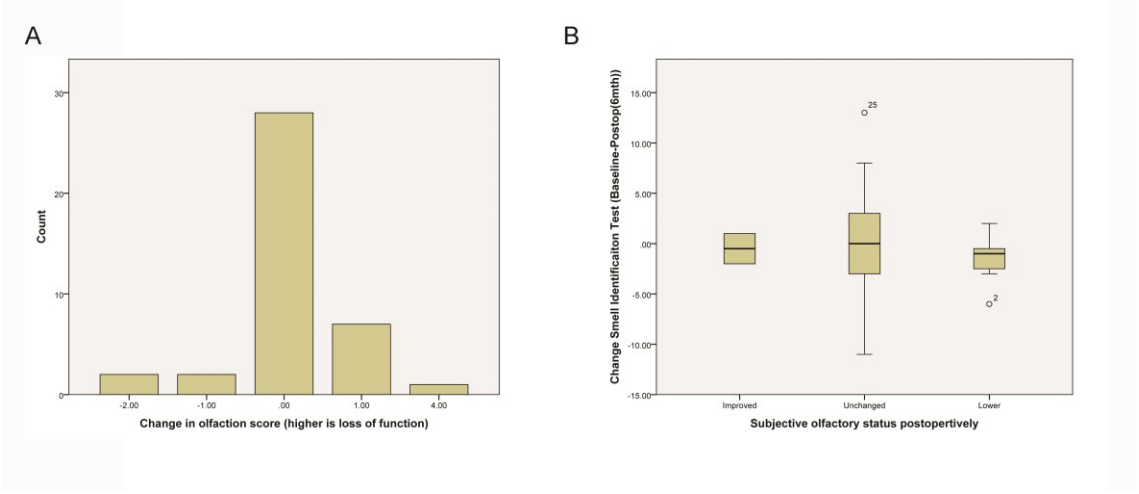
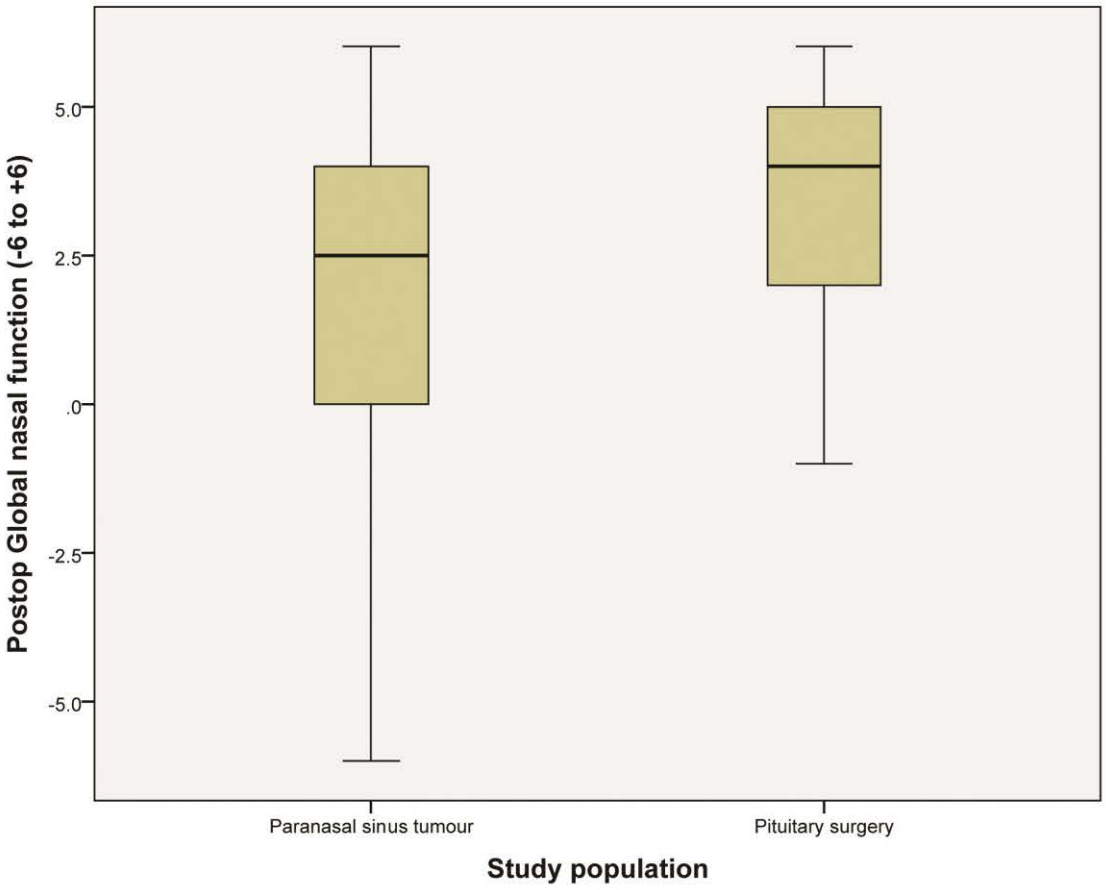


Figure 6.5

The overall post-operative rating of “global nasal function” by patients on a scale -6 to +6 favours the pituitary group as expected.



Tables

Table 6.1

Baseline data for the study population. SIT: Smell Identification Test. SNOT22: Sinonasal Outcome Test 22. Global nasal function (score -6 to +6). Loss of smell or taste (rated 0 to 5)

Outcome	**Pituitary (n=40)**	**Sinonasal tumour (n=58)**	**p-value**
Age	50.95±15.31yrs	52.35±18.51yrs	0.70
Gender (female)	47.5%	52.5%,	0.29
SIT 40	31.22±3.72	Not performed	n/a
Nasal symptom score	2.75±3.40	1.46±0.11	0.01
SNOT22	1.02±0.80	1.27±0.89	0.16
Global nasal function	4.0(IQR 6)	-2.0(IQR4)	<0.01
Sense of loss of smell or taste	0(IQR1)	0(IQR3)	0.02

Chapter 7

Survival outcomes for stage-matched endoscopic and open resection of olfactory neuroblastoma

Abstract

Objective

Advanced stage olfactory neuroblastoma still remains a condition that requires aggressive multimodal therapy to achieve optimal outcomes. Debate exists over the application of aggressive endoscopic endonasal resection of tumour in this situation. This study aims to assess stage matched open and endoscopic surgical therapy, in conjunction with adjuvant therapies, in the management of olfactory neuroblastoma.

Methods

A prospective cohort of patients with olfactory neuroblastoma from six cancer institutions was undertaken. Classification was based on dural involvement, Kadish stage, nodal disease and Hyam's grading. The treatment approach and margin status were sought. At follow-up, local control, nodal status, and evidence of distal metastases were recorded. Any subsequent therapy for ENB either at the primary, regional or distant site was sought. Patients without recent follow-up (<6month) were contacted prospectively. Statistical analyses to identify risk factors for developing recurrence and survival differences were performed.

Results

113 patients were recruited from six difference centres (age 49.7+/-13.2yrs. 46% female). Local disease stage as presentation was Kadish A 9.7%(11), Kadish B 26.5% (30), Kadish C 63.5%(72.. One hundred and nine patients had an operation with curative intent with 61.5% undergoing endoscopic resection. Endoscopic surgeon was employed in 53.5% of Kadish C tumours. The within Kadish Stage survival analysis favoured the endoscopic subgroup for Kadish C (log rank p=0.017) non-significant for Kadish B (log rank p=0.39).

Conclusion

Olfactory neuroblastoma is a tumour associated with delayed neck disease, long term recurrence and a survival rate, which despite being higher than other sinonasal malignancies,

still warrants aggressive multimodal therapy. The endoscopic approach can achieve margin negative surgical clearance, even in advanced Kadish C disease, with favourable outcomes to open craniofacial resections.

Introduction

There has been a significant adaptation of the endoscopic endonasal route to the resection of sinonasal malignancies in the past decade. The model malignancy for endoscopic resection is olfactory neuroblastoma, with its nasal cavity origin, large exophytic component and local invasion. There are sensible limits to what can be removed from an entirely endoscopic ventral route. The principals of the surgical approach not crossing a major neurovascular plane, such as tumour extending beyond the mid-orbital point, for the endonasal approach, this represents disease better addressed by alternate routes. Similarly, tumour extending into the premaxillary tissue often involves resection of skin and a trans-facial approach. Finally, tumour involving the hard palate or alveolar process is likely to be removed in conjunction with an inferior maxillectomy and not an endoscopic only approach.

However, in skilled endoscopic centres, the size of the tumour and degree of intra-cranial extension are not limitations to endoscopic resection. Likewise, vascularized flaps, used in the reconstruction of the subsequent skull base defect, provide comparable rates of closure to open surgery[(81)]. Although the sino-nasal tract is not sterile, infective complications such as meningitis also appear to be very low[(136)]. There is evidence that an endoscopic approach in skull base tumour surgery may provide superior neurological[(2)], visual[(3)] and functional[(4)] outcomes compared to open approaches to the same area[(5)]. Additionally, patients undergoing endoscopic surgery have a faster recovery and less in-hospital time post-surgery [(6)]. Despite attempts to compare endoscopic and open approaches, deponents of endoscopic surgery for malignancy highlight the imbalance of lower staged tumours being treated via an endoscopic only approach[(137, 138)]. Unfortunately, attempts at systematic review of published studies on the management of olfactory neuroblastoma are also plagued by this bias[(139-142)]. Thus, the conclusions for most of these reviews are that “for appropriately selected patients” the endoscopic approach may be appropriate. This study attempts to bring together prospective

data from stage-matched patients with olfactory neuroblastoma to compare outcomes from surgical excision performed via an endoscopic or open craniofacial approach.

Methods

Study design

A cohort analysis was performed on all patients treated for olfactory neuroblastoma. Multicentre retrospective and prospective data was collected. The study had ethical approval from the local Human Research Ethics Committee (HREC12/177). All patients with prospective follow-up provided informed consent before enrolment. Data collection was used using a locked-validated excel spreadsheet to collate data consistently from all sites.

Patient population and staging

Patients with a histological diagnosis of olfactory neuroblastoma that were treated across six tertiary hospitals were included. The recruitment centres were chosen as they had known oncologic services that included endoscopic skull base surgical expertise to ensure that definitive endoscopic, margin negative surgical resections were performed rather than 'debulking' procedures. The tumours were classified based on dural involvement, Kadish stage, nodal disease and Hyam's grading.

Treatment characteristics

Treatment modalities to the primary site and neck included radiotherapy, surgery and combinations. The treatment approach was classified as endoscopic, endoscopic assisted or open craniofacial. Margin status from surgery was defined as microscopically positive or clear. Gross total resection was the goal of every surgical procedure. The surgical complications of infection (meningitis, ventriculitis), new onset neurological deficits, epistaxis and postoperative

cerebrospinal fluid leak were collected. The use of radiotherapy and/or chemotherapy was defined as none, neoadjuvant or adjuvant. The total radiation dose (Gy) was recorded.

Follow-up data collection

At last follow up- visit, within 6 months, the status of local control (recurrence/no recurrnce), nodal status, and evidence of distal metastases were recorded. Any subsequent therapy for ENB either at the primary, regional or distant site was sought. Patients without recent followup (<6month) were contacted prospectively. Dates of any recurrence and/or subsequent therapy were recorded.

Statistical analysis

Disease-free survival (DFS) was calculated following primary treatment of olfactory neuroblastoma. Chi squared analysis was used to compare groups by proportions. Pearson correlation, regression analysis and Kaplan Meier product limit method were performed to identify risk factors for developing recurrence or survival. Statistical differences between actuarial curves were tested by the log rank test. ANOVA was used to compare age and radiation dosing between groups. Statistical analyses were performed using SPSS v 20.0 (Statistical Package for the Social Sciences, Chicago, IL). All *p*-values were two-tailed and a value of $p<0.05$ was considered statistically significant.

Results

Patient population

113 patients were recruited from six difference centres (age 49.7+/-13.2yrs. 46% female). Local disease stage at presentation was Kadish A 9.7%(11), Kadish B 26.5% (30), Kadish C 63.5%(72). One hundred and nine patients underwent curative surgical therapy. Tumour histological grade for Hyam's grading of grade I 6.2%, II, 31.9%, III 28.3% and IV 5.3%. Dural involvement was recorded as being present in 52.2% of patients. Nodal disease was present in 7.1% of

patients at presentation. All primary nodal disease was ipsilateral level 2 disease. Median follow- up was 41.5 months (IQR58.2 months).

Perioperative treatment characteristics

Surgical approach included endoscopic-only 59.3%(67), endoscopic assisted 16.8%(19) and open craniofacial resections in 20.4%(23) and 4 patients having only radiotherapy/chemoradotherapy. Surgical margins were clear in 74.1% and positive in 25.9% of patients post-surgery. Postoperative complications were recorded in all but one case and were identified in 16.7% of patients Complications included four (3.7%) with postoperative infection, five (4.6%) with neurological deficits, two (1.9%) with epistaxis and eight (7.4%) with postoperative CSF leaks. Radiotherapy was used as adjuvant therapy in 75.2%, neo-adjuvant treatment in 9.2% and surgery alone in 15.6%. Total doses were 57.0±7.1Gy with a range (23Gy-74Gy) over 30.4±6.0 fractions (range 11-55). The use of radiotherapy increased with Kadish stage (X^2 13.0, p=0.011) and is presented in Table 1. Chemotherapy was used in only 29.3% of patients and increasingly offered with Kadish stage (X^2 13.1, p=0.041), Table1.

Overall Disease free survival

Of the 113 patients, local recurrence occurred in 15(13.3%) and regional disease in 10 (8.8%) patients. Metastatic disease occurred in 17 (15%). The 5 and 10 year overall disease specific survival rates were 87%(SE48) and 66%(SE10). There was no clear relationship between Kadish stage and nodal disease (p=0.43) but a trend between Kadish stage and the development of metastatic disease (p=0.06), Table 2. Disease free survival by Kadish Stage is presented in Figure 1 (log rank p=0.14 between curves). The distribution of disease characteristics between Kadish stage is presented in Table 3.

Endoscopic only versus open resections

The characteristics of patients with an open (and assisted) versus purely endoscopic resection are presented in the Table 4. There were 30 Kadish B and 71 Kadish C tumours. These characteristics between the endoscopic only resected tumours and the open (and assisted) tumours were very similar. There were two important differences. Firstly, the Kadish C patients were older in the endoscopic only group (45.7±13.8 v 52.2±12.1, p=0.04) and consistently, the ability to achieve a clear surgical margin was greater in endoscopic, compared to open surgery, groups for both Kadish B (71.4% v 90%,p=0.001) and Kadish C (53.1%v 84.2%, p=0.001) subgroups. This was important as surgical margin status was a major predictor of survival for the group as whole (Figure 2, log rank p=0.004). The within Kadish Stage survival analysis favoured the endoscopic subgroup for Kadish C (log rank p=0.017, figure 3b) non-significant for Kadish B (log rank p=0.39, figure 3a).

Other factors contributing to survival

Hyams grade did not appear to influence overall disease specific survival (log rank p=0.17). This was also non-significant when analysed in cox-regression and adjusted for Kadish stage (p=0.61). Dural involvement was a significant factor in survival analysis with worse outcomes associated with patients displaying dural involvement (figure 4, Log rank p=0.032). Lymph nodes at presentation did not appear to affect survival as a single factor (log rank p=0.82) or when adjusted for Kadish stage (Cox regression p=0.92). However, delayed nodal disease was major predictor of mortality (log rank p<0.001, Figure 5), despite subsequent therapy, and was still significant when adjusted for Kadish stage in cox regression (p=0.011).

Discussion

Oncologic training is critical for the success of patients managed via endoscopic only approaches. Careful assessment, accurate staging, negative margin tumour resection and

appropriate use of (neo)adjuvant therapy are critical to successful outcomes. In this series, the majority of olfactory neuroblastomas managed were Kadish C and the majority (53.5%) removed by endoscopic only approaches. This study population differs to previous reports on the endoscopic management of olfactory neuroblastoma[143-148] and those in the Deviah and Komotar meta-analyses[138, 142], in which the majority of Kadish C cases were managed in conjunction with a craniotomy. However, both surgical expertise and equipment have evolved in the past 10 years. Most intracranial extension is managed endoscopically in this study's participating institutions. Open approaches are appropriate when there is disease lateral to the mid-orbital point, extensive involvement of the posterior table of the frontal sinus and intra-orbital disease. However, extensive dural and intracranial involvement is not a limitation. Open approaches are utilized when surgical dissection may cross neurovascular planes (lateral to mid orbit), present issues with reconstruction (needing to cranialize the frontal sinus) or require an orbital exenteration (although this can be performed endonasally, patient benefit is negligible).

The ability of the surgeon to achieve a margin negative resection was critical in this study. The clear margin status of open resections of patients with Kadish C tumours was less than endoscopic cases (53.1%v 84.2%, p=0.001). There may be inherent bias in the types of Kadish C tumours being treated by each approach. However, the endoscopic approach is advantageous as much of the tumour bulk, which is initially visualised, is exophytic in nature. Often, it is only the base of the tumour that has extension and invasion into local structures. When a tumour is de-bulked endoscopically, it is this exophytic component that is removed first. The invasive base of the tumours is often accurately localised compared to a purely open craniofacial resection. The rate of clear margin resection was lower in our open group. In comparison, the International Collaborative Study by Ganly[149] , primarily an assessment of open surgeries, reported a 71% clear margin status (95/329). Other publications, which

include primarily Kadish C and open resections, report clear margin status from 42-46%[150, 151] through to 78%-88%[152, 153]. In addition to other publications, most of these studies support this study's finding that positive microscopic margin status remains a poor predictive factor [154, 155]. For the endoscopic groups, margin negative resections varies from 85% in a larger population of sinonasal malignancies [156] to 100% in smaller groups [157].

There is still debate regarding optimal staging systems. Both Kadish[158] and Dulguerov[143] have been shown to be superior to alternatives and each other. This study only utilized the Kadish system and may not accurately reflect the diversity of tumours seen within each stage, especially Kadish C. A selection bias may be introduced here, in particular to orbital involvement. However, extensive Kadish C tumours involving the infra orbital spaces, such as the infratemporal fossa, may bias the endoscopic group in reverse. Limitations exist with all staging systems and it is unlikely that rapid advancements will be made, as large numbers of patients will be required to refine and prove superiority over currently used systems. However, this is an area for future research.

The data from these multiple centres, performing endoscopic resections for advanced stage olfactory neuroblastoma, strongly support the current practice at many institutions. The endoscopic endonasal approach can provide an aggressive margin negative resection with survival outcomes equivalent to or better than open resections. The ability to assess and carefully resect the infiltrative component of the tumour may underscore this observation. Whether open or endoscopic, the oncologic principal of complete resection with microscopic negative margins, even in a tumour known to be radiation-sensitive, is still critical [154].

Conclusion

Olfactory neuroblastoma is a tumour associated with delayed neck disease, long term recurrence and a survival rate, that despite being higher than other sinonasal malignancies[154], still warrants aggressive multimodal therapy. The endoscopic approach can achieve margin

negative surgical clearance, even in advanced Kadish C disease, with favourable outcomes to open craniofacial resections.

Figures

Figure 7.1

Overall and Kadish stage factored disease free survival curve analysis

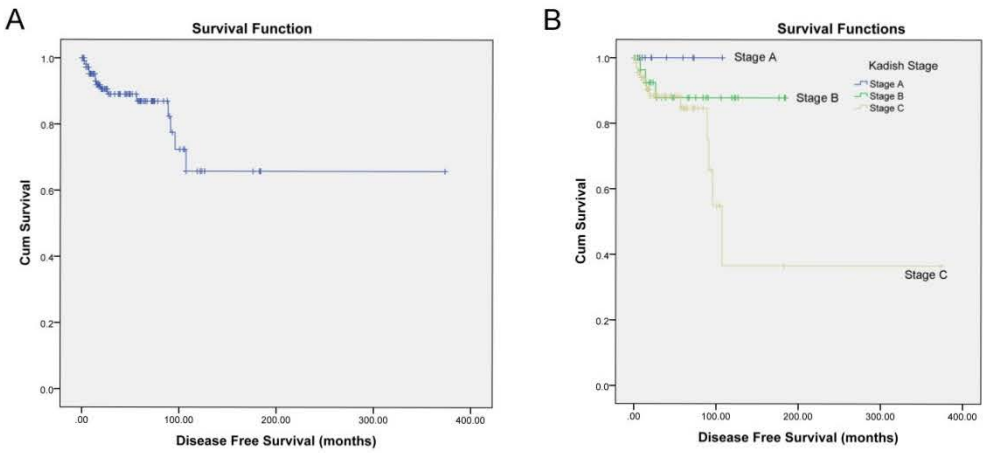


Figure 7.2

Survival and surgical margin status for the whole group.

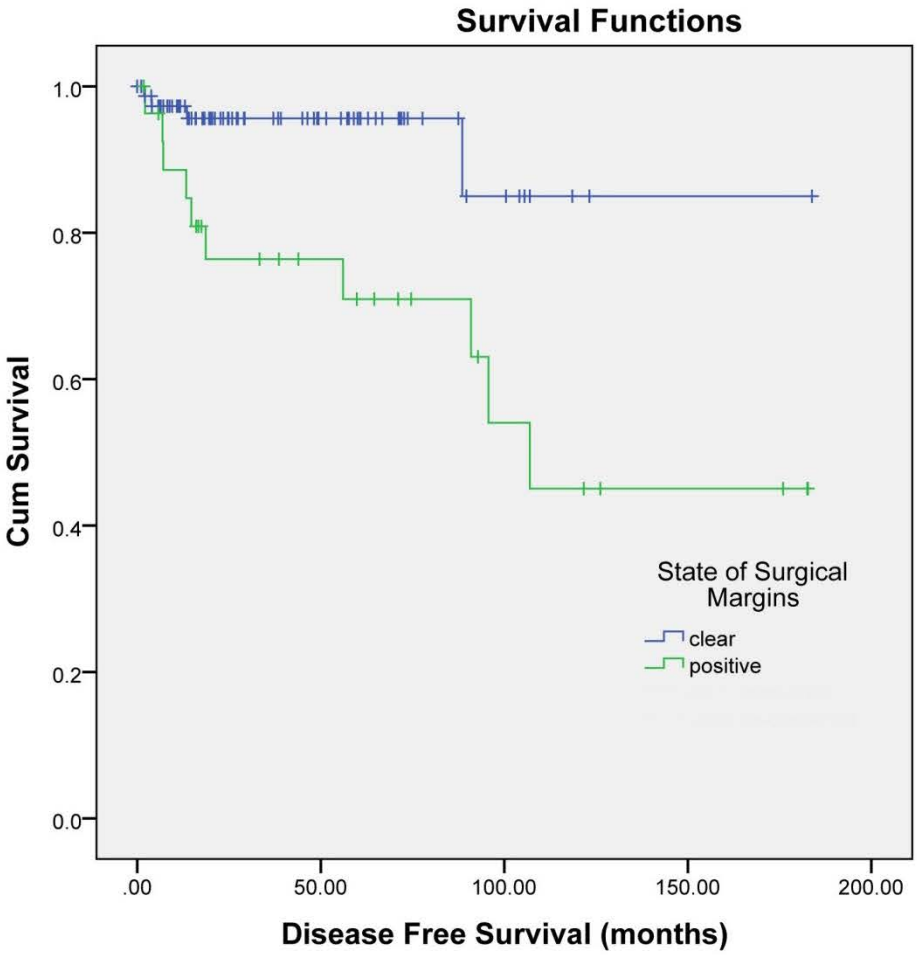


Figure 7.3

With-in stage survival analysis Kadish B (a) and Kadish C (b)

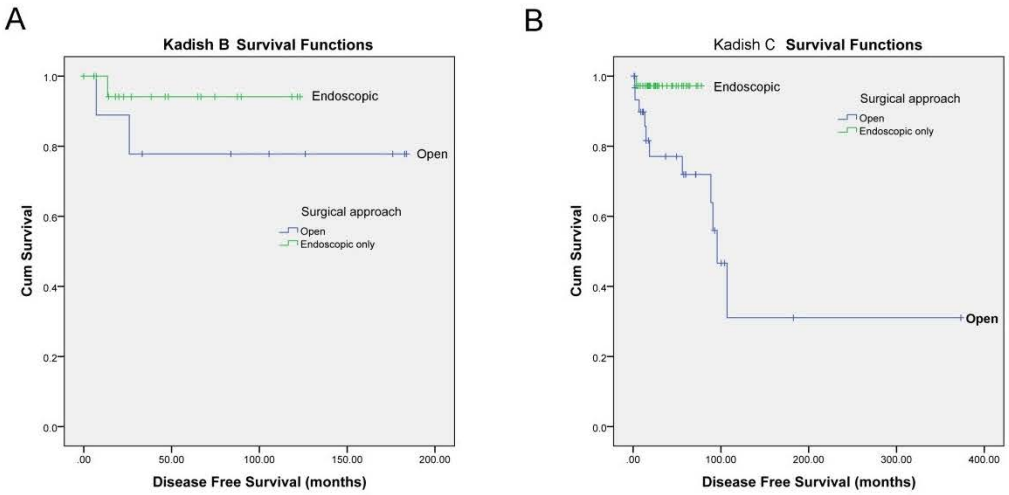


Figure 4

The presence of dural involvement and survival analysis.

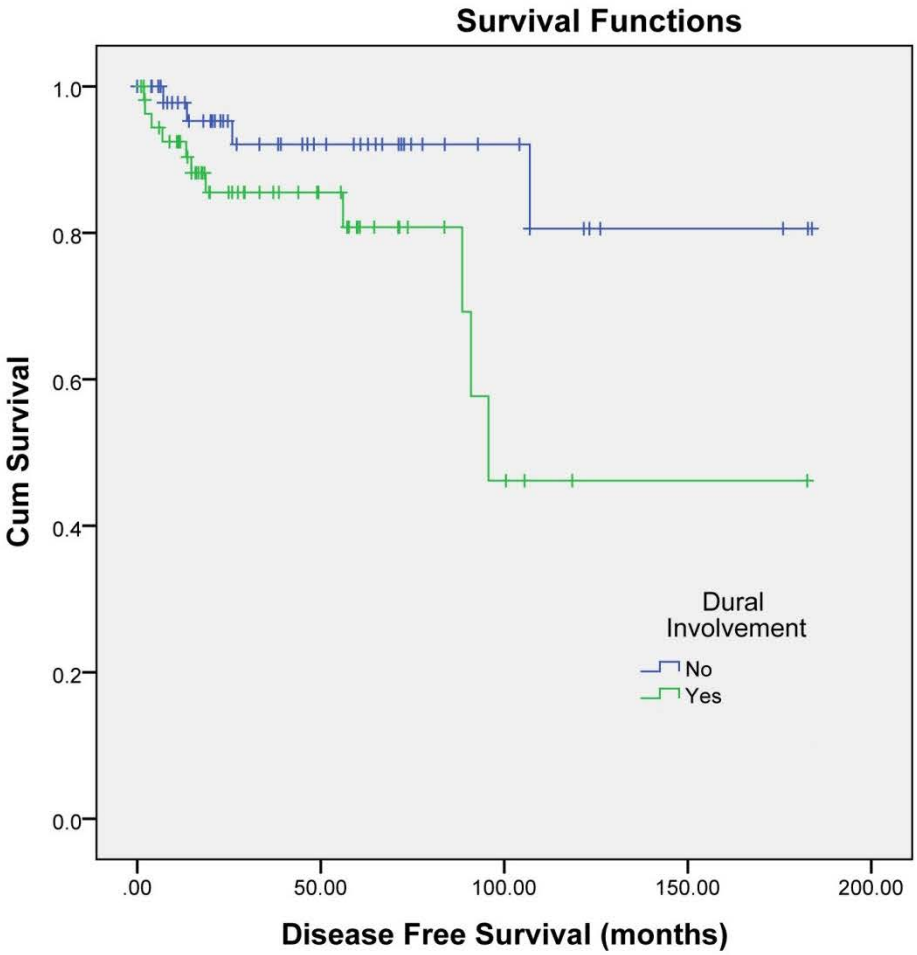
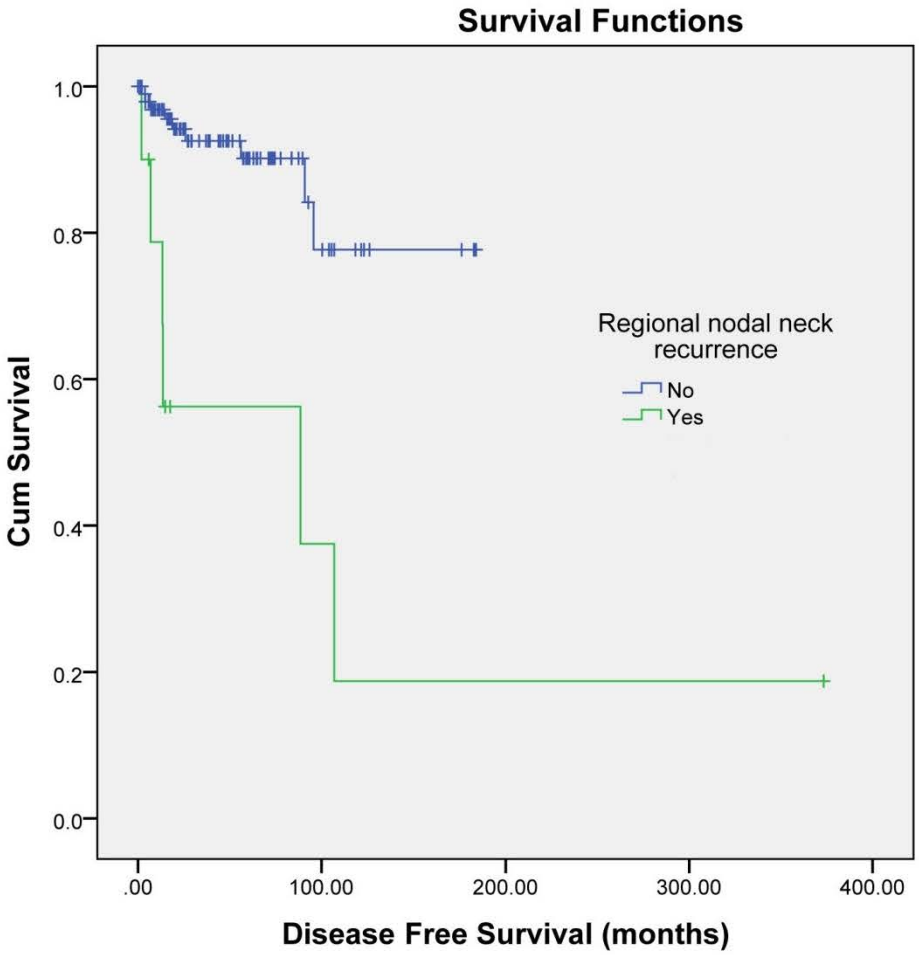


Figure 5

Survival analysis with delayed neck disease



Tables

Table 7.1

Adjuvant therapies by Kadish stage at presentation

	Kadish Stage (% within stage)			
Radiotherapy	A	B	C	p=0.011
Neoadjuvant	0	3.7%	12.7%	
Adjuvant	54.5%	74.1%	78.9%	
None	45.5%	22.2%	8.5%	
Chemotherapy				p=0.41
Neoadjuvant	0%	13.3%	12.5%	
Adjuvant	0%	10.0%	22.2%	
None	100%	76.7%	65.3%	

Table 7.2

Development of nodal or distant disease based on Kadish stage at presentation

	Kadish Stage (% within stage)			
Regional	A	B	C	p=0.427
Neck free of disease	100%	93.3%	88.9%	
Nodal recurrence	0%	6.7%	11.1%	
Distant				p=0.064
No distant disease	100%	93.3%	79.2%	
Metastasis	0%	6.7%	20.8%	

Table 7.3

Baseline data for the entire study population

	Kadish Stage (% within stage)			
	A (n=11)	B (n=30)	C (n=72)	P value
Age	52.8±15.2	48.9±12.2	49.5±13.5	0.70
Gender (female %)	54.5%	56.7%	40.3%	0.27
Hyams Grade				0.20
1	30.0%	5.0%	5.9%	
2	40.0%	35.0%	49.0%	
3	30.0%	50.0%	373.%	
4	0%	10.0%	7.8%	
Surgical approach				0.09
Endoscopic	81.8%	74.1%	53.5%	
Open/Endoscopic assisted	9.1%	3.7%	23.9%	
Open	9.1%	22.2%	22.%	
Nodal disease at presentation	0%	10%	7%	0.54
Radiation use	54.5%	70.0%	90.4%	0.003
Dosing (Gy)	52.7±4.1	57±4.5	57.5±7.9	0.28

Table 7.4

Open versus endoscopic resection

	Open (n=42)	Endoscopic only(n=67)	P value
Age	45.6±1.9	51.5±11.9	0.02
Gender (female %)	50%	43.3%	0.49
Kadish			0.06
A	4.8%	13.4%	
B	16.7%	29.9%	
C	78.6%	56.7%	
Hyams Grade			0.36
1	6.1%	11.4%	
2	39.4%	52.3%	
3	42.4%	31.8%	
4	12.1%	4.5%	
Nodal disease at presentation	7.1%	7.6%	0.93
Radiation use	95.2%	77.6%	0.01
Dosing (Gy)	57.6±5.4	56.6±8.6	0.55
Margin status (% clear)	51.2%	88.1%	<0.001

Table 7.5

Kadish B (n=30 with n=27 having surgery)

	Open (n=7)	Endoscopic only(n=20)	P value
Age	42.6±11.7	49.7±11.1	0.16
Gender (female %)	42.9%	60%	0.66 (Fishers)
Hyams Grade			0.85
1	0%	10.0%	
2	42.9%	40.0%	
3	42.9%	40.0%	
4	14.3%	10.0%	
Nodal disease at presentation	0%	15%	0.55(Fishers)
Radiation use	100%	70.%	0.1
Dosing (Gy)	57.3±3.8	56.9±6.0	0.88
Margin status (% clear)	71.4 %	90%	0.001

Table 7.6

Kadish C (n=72 with n=71 having surgery)

	Open (n=33)	Endoscopic only(n=38)	P value
Age	45.7±13.8	52.2±12.1	0.04
Gender (female %)	48.5%	34.2%	0.22
Hyams Grade			0.25
1	4.2%	7.7%	
2	37.5%	61.5%	
3	45.8%	26.9%	
4	12.5%	3.8%	
Nodal disease at presentation	9.1%	5.4%	0.55
Radiation use	97%	86.8%	0.13
Dosing (Gy)	58.1±5.8	57.1±9.8	0.65
Margin status (% clear)	53.1%	84.2%	0.005

Chapter 8

Conclusion

The ability of endoscopic surgeons to accurately orientate the orbit and skull base, even in the presence of massive and obstructive pathology, has expanded the role of endoscopic surgery to tumour management. The orbital floor, as a landmark is critical for an endoscopic surgeon. Secondly, once the skull base has been identified, usually in sphenoid, the ability to resect this barrier, the craniotomy or craniectomy, and have techniques that can provide a robust, evidence based reconstruction has further expanded the diversity of pathology that can be addressed via an endonasal route. However, there are still some key surgical and oncologic principals that must be preserved. Three foundations exist for successful endoscopic surgery for malignant tumours. Firstly, the resection should be defined with frozen section control of surgical margins. The analysis of both open and endoscopic management of olfactory neuroblastoma highlights the importance of resection beyond microscopic margins. Few endoscopic tumour removals are 'en-bloc' but margin control is still essential. The surgical approach that is best for the patient is pre-determined by the tumor and pre-operative imaging, not surgeon skill or expertise. Minimal access rarely implies minimally invasive for the management of malignancy of the skull base. Anatomy should not be retained at the expense of gaining adequate access for tumour removal. Finally, there should be no hesitancy in removing macroscopically involved tissue, such as dura, periorbita and other important structures. There are techniques that are robust, with low morbidity, which can be employed to reconstruct these barriers. While the biology of some tumours may afford an approach of gross, but not microscopic, removal from dura, carotid and orbital structures with successful adjuvant therapy, this is not standard care and yet to be proven as effective therapy for

malignancy[159]. An endoscopic approach should not prevent the surgeon from removing obviously involved anatomical barriers at the time surgery. These principals differ from managing benign conditions, such as inverted papilloma, in which preserving anatomical barriers to spread it paramount or when balancing the morbidity of loss of function with completeness of resection in conditions such as pituitary adenoma or craniophyarngioma.

Proponents of the traditional craniofacial approach (tCFR) argue an en bloc resection possible with the tCFR, where as it is impossible with endoscopic approaches considering it, at best, "piecemeal resection" of the tumor. Proponents of the endoscopic approach, however, are of the opinion that in resecting tumors involving the ventral skull base, whichever the approach; an *en bloc* resection is rarely possible. In fact, optimum endoscopic visualization enables a wide-field three-dimensional resection close to an en bloc resection in most cases. The data presented from the olfactory neuroblastoma study suggests that the endoscopic surgon might have the best opportunity to visualize and control the origin or infiltrative component of the tumour. Proponents of both approaches agree, the resection is aimed at achieving negative margins, and this is supported in the data assessed with the principals of oncologic resection maintained[160].

The endoscopic approach offers a number of other advantages[161] . The operation time is shorter, associated with less morbidity and shorter hospital stay [162]. Patients do not experience the serious complications that can be associated with the approach in tCFR nor are they likely to be subject to the subsequent reduction in quality of life. Nicolai et al.,[163] reported a complication rate of 6 percent following endoscopic resection of malignant tumor compared to 16 percent after craniofacial resection. The most common complication after

endoscopic approach was CSF leak, followed by mucocele formation. Life-threatening complications, such as intra-cranial bleeding and infection are still a risk regardless of the approach.

There is good evidence that vascularized flaps are now the accepted standard for reconstruction of large skull base defects[164]. Although not always available, when the ability to use vascularized mucosa in closing the endoscopic trans-nasal craniotomy, it appears warranted. Donor morbidity is not minimal, as crusting may take 3-4months to fully resolve [11, 165]. However, for many patients, there is also a site of secondary healing where pathology has already been resected. The addition of the nasoseptal flap in this situation does not appear to increase recovery or impair long term sinonasal function [11, 128]. Vascularized mucosa is not always required. While in large (>1cm) defects, post-radiotherapy, high-flow cisterns and in the setting of raised intracranial pressure they are usually employed, free grafts are still often used for simple fistula and sella defects[14, 134]. Techniques have developed to leave the option of raising a flap until absolutely necessary and are often referred to as 'rescue flaps' [133, 166]. However, in partially raising these flaps, without respecting the olfactory epithelium, some authors have reported a 26% loss of smell in their postsurgical patients [167]. Additionally, it may be possible to leave part of the pedicle and return to harvest the flap, the delayed flap. Good vascularity appears to still be maintained in this approach and it remains an alternative [168]. However, given our better understanding of how to reduce reconstruction morbidity and a surgical desire to avoid performing sinonasal dissection at the end of a surgical case with an open intracranial cavity, the flap is raised as part of the initial approach in our institution.

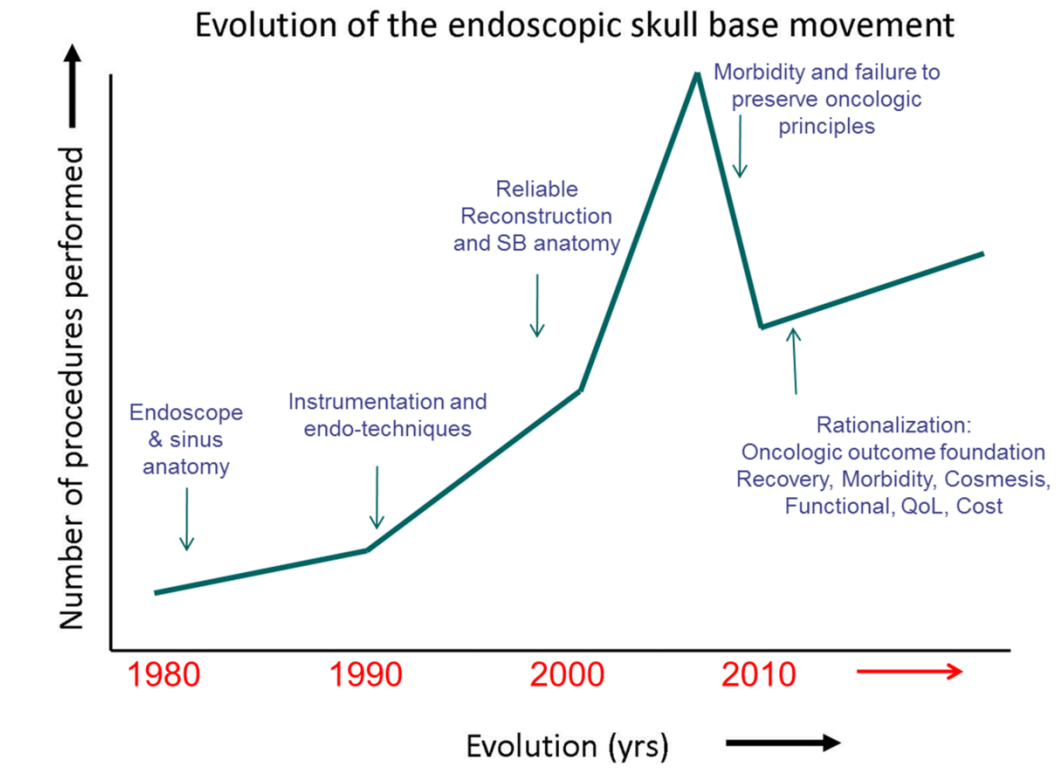
This study demonstrates that the evolution of endoscopic techniques has evolved to a level where potential superiority exists in the management of olfactory neuroblastoma via and endoscopic route. This evidence base supports the decision to employ an endoscopic trans-nasal craniotomy not only for the primary outcome of oncologic success but also in the secondary goals of reduced perioperative morbidity and local sinonasal function. In the published literature, outcomes of endonasal surgery for other tumours are favourable. However, there exists a publication bias in favour of reports on successful surgery which has been noted in other disciplines [169]. In endonasal skull base surgery, the mandatory learning curve of the surgeon calls for specific training programs addressing the technical demands and also crisis management [22, 170-174]. In addition, advanced skull base techniques should be undertaken only in centres where all other surgical approaches can be performed, if required [175]. There are several minimally invasive open approaches, such as keyhole supraorbital craniotomy[176], that need to be considered when under taking treatment planning[177]. Constant training of the multidisciplinary skull base team should help keep the rate of complications minimal [22, 178]. Finally, although the evolution of the endoscopic trans-nasal craniotomy appears to offer lower morbidity in many key functional domains; cerebrospinal fluid (CSF) leak, neurological morbidity, post-operative visual function, post-operative anosmia, post-operative diabetes insipidus (DI), and post-operative obesity/hyper-phagia, there is some mounting evidence that recurrence rates may be higher in benign or slow growing malignancy (meningioma, craniopharyngioma, and chordoma) [179]. It is important that the evolution of endoscopic skull base surgery (figure 8.1) does not leave patients with persistence and recurrent disease, slowly invading into even more difficult-to-treat areas of their skull base because the window for a comprehensive and adequate treatment was not undertaken early in the course of their illness. While, in malignant disease, the first resection should always be complete, there is a role for sub-total resection of benign neoplasia. The judgement, expertise and decision making here, is not easy. For benign tumours, no surgeon wishes to have patient

morbidity dictated by their treatment. However, benign neoplasia is cured by completeness of resection (cf malignancy). Patients with subtotal removal need to be carefully monitored, adjuvant therapies considered and early intervention if growth continues. This process is only possible where the skull base team has made a conscious decision to follow this path and not because surgeon skill or comfort dictated it. The potential exists for a generation of “skull base cripples” in which poorly conceived partial resections and suboptimal patient outcomes adversely affects the advances, as a whole, which have been made by the sub-speciality in the past decade. Perseverance in disseminating new research, improving basic endoscopic training and ensuring continuation of adequate education and skill development, will provide us protection from this outcome.

Figures

Figure 8.1

The evolution of endoscopic skull base surgery from anatomical, technical and instrumentation advancements. We are now in a period of rationalisation of benefit versus limitation.



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