An Algorithm for Surgical Approach to the Anterior Skull Base

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Abstract

Objective To characterize our experience with the surgical management of anterior skull base malignancy, and to propose an algorithm for surgical approach to anterior skull base malignancies.

Design Retrospective review.

Setting Academic cranial base center.

Participants Sixty-seven patients who underwent resection of paranasal sinus or anterior skull base malignancy with an endoscopic, craniotomoscopic, or traditional anterior craniofacial approach.

Outcome Measures Complications, recurrence, and survival.

Results There were 48 males and 19 females, ranging from 6 to 88 years old. There were three groups: endonasal endoscopic resection ($n = 10$), craniotomoscopic resection ($n = 12$), and traditional craniofacial resection ($n = 45$). The most common tumor pathologies included esthesioneuroblastoma, squamous cell carcinoma, and sinonasal undifferentiated carcinoma. Patients with T3/T4 disease were less likely to undergo endoscopic resection ($p = 0.007$). The 5-year disease-free survival was 82.1% overall, with no statistically significant differences among approaches. There were no differences in orbital complications, meningitis, or cerebrospinal fluid leak. Use of a transfacial incisions predisposed patients to surgical site infection and sinocutaneous fistulae. An algorithm for surgical approach was developed based on these results.

Conclusion Sinonasal and skull base malignancies can be safely surgically addressed via several approaches. Surgical approach should be selected algorithmically based on preoperative clinical assessment of the tumor and known postoperative complication rates.

Keywords

- ▶ skull base surgery
- ▶ sinonasal malignancy
- ▶ CSF leak
- ▶ sinocutaneous fistula

Introduction

Paranasal sinus malignancy with anterior skull base involvement was traditionally resected via a craniofacial resection, an

approach that included a transfacial incision combined with a craniotomy. Originally described by Ketcham et al in 1963,¹ this approach remains a mainstay in the treatment of advanced anterior skull base malignancy, but was initially associated with significant morbidity.^{2–7} Over time, advances in surgical technique and improvement in perioperative care have contributed

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to a decreased incidence of complications. In the last decade, the biggest technical development has been the introduction of the endoscope as an adjunct to the surgical approach to skull base pathology. Initially applied to the treatment of inflammatory sinus disease and benign sinonasal tumors, more recently, authors have described the endoscopic endonasal approach (EEA) and craniotomoscopic approach (CEA) for resection of anterior skull base malignancy. In appropriately selected patients, these techniques have been demonstrated to have acceptable oncologic outcomes.^{8,9} Furthermore, EEA and CEA have several potential advantages over traditional craniofacial approaches, including better visualization of deep structures, potential reduction of frontal lobe retraction, and decreased rate of postoperative sinocutaneous fistula.^{10–12} Conversely, cerebrospinal fluid (CSF) leak rate has been reported to be higher in EEA compared with traditional approaches.^{5,9,13}

The appropriate use of endoscopic and endoscopic-assisted approaches depends on the preoperative radiographic and clinical characteristics of the tumor, and it should be continually reevaluated in light of the risk of postoperative complications and long-term outcomes. Most studies comparing approaches to the anterior skull base malignancies are small or limited to specific pathologies,^{14–17} with several larger studies demonstrating single-institution results for endoscopic approaches.^{8,9} Thus, it remains unclear which cases can and should be approached endoscopically. The purpose of this study is to report the complications and outcomes from endoscopic, endoscopic-assisted, and traditional craniofacial approaches for resection of anterior skull base malignancy at a tertiary care cranial base center. The assessment of surgical outcomes was analyzed for factors that should be considered to determine an appropriate surgical approach, and an algorithmic guideline is proposed.

Methods

Approval of this study was obtained through the Massachusetts Eye and Ear Infirmary (MEEI) Institutional Review Board. Surgical databases from the Cranial Base Center at MEEI were interrogated for all cases of anterior skull base surgery performed for the indication of anterior skull base or paranasal sinus malignancies from May 2007 through May 2014. Billing records were queried for CPT codes relating to sinonasal and skull base neoplasms to ensure completeness. Patients with benign neoplasms and patients with sinonasal malignancy that did not involve the skull base were excluded from the study. Patients were divided into groups based on surgical approach. Using operative reports, the surgical approach was documented as either endonasal endoscopic (EEA; endoscopic approach without craniotomy or transfacial incision), or craniotomoscopic (CEA; endoscopic approach with craniotomy, but without transfacial incision), or an “open craniofacial” approach (transfacial approach, with or without craniotomy). The endoscopic and craniotomy portions of the CEA approach were done in a simultaneous, rather than staged, manner. Orbital involvement was defined as invasion of the orbital fat, and in all cases resulted in orbital exenteration; cases with tumor involvement only of the periorbital fat resulted in sparing of the eye. Likewise, intradural involvement was defined as invasion through the dura; cases

with tumor adjacent to the dura were not considered intradural. In all cases, the goal of surgery was gross total resection. Patients who did not undergo surgical therapy were excluded. Demographic information, medical comorbidities, past treatment data, and tumor characteristics were collected from the hospital's electronic and paper medical records. Preoperative staging was assessed based on imaging, using the modified Duguev TNM staging for esthesioneuroblastoma and AJCC staging system for other nasal cavity and paranasal sinus pathology where applicable.^{18,19} Records were reviewed individually for postoperative complications, including CSF leak, diplopia, vision changes, intracranial infection, sinocutaneous fistula, mucocoele, skin breakdown, and chronic rhinosinusitis. Outcomes including follow-up period, recurrence, and survival were also recorded.

Data were analyzed with Microsoft Excel (version 12.1.0, Microsoft, Redmond, Washington, United States) and JMP statistical software (version 11.0.0, SAS, Cary, North Carolina, United States). Standard descriptive statistics are reported, including frequencies and percentages of the variables of interest. Correlations between surgical approach and parameters of interest were calculated with both chi-square tests and Fisher exact tests to ensure accuracy with small sample sizes. Kaplan–Meier curves were created describing overall survival, and significance was tested using log-rank test.

Results

Sixty-seven cases of surgically resected anterior skull base malignancy were included over the 6-year period from 2007 through 2014. Ten of these cases were exclusively endoscopic (EEA), and 12 cases were craniotomoscopic (CEA); in both of these groups, the majority of cases were performed in the second half of the study period. Forty-five cases were performed with a traditional craniofacial approach.

Demographic statistics and tumor characteristics are listed by group in ▶ **Table 1**. The average age in our cohort was 58.2 years (range: 6–88), and the majority of patients were male (48 men, 19 women). The most common pathologies in our cohort were esthesioneuroblastoma (25.4%), sinonasal undifferentiated carcinoma (19.4%), squamous cell carcinoma (19.4%), and melanoma (10.4%). Of the 67 patients, 15 (22.4%) had undergone prior skull base surgery (excluding endoscopic biopsy) before presenting to our cranial base center for further treatment; 7 (10.4%) had undergone previous endoscopic resection, and 8 (11.9%) had undergone previous open resection. A total of 13.4% had undergone prior nonsurgical therapy with radiation and/or chemotherapy. In all cases, previous chemotherapy and/or radiation done at outside institutions were performed for cure, rather than as neoadjuvant therapy. Tumor stage was significantly shifted toward higher stage disease: 70.1% had T3/T4 disease and 13.4% presented with T1/T2. Certain pathologies (sarcoma, glomangiopericytoma, and adnexal carcinoma) and recurrent tumors with unknown staging at time of initial presentation staging were not staged. Patients undergoing EEA were significantly less likely to have T3/T4 disease, relative to those patients requiring a craniotomy ($p = 0.0077$). Orbital invasion (through periorbital fat) and intradural involvement, as determined by imaging and intraoperative findings, were not significantly

Table 1 Characteristics of all patients undergoing anterior skull base surgery, by approach

Characteristic	EEA	CEA	Open	Total	p-Value ^a
Number of cases (%)	10 (14.9%)	12 (17.9%)	45 (67.2%)	67 (100%)	
Male	5	10	33	48	0.23
Female	5	2	12	19	
Age (y)	60.2	61.6	56.9	58.2	0.66
Pathologies					
Esthesioneuroblastoma	2	5	10	17 (25.4%)	
SNUC	2	2	9	13 (19.4%)	
SCC	0	1	12	13 (19.4%)	
Melanoma	1	1	5	7 (10.4%)	
Adenocarcinoma	2	1	3	6 (9.0%)	
Sarcoma	2	1	2	5 (7.5%)	
Adenoid cystic	0	1	2	3 (4.5%)	
Other ^b	1	0	2	3 (4.5%)	
T stage					
1 or 2	4	0	5	9	0.0077
3 or 4	3	9	35	47	
Not staged ^c	3	3	5	11	
Intraoperative findings					
Orbital involvement	3 (30%)	2 (16.7%)	20 (44.4%)	25	0.17
Intradural component	5 (50%)	10 (83.3%)	20 (44.4%)	35	0.052

Abbreviations: CEA, craniotomoscopic approach; EEA, endonasal approach; SCC, squamous cell carcinoma; SNUC, sinonasal undifferentiated carcinoma.

^ap-Value statistic calculated with analysis of variance (age) or Fisher exact test (all others).

^b"Other" includes basal cell carcinoma, microcystic adnexal carcinoma, and glomangiopericytoma.

^cCertain pathologies (sarcoma, glomangiopericytoma, and adnexal carcinoma) and recurrent tumors with unknown staging at time of initial presentation staging were not staged.

different between groups ($p = 0.17$ and 0.052 , respectively). Adjuvant radiation therapy and/or chemotherapy were used in 82.1 and 61.2% of cases, respectively, without statistically significant differences between groups ($p = 0.20$ and 0.11 , respectively).

Complications are shown in **Table 2**, divided by surgical approach. Four patients (6.0%) had a CSF leak postoperatively, one each from the EEA and CEA cohorts, and two from the open cohort. Three of these cases resolved without intervention, and one required placement of a lumbar drain. Four

Table 2 Complications occurring after surgery, by approach

Complication	EEA	CEA	Open	Total	p-Value ^a
CSF leak	1 (10.0%)	1 (8.3%)	2 (4.4%)	4 (6.0%)	0.32
Meningitis/cerebritis	0 (0.0%)	1 (8.3%)	3 (6.7%)	4 (6.0%)	0.89
Vision changes	1 (10.0%)	4 (33.3%)	9 (20.0%)	14 (20.9%)	0.37
Diplopia	0 (0.0%)	3 (25.0%)	7 (15.6%)	10 (14.9%)	0.29
Epiphora	2 (20.0%)	3 (25.0%)	12 (26.7%)	17 (25.4%)	0.96
Wound infection	0 (0.0%)	1 (8.3%)	12 (26.7%)	13 (17.9%)	0.034 ^b
Sinocutaneous fistula	0 (0.0%)	1 (8.3%)	11 (24.4%)	12 (17.9%)	0.067 ^b
Chronic rhinosinusitis	0 (0.0%)	3 (25.0%)	4 (8.9%)	7 (10.4%)	0.14
Mucocele	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	–

Abbreviations: CEA, craniotomoscopic approach; CSF, cerebrospinal fluid; EEA, endonasal approach.

^ap-Value statistic calculated with Fisher exact test.

^bp-values for wound infection and sinocutaneous fistula were calculated by comparing transfacial incision group (Open) with nontransfacial incision group (EEA + CEA).

patients (6.0%) developed meningitis, which was treated with antibiotic therapy. One patient had a cerebellar stroke in the immediate perioperative period without long-term neurological complications. Orbital complications included 14.9% of patients experiencing diplopia, 20.8% with subjective worsening of vision, and 25.4% with epiphora. Notably, there were no significant differences between the three study groups for any specific orbital or intracranial complication. However, when comparing the traditional craniofacial group to the EEA or CEA groups, the rate of wound infection was found to be statistically significantly higher ($p = 0.034$), while the development of a sinocutaneous fistula approached significance ($p = 0.067$).

Oncologic outcomes are illustrated in ►Figs. 1 and 2. The average period of follow-up was 27.4 months (range: 1.6–88.0 months). Locally recurrent or persistent disease was seen in 38.8% of patients, and this presented on average 9 months after surgical intervention. The overall 5-year survival was estimated at 82.1%. The difference between the groups did not show a significant difference ($p = 0.75$). Five-year disease-specific survival was 87.1% overall. Disease-free survival was higher for those patients with negative surgical margins than for those with positive surgical margins (►Fig. 2; $p = 0.016$), and the differences between approaches did not meet statistical significance ($p = 0.093$). Margin status was not different between the three approaches ($p = 0.82$).

Discussion

In the past decade, there has been a significant interest in applying endoscopic techniques to access the anterior skull base; this development has paralleled a general trend toward less invasive procedures across many surgical specialties.^{2,20} Although traditional craniofacial resection remains the gold

* Note: The relative drop in survivorship in the endoscopic group at 46 months is due to a single patient, and proved not to be statistically significant.

Fig. 1 Overall survival in patients, by approach.

Fig. 2 Disease-free survival, by margin status (0 = negative, 1 = positive).

standard, several recent studies have suggested that EEA and CEA are oncologically sound in appropriately selected patients,^{8,9} and have equivalent or reduced postoperative complications.^{21–23} In the present study, we characterize our cranial base center's evolution regarding endoscopic skull base surgery, as well as the outcomes achieved with various surgical approaches.

With an average follow-up of 27.4 months (range: 1.6–88.0), our projected disease-free survival rate was 83.1%. Much of the literature regarding anterior skull base surgery focuses on open approaches for esthesioneuroblastoma, and the disease-free survival rate in this group ranges from 33 to 87%.^{15,18,24–27} Smaller series have also reported endoscopic and endoscopic-assisted resection of esthesioneuroblastoma, with favorable outcomes.^{14,17,28,29} Given the more favorable prognosis of esthesioneuroblastoma relative to other anterior skull base malignancies,^{9,28} several studies have also looked at EEA and CEA for all skull base pathologies, and report 5-year disease-specific survival of 82 to 87%.^{8,9,30} In aggregate, our data are comparable to these published statistics; when separated by surgical approach, there was no significant difference between groups, though it is important to note that we had significantly different numbers in the open ($n = 45$) versus EEA ($n = 10$) and CEA ($n = 12$) groups. The data support the assertion that EEA and CEA are appropriate in carefully selected patients. In our cohort, patients undergoing exclusively endoscopic approaches were more likely to have lower stage disease ($p = 0.0077$), which reflects a preoperative surgical decision to use an open approach in patients for whom there is concern about obtaining an adequate margin.

Potential complications after surgery are another important factor when considering a surgical approach. EEA and CEA avoid a transfacial incision, reducing the likelihood of surgical site infection and sinocutaneous fistula.¹² In the present study, the number of surgical site infections was significantly higher in patients with transfacial incisions

($p = 0.034$), and sinocutaneous fistulae also tended to be more common in open approaches ($p = 0.067$). Notably, one sinocutaneous fistula developed in a patient without a transfacial incision, in the setting of sinusitis after chemoradiation therapy. Another important complication is CSF leak, which has been reported to be higher in cases of exclusively endoscopic repair.^{5,9,13} In our cohort, four patients developed a CSF leak (6%), without significant differences between groups, which is comparable with other published data.^{9,13,31}

Debate remains as to whether the endoscopic approach to the anterior skull base, in which en bloc resection is not performed, can achieve adequate surgical margins.^{28,29,32} Even in traditional open approaches, obtaining a true en bloc resection can be difficult.^{33,34} Occasionally, surgical resection may be attempted even if complete extirpation is not possible, with postoperative chemoradiation used as adjunct therapy. In our cohort, 43.2% of patients had positive or close surgical margins on pathology, and there was an expected trend toward improved survival in those patients who had negative margins (►Fig. 2). We did not show a difference in surgical margin status between the EEA, CEA, and open groups. From our data, we cannot conclude that endoscopic or endoscopic-assisted approaches result in an increased risk of a positive margin.

Because endonasal and craniotomoscopic resection of skull base lesions are still relatively new, there is no established algorithm for determining the most advantageous approach to the anterior skull base, and the use of EEA and CEA continues to expand. Several authors have suggested that size, location, and the presence of nearby neurovascular structures should be considered in planning an endonasal

approach.^{10,23,35} We suggest an algorithm for approach to the anterior skull base in ►Fig. 3. Some lesions will be considered too extensive to resect (either open or endoscopically) and will be treated nonsurgically; these are excluded from this algorithm. First, the surgeon must determine whether there are contraindications to an endoscopic approach. Involvement of the nasal bones, anterior table of the frontal sinus, or skin overlying the nasal dorsum or frontal sinus, and frank involvement of the eye (requiring exenteration) are better treated with a traditional open approach that incorporates a transfacial incision.^{23,34} Next, the surgeon should consider the extent of intracranial extension. In patients with superficial tissue involvement requiring a transfacial incision, any involvement of the brain parenchyma should be approached with a craniotomy; a transfacial incision only may be done if there is no intracranial component. In patients who do not require a transfacial incision, and who do not have any intracranial component, we prefer an endoscopic approach, whereas intracranial involvement in this subset requires consideration of the lateral extension of tumor invasion. Some authors have suggested that extension lateral to the midorbital plane be considered the boundary of what is resectable endoscopically.²³ Lastly, reconstruction must be considered, as anterior skull base resection can result in a large dural defect. We use a pedicled nasoseptal flap for the majority of our endoscopic reconstructions, particularly if adjuvant therapy is planned; if this tissue is not available (due to tumor involvement or previous resection), we prefer craniotomy for layered reconstruction with a pericranial flap. Several studies propose algorithms for reconstruction of these defects.^{35,36}

Fig. 3 Algorithm for surgical approach to the anterior skull base.

There are several limitations of this study. As with many other studies, the cohort size is relatively small. Although we were able to show several significant findings, the ability to detect differences between the EEA, CEA, and traditional craniofacial approaches is limited. Additionally, because the endoscopic and cranioendoscopic approaches are still relatively new techniques, our follow-up period is limited at ~27 months, and will require continued monitoring.^{18,24–26,28} Finally, as these techniques have been evolving over the past 15 years at our institution, our review of outcomes is necessarily retrospective and subject to selection bias by the surgical team.

Conclusion

Sinonasal and anterior skull base malignancy remains a complicated problem, and surgical resection can be performed with multiple techniques. Endoscopic, endoscopic-assisted, and traditional craniofacial approaches are oncologically sound techniques, and their appropriate use depends on tumor stage as well as other tumor characteristics and the options for reconstruction. When using endoscopic techniques, the principles of oncologic surgery must remain the same, including complete tumor extirpation, sound skull base reconstruction, and multimodality treatment; surgical teams should be able to convert from endoscopic to open techniques (and vice versa) depending on the individual patient and pathology. The morbidity of each approach must also be considered. Postoperative complication rates were similar in the endoscopic and transfacial surgical groups, with an increased risk of wound infection in the latter group. Given the surgical and oncologic complexity of these malignancies, patients with skull base tumors should be treated at multidisciplinary cranial base centers with a full armamentarium of resources, including otolaryngologists, neurosurgeons, and medical and radiation oncologists.

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