Chapter 6
Endoscopic Resection of Sinonasal Tumors

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Introduction

Due to the close proximity of the orbit, brain, cranial nerves, and major vessels, surgical resection of sinonasal tumors is technically challenging with associated morbidity and mortality. The traditional gold standard procedure for skull base masses has typically been an open transfacial or craniofacial resection (CFR) with favorable results. Over the last three decades, endoscopic endonasal approaches (EEAs) for the resection of skull base masses have emerged as a viable alternative for carefully selected patients.

The introduction of endoscopic sinus surgery revolutionized the surgical treatment of sinonasal disorders. Improved training through inflammatory sinonasal surgery provided increased experience with the treatment of cranial base lesions including cerebrospinal fluid (CSF) leaks and pituitary tumors. In the early 1990s, the first reports were published on endoscopic resections of benign sinonasal tumors including inverted papillomas and angiofibromas [1–4]. Studies demonstrated improved local tumor control and decreased morbidity compared with standard open approaches for the treatment of benign tumors [5–8]. Technological advances including surgical navigation, ultrasonic Doppler probes, extended high speed drills, endoscopic bipolar cautery, hemostatic agents, and microdissection instruments further provided the basis for advancement in endoscopic tumor management

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[9]. With increasing technology and endoscopic surgical experience with benign sinonasal tumors, there was a natural progression to endoscopic approaches for skull base malignancies. In the late 1990s, the first reports of endoscopic assisted approaches combined with a craniotomy were published and evolved to an entirely endoscopic approach to skull base malignancies [10–12]. Initially, endoscopic approaches were reserved for early stage sinonasal malignancies of the nasoethmoidal complex but not encroaching on the anterior skull base, with a combined cranioendoscopic approach (CEA) reserved for more advanced tumors. As endoscopic experience with resection of sinonasal malignancies evolved, the indications were expanded to include the resection of the anterior skull base with the adjacent dura. Now, expanded endonasal approaches are used to access the anterior, middle, and posterior cranial fossa.

The outcome of any alternative method of treatment for sinonasal malignancies should be compared with the traditional open CFR [13, 14]. Due to the rarity and heterogeneity of skull base malignancies, it is difficult to compare the outcomes of an endoscopic versus open CFR. However, current evidence supports an endoscopic endonasal resection of select skull base malignancies with similar (or improved) outcomes to traditional open CFR but with decreased morbidity [13, 15–28].

Resection of Skull Base Malignances: General Principles

Regardless of the approach used, the primary oncologic principle is to achieve complete tumor removal with negative resection margins. This goal must be tempered with good judgment as with all surgical procedures. The general principle in choosing an approach for resecting a sinonasal or skull base tumor involves one with the most direct route to the pathology as well as the least manipulation of vital neurovascular structures. The ideal surgical approach for resection of a skull base malignancy allows for adequate exposure to facilitate resection of the tumor with negative margins, identification and protection of critical neurovascular structures, minimizes facial scarring and cosmetic deformity, preserves function (neurological, nasal breathing, olfaction, etc.), as well as facilitates reconstruction of the surgical defect. The position of the tumor relative to the cranial nerves usually guides the decision of the optimal approach, with the overarching principle of avoiding crossing the plane of cranial nerves when feasible. Further considerations for choosing a treatment modality include histology, tumor stage, molecular profile, previous treatments, and patient comorbidities.

The general philosophy behind endoscopic resection of sinonasal tumors is centered on the observation that many intranasal tumors have a small area of tissue invasion with a focal attachment point even with large tumor volume filling the sinonasal cavity [29]. Tumor growth into the sinuses and skull base is often due to erosion rather than direct invasion [29]. In cases of small tumor volume, initial attempts are made to resect the entire tumor en bloc. However, with larger tumors this is generally not possible. In these cases, the initial resection commences with piece-meal debulking. While debulking violates the tumor plane, the normal tissue planes are not interrupted as the tumor is residing in an air-filled cavity without surrounding attachment. Piece-meal debulking is continued until the tumor pedicle and its relationship to the skull base are identified, followed by an en bloc resection of the pedicle and a surrounding margin. Additional frozen sections are used to confirm clear margins. The tumor origin site, relationship to the skull base, as well as preoperative imaging guide the decision to perform an anterior skull base resection. Involved structures including the dura and periorbita should be completely resected to negative margins as they would with an open CFR. If margins cannot be safely cleared with a purely endoscopic approach, conversion to an endoscopic assisted or open approach should be considered [30].

As with any oncologic surgery, the key principle is to obtain complete tumor resection with negative margins for both locoregional control and overall survival. It is well known that positive resection margins impact tumor recurrence and negatively impacts survival [17]. Endoscopic approaches for sinonasal malignancies have been criticized for a non-en bloc resection with a piece-meal tumor removal. Initial concerns included compromised oncological integrity with tumor seeding and for the theoretical inability to obtain negative margins reducing locoregional control and survival [31–33]. While theoretically ideal, an en bloc resection is not always possible even with open resections due to fragmentation of the specimen and proximity to vital structures. In a multi-institutional study, Patel et al. demonstrated that even in traditional open approaches, resection margins are close or positive in 31.6% of patients [34]. Studies have shown that endoscopic transnasal resections of skull base malignancies have similar rates of negative margins compared to open resections [21, 28, 35–37]. In a retrospective review by Cohen et al. on 23 patients treated with an open CFR and 18 patients with an endoscopic approach, resection margins were close/positive in 17% in both groups [18]. Currently, there is no evidence to support that debulking increases the risk of local recurrence or decreases survival [29]. In a study of 30 patients undergoing open CFR for skull base malignancies, piece-meal excision resulted in similar survival rates compared with en bloc resection in cases of positive margins as well as in cases of negative margins [36]. Studies have shown that the single most significant prognostic indicator for tumor recurrence is positive resection margins rather than en bloc resection [35, 36, 38]. Ultimately, the act of obtaining negative margins is more important than the method of tumor removal.

Depending on the histology and extent of the neoplasm, the goal of surgery may vary. The most common sinonasal malignancies include squamous cell carcinoma, adenocarcinoma, adenoid cystic carcinoma, mucosal melanoma, nasopharyngeal carcinoma, olfactory neuroblastoma, and sinonasal undifferentiated carcinoma. In most cases, the goal is complete excision with acceptable morbidity. Olfactory neuroblastomas (ONB) generally arise in the olfactory groove. The mainstay of treatment involves complete surgical resection with or without radiation. An endoscopic anterior skull base resection is performed with unilateral or bilateral excision of the cribriform plates and overlying dura if necessary. In most cases, the olfactory bulbs will need to be resected. Long-term follow-up is essential as recurrences occur at a mean period of 6 years [9]. Squamous cell carcinoma (SCCa) is the most common sinonasal malignancy. For early-stage, resectable tumors, the mainstay of treatment for SCCa is radical surgery with or without adjuvant therapy. While many cases are suitable for an endoscopic approach, open or combined approaches may be indicated in advanced tumors [39]. Adenocarcinomas occur mainly in the ethmoid sinuses (85%) and are associated with wood and leather dust exposure. Surgery, either through an EEA, CEA, or open CFR, remains the first treatment of choice for these tumors, with a role for adjuvant therapy in advanced cases [39]. Adenoid cystic carcinomas mainly occur in the maxillary sinus (60%), followed by the nasal cavity (25%) and ethmoids (15%). The mainstay of treatment is surgery generally followed by radiation. These tumors recur locally, frequently metastasize distally, and are often complicated by perineural invasion making complete resection difficult. In these cases, the goal of surgery is to resect as much as possible while limiting injury to cranial nerves if possible. Adjuvant radiation is an important aspect of treatment in these cases. Mucosal melanoma is a very aggressive but rare sinonasal malignancy (5%). The treatment of choice is radical surgery with negative margins when possible; however, prognosis is generally poor (5-year OS <30%) [39]. In high-grade malignancies involving critical structures (i.e., brain, carotid artery, cavernous sinus, optic nerves), complete resection is not possible. In these cases, chemoradiation may be considered as first line with surgical salvage of residual tumor following treatment. Additionally, there is a role for endoscopic debulking of tumors in palliative cases to relieve symptoms such as visual loss caused by tumor compression, nasal obstruction, epistaxis, or pain [29].

Advantages of an Endoscopic Approach

There are multiple advantages of the endoscopic approach for the resection of skull base malignances. The primary benefit of the endoscope is enhanced visualization with no loss of light and avoidance of "line-of-sight" problems. Angled endoscopes allow for visualization around obstructing corners that can minimize displacement of normal tissues. Contrary to initial criticism, proponents of the endoscopic approach cite the improved visualization of the tumor margin interface provided by the endoscope. This allows complete resection of the tumor origin, increased margin assessment, and may ultimately provide superior tumor excision [9, 23, 29]. Endoscopic surgery may be tailored to the individual tumor avoiding unnecessary skull base or orbital violation and frontal lobe retraction that may decrease morbidity. Furthermore, postoperative surveillance of the skull base resection cavity with in-office endoscopy allows for early recognition of recurrent disease prior to onset of symptoms or radiographic evidence.

While an open transfacial or craniofacial resection is considered the gold standard procedure for skull base malignancies, there is associated morbidity with these approaches including scarring, wound complications, prolonged brain retraction, extended hospital stays, and the need for free tissue reconstruction in certain cases.

Major postoperative complications with open approaches have reported ranges of 35–63% with perioperative mortality rates ranging from 0% to 13% [34, 37, 38]. Endoscopic endonasal approaches have several advantages over open approaches including avoidance of craniotomies and facial incisions as well as decreased brain retraction. Multiple studies have shown that in comparison to open approaches, patients undergoing endoscopic resection have shorter operating room times, lower intraoperative blood loss, decreased rates of postoperative complications, and decreased hospital and ICU stays. Furthermore, endoscopic approaches have decreased perioperative morbidity and mortality compared to open approaches, with preserved oncologic integrity [20, 23, 25, 31, 34, 38].

Quality of life (QOL) is an important factor in discussing surgical approaches. Multiple validated questionnaires have been developed to determine QOL specifically after undergoing endoscopic or skull base surgery. The Anterior Skull Base Surgery Questionnaire (ASBSQ) is a validated, multidimensional disease-specific questionnaire for anterior skull base neoplasms [40]. Using the ASBSQ, a retrospective study analyzing 78 patients undergoing open or endoscopic approaches for skull base tumors found that endoscopic resection results in significant improvement in overall QOL, especially in domains pertaining to physical function and emotional impact [41]. The Sinonasal Outcome Test (SNOT-22) questionnaire specifically focuses on parameters relating to sinonasal function, including sinus specific domains as well as psychological and sleep domains that assess general health. In a retrospective review of 108 patient undergoing endoscopic surgery for lesions involving the skull base, there was no significant change in QOL from baseline at 3 or 6 months postoperatively [40]. Furthermore, a more extended endoscopic approach involving resection of the skull base was not associated with worse QOL outcomes. In contrast to other studies, Glicksman et al. actually found an improvement in each domain of SNOT-22 scores in patient undergoing an endoscopic resection of sinonasal tumors that was sustained over a 2-year period [42].

Limitations of an Endoscopic Approach

While endoscopic endonasal approaches provide significant advantages, it is important to emphasize that not all skull base malignancies are amenable to an endoscopic surgical resection. Endoscopic approaches are utilized in carefully selected patients based on extent of tumor spread, histology, previous treatments, and patient comorbidities. Contraindications to a purely endoscopic approach include tumors with involvement of the dura beyond the mid-orbital roof, intraorbital extension, extension into facial or orbital soft tissues, and involvement of the anterior table or lateral recess of the frontal sinus [9]. Relative contraindications include lateral extension into the lateral wall of the maxillary sinus and infratemporal fossa as well as gross brain parenchymal involvement. In these cases, a CEA or open CFR may be beneficial. Table 6.1 outlines the general indications as well as contraindications of an endoscopic approach.

Table 6.1 Indications and contraindications for endoscopic resection of sinonasal malignancies

Indications	Relative contraindications	Absolute contraindications
Maxillary sinus tumors	Lateral extension into lateral wall of maxillary sinus	Need for total maxillectomy
Ethmoid sinus tumors involving the ethmoid roof, lamina papyracea, cribriform plate		Tumor involvement of nasal bones, palate, subcutaneous tissues, and skin
Sphenoid sinus tumors	Disease lateral or superior to carotid or optic nerve Cavernous sinus involvement ICA encasement	
Frontal sinus tumors limited to medial aspect		Anterior table or lateral recess of the frontal sinus
Pterygopalatine fossa and limited infratemporal fossa tumors	Lateral extension into infratemporal fossa	
Tumor infiltration into periorbita		Intraorbital extension Orbital soft tissue (fat, muscle, globe) involvement
Tumor infiltration into anterior skull base dura	Gross brain parenchyma involvement	Involvement of dura beyond mid-orbital roof

A significant obstacle encountered with endonasal skull base surgery was the ability to reconstruct the skull base. While postoperative cerebrospinal fluid (CSF) leaks can occur with open approaches, early studies demonstrated higher rates with an endoscopic approach. Historically, the skull base was repaired with free tissue grafts and evolved into multilayered grafting usually combining inlay and onlay techniques. Despite advances, CSF leaks remained high with rates ranging from 10% to 30%, which was much higher than traditional approaches [9]. Perhaps the most significant advancement in skull base surgery was the pedicled nasoseptal flap described by Hadad et al. in 2006, which has significantly reduced the incidence of postoperative CSF leaks [43]. Based on the posterior nasoseptal artery, the flap can provide enough tissue to cover the defect created by an anterior cranial base resection. In a prospective review of high-flow skull base leaks, the nasoseptal flap was successful in 94% [44]. Further advances in reconstructive techniques involve the transfrontal pericranial flap, transpterygoid temporoparietal fascia flap, inferior and middle turbinate flap, Oliver palatal flap, and even free tissue reconstruction [9]. With these advancements, studies have demonstrated comparable postoperative CSF leak rates to open approaches [25, 45].

Another significant issue with endoscopic techniques is chronic nasal crusting. Removal of normal sinonasal mucosa can affect sinonasal ciliary clearance and the ability to humidify airflow. However, crusting can also be seen in open approaches, and frequent use of saline and in-office debridements can help mitigate this.

Approaches

Successful endoscopic endonasal surgery requires optimization of the sinonasal corridor. The extent of the tumor is ultimately what determines the surgical approach and which structures will need to be exposed and removed. A wide surgical corridor requires removing enough bone at the skull base to expose key anatomical landmarks. A binary approach increases the size of the surgical corridor, provides more room for instrumentation, and allows for a two surgeon/four handed technique. Furthermore, it is important to take into consideration the anticipated reconstruction needs. Expanded endonasal approaches have proven to provide safe anteromedial access to the entire ventral skull base along the sagittal and coronal planes [46–50]. Endonasal approaches are classified according to their orientation in the sagittal and coronal planes. The sphenoid sinus is located at the epicenter of these two planes and is generally the starting point for many of the approaches.

In the sagittal plane, median approaches (between the carotid arteries) extend rostro-caudally from the frontal sinus to the body of C2 allowing resection of tumors involving the anterior, middle, and posterior cranial fossa [49, 50]. The transfrontal approach provides access to the floor and posterior wall of the frontal sinus [50]. The transcribriform module extends from the crista galli to the planum sphenoidale in an anterior–posterior direction, and across the ethmoid roof (fovea ethmoidalis) to the orbital roof either bilaterally or unilaterally. This is most often used for sinonasal malignancies and olfactory groove meningiomas. The transplanum approach allows access to suprasellar lesions with suprasellar extension, such as large pituitary tumors and craniopharyngiomas. The optic canals limit the approach posterolaterally [46]. The transsellar approach is the standard approach for pituitary tumors but can also be combined with other approaches such as the transplanum/transtuberculum for extrasellar extension [50]. This approach is limited laterally by the cavernous internal carotid artery (ICA). The transclival approach spans the sphenoid bone and clivus from the posterior clinoids to the foramen magnum [49]. This approach can be further subdivided into superior, middle, and inferior transclival approaches. Through the trans-odontoid approach, one can access the upper cervical spine (C1 and C2) as well as the foramen magnum [48]. This approach is limited laterally by the parapharyngeal ICA and vertebral arteries, and inferiorly by the nasopalatine line (line tangential to the inferior edge of the nasal bones and the posterior edge of the hard palate) [48].

In the coronal plane, paramedian approaches (lateral to the carotid arteries) are divided into anterior, middle, and posterior planes corresponding to the respective cranial fossa [46]. The anterior coronal plane includes the supraorbital and transorbital approach. The supraorbital approach removes the medial orbital wall allowing access to the medial and superior orbit. The transorbital approach is used for intraconal lesions inferior and medial to the optic nerve, with access between the inferior and medial rectus. The middle coronal plane extends from the sphenoid sinus to the floor of the middle cranial fossa superior to the petrous ICA [46]. Middle coronal approaches allow access to the lateral recess of the sphenoid sinus, medial petrous

Table 6.2 Classification of expanded endonasal approaches to the skull base

Saggital plane (median)		Coronal plane (paramedian)
Transfrontal		Anterior coronal plane • Supraorbital • Transorbital
Transcribriform		Middle coronal plane • Transpterygoid • Medial petrous apex • Cavernous sinus/ quadrangular space (Meckel's cave) • Infratemporal approach
Transtuberculum/transplanum		Posterior coronal plane • Petroclival approach • Infrapetrous • Parapharyngeal space
Transsellar		
Transclival	Superior third: Dorsum sella and posterior clinoids to Dorello canal	
	Middle third: Dorello canal to Jugular foramen	
	Inferior third: Jugular foramen through the cervicomedually junction and foramen magnum	
	Panclival	
Transodontoid and foramen magnum/craniovertebral junction approach		

apex, middle cranial fossa superior to the petrous ICA, cavernous sinus, and the infratemporal skull base. Meckel's cave and the cavernous sinus can be accessed lateral to the paraclival ICA and superior to the petrous ICA. This access requires a transpterygoid approach with dissection between the vidian nerve and second division of the trigeminal nerve, V2 [47]. Lateral access into the infratemporal fossa requires a medial maxillectomy with a Denker's approach for full access to the posterolateral wall of the maxillary sinus. The posterior coronal plane extends from the foramen magnum across the occipital condyle and hypoglossal canal to the jugular foramen, allowing access to the petrous internal carotid artery, petrous apex, hypoglossal canal, jugular foramen, and parapharyngeal space. The eustachian tube must be resected to allow full access to the infrapetrous area that can allow access to pathology that cannot be reached in a medial approach. Table 6.2 outlines the classification of endonasal approaches to the skull base [46–51].

Open Craniofacial Resection of Sinonasal Malignancy: Outcomes

When discussing alternative methods in the treatment for sinonasal malignancies, comparisons should be made with the traditional/gold standard open CFR [13, 14]. Due to the rarity and heterogeneity of skull base malignancies, randomized controlled trials comparing endoscopic and open approaches are generally not feasible. Furthermore, small sample sizes, relative rarity of sinonasal malignancies, and lack of balanced patient distributions between surgical approaches make comparisons difficult. These issues are largely unavoidable as more advanced tumors tend to undergo an open surgical approach. The data supporting the use of endoscopic approaches is primarily through retrospective chart reviews with data primarily centered on survival (overall survival, disease free survival), control of disease (locoregional control, distant metastasis), and surgical complications. However, current evidence based on case series, multi-institutional cohorts, large database studies, and systematic reviews has demonstrated that an endoscopic approach to select patients with sinonasal malignancies is an acceptable approach without compromising survival.

Although comparing the two approaches is difficult, studies on open CFR provide a benchmark to analyze survival outcomes with endoscopic endonasal approaches. In 2001, Dulguerov et al. [52] published a retrospective review of 220 patients undergoing treatment for nasal and paranasal sinus malignancies treated at two institutions. Patients were treated with either surgery (open resection), radiation, chemotherapy, or a combination. The most common histology was SCCa occurring in 57.3%, and patients with ONB, melanoma, and sarcoma were excluded. Overall survival (OS) was 75%, 60%, and 47% at 2-, 5-, and 10-years, respectively. Intracranial and orbital extension as well as histology were independent predictors of disease-specific survival (DSS), with adenocarcinoma and glandular carcinoma affording improved survival compared to those with SCCa and sinonasal undifferentiated carcinoma (SNUC). Furthermore, positive margins were a predictor of survival with a 5-year DSS of 25% for those with positive margins and 64% with negative margins ($p < 0.0001$). In 2003, Patel et al. [34] published the largest multicenter, international cohort including 1307 patients with malignant tumors of the skull base undergoing open CFR at 17 institutions. This study included patients with ONB and melanoma in contrast to the previous study, with expected results of ONB conferring a favorable prognosis (DSS 82.6%) and melanoma a poor prognosis (DSS 19.2%); 32% of patients had close/positive margins that independently affected recurrence-free survival (RFS) and DSS. Utilizing the same cohort of patients, Ganly et al. [53] performed a sub-group analysis on 334 patients focusing on those with primary tumors located in the paranasal sinuses. The results of these studies as well as the results from a similar study by Howard et al. [54] are summarized in Table 6.3 [34, 52–54].

Endoscopic Approaches for Sinonasal Malignancy: Outcomes

Studies on endoscopic approaches are often plagued by small sample sizes due to the approach being relatively new and the rarity of sinonasal malignancies in general, with larger series often including a variety of histologies. Studies evaluating the efficacy of a purely endoscopic approach for sinonasal malignancies are mainly centered on retrospective reviews, with comparable outcomes to open resections [14, 32, 33, 55–76]. Several studies have reported results in cohorts of mixed histologies, while others have reported on the efficacy of an endonasal approach in a selected histologic population. Despite these limitations, there is a growing body of evidence to support a purely endoscopic approach to selected sinonasal malignancies [14, 32, 33, 55–57, 59–76].

Table 6.3 Compiled outcomes of open resections for sinonasal malignancy

Author	Mean follow-up (months)	Histology	N (%)	5-year overall survival (%)	5-year disease-specific survival (%)	5-year recurrence-free survival (%)
Dulguerov et al. (2001) [52]	72	*Overall*	*220*	*60*	*63*	*59*
		SCCa	126 (57.3)	ND	60	58
		Adenocarcinoma	25 (11.4)	ND	78	69
		Salivary gland carcinoma	39 (17.7)	ND	79	68
		SNUC	30 (13.6)	ND	40	41
Patel et al. (2003) [34]	25	*Overall*	*1307*	*54*	*60*	*53*
		SCCa	375 (28.7)	44.4	53	49.9
		Adenocarcinoma	210 (16.1)	51.5	57.5	53.1
		Salivary gland carcinoma	124 (9.5)	45.5	53	44.3
		SNUC	39 (3)	37.3	41.9	45.5
		Melanoma	53 (4)	18.3	19.2	19.2
		ONB	151 (11.6)	77.8	82.6	64.3
		Other	355 (27.1)	*ND*	*ND*	*ND*
Ganly et al. (2005) [53]	19	*Overall*	*334*	*48.3*	*53.3*	*45.8*
		SCCa	101 (30.2)	43	44	38
		Adenocarcinoma	107 (32)	45	52	46
		Salivary gland carcinoma	32 (9.6)	65	70	60.5
		SNUC	14 (4.2)	0	0	0
		Melanoma	21 (6.3)	*ND*	*ND*	*ND*
		Other	59 (17.7)	*ND*	*ND*	*ND*

Table 6.3 (continued)

Author	Mean follow-up (months)	Histology	N (%)	5-year overall survival (%)	5-year disease-specific survival (%)	5-year recurrence-free survival (%)
Howard et al. (2006) [54]	63	*Overall*	*259*	*65*	*59*	*ND*
		SCCa	34 (13)	53	ND	ND
		Adenocarcinoma	62 (24)	58	ND	ND
		Salivary gland carcinoma	19 (7.3)	61	ND	ND
		SNUC	15 (5.8)	ND	ND	ND
		Melanoma	8 (3.1)	ND	ND	ND
		ONB	56 (21.6)	74	ND	ND
		Other	65 (25.1)	ND	ND	ND

SCCa squamous cell carcinoma, *SNUC* sinonasal undifferentiated carcinoma, *ONB* olfactory neuroblastoma, *ND* not defined

The largest studies supporting a role for endoscopic approaches generally come from those analyzing a purely endoscopic endonasal approach (EEA) or a combined cranioendoscopic approach (CEA), where an endoscopic approach is combined with a frontal or subfrontal craniotomy. In 2008, Nicolai et al. [25] published a retrospective review on 184 patients undergoing an EEA (72.8%) or CEA (27.2%) for various sinonasal malignancies. The 5-year DSS for the entire cohort was 81.9%, significantly varying from 91.4% in the EEA group to 58.8% in the CEA group ($p = .0004$). Although DSS was significantly improved in the EEA group, there was a higher proportion of patients with T3/T4 and Kadish C tumors undergoing CEA. The authors concluded that an endoscopic approach (with or without a combined craniotomy) is an effective alternative approach to sinonasal malignancies. Hanna et al. published a similar study on 120 patients undergoing EEA (77.5%) or CEA (22.5%) for sinonasal malignancies [21]. A significantly higher proportion of patients with T3/T4 underwent a CEA, while T1/T2 tumors were more likely to have an EEA. The 5-year DSS and OS rates were 87% and 76% overall. While these results were comparable to those published by Nicolai et al., there was no significant difference in DSS or OS between the EEA and CEA groups despite the higher disease stage in the CEA group. The authors concluded that this may be due to a difference in the indications for a CEA between the two studies. Hanna et al. noted that EEA was generally reserved for patients with relatively earlier stage disease with no or limited invasion of the skull base. In contrast, Nicolai et al. described a shift in their surgical approach in the latter part of their study where they expanded the indications of EEA to include select patients with skull base invasion and focal dural infiltration. More recently, Abdelmeguid et al. published a retrospective review of 239 patients undergoing EEA (70%) or CEA (30%) [15]. In contrast to the previously mentioned studies, a CEA involved an endoscopic approach combined with a bifrontal craniotomy, Caldwell-Luc, facial incision, or transoral resection. The 5-year DSS and OS was 84.6% and 73.9%, respectively. Similar to the Hanna et al. study, there was no significant difference in OS or DSS between the EEA and CEA groups. Survival varied significantly according to pathology with sinonasal mucosal melanoma having the lowest 5-year OS compared with ONB (41.1% vs. 83.5%, respectively). These studies add to the growing body of evidence in support of endoscopic approaches in select sinonasal malignancies, including highly aggressive tumors such as sinonasal melanoma and SNUC. The results of several of the largest cohorts are summarized in Table 6.4 [15, 21, 25].

Table 6.4 Compiled outcomes of EEA and CEA for sinonasal malignancy

Author	Mean Follow-up (months)	Histology (N)	N (%)	T1	T2	T3	T4a	T4b	5-year overall survival (%)	5-year disease-specific survival (%)
Nicolai et al. (2008) [25]	34.1	Adenocarcinoma [68] SCCa [25] ONB [22] Adenoid cystic carcinoma [13] Melanoma [17] SNUC [5] Other [34]	*Total* 184	52	26	32	17	35	ND	81.9
			EEA 134 (72.8)	49	25	20	9	12		91.4[a]
			CEA 50 (27.2)	3	1	12	8	23		58.8
Hanna et al. (2009) [21]	37	ONB [17] Adenocarcinoma [14] Melanoma [14] SCCa [13] Adenoid cystic carcinoma [7] SNUC [2] Other [53]	*Total* 120	25	25	21	29		76	87
			EEA 93 (77.5)	32	31	17	20			
			CEA 27 (22.5)	0	5	36	59			
Abdelmeguid et al. (2019) [15]		ONB [54] Melanoma [41] SCCa [38] Adenocarcinoma [20] Adenoid cystic carcinoma [19] SNUC [12] Other [55]	*Total* 239	41	37	65	95		73.9	84.6
			EEA 167 (70)	70		96				
			CEA 72 (30)	8		64				

EEA endoscopic endonasal approach, *CEA* cranioendoscopic approach, *SCCa* squamous cell carcinoma, *ONB* olfactory neuroblastoma, *SNUC* sinonasal undifferentiated carcinoma, *ND* not defined

[a] significant difference between approaches

In 2016, Rawal et al. performed a systematic review and meta-analysis on 952 patients undergoing EEA or CEA for sinonasal malignancies [27]. Fifteen studies (*n* = 759) allowed only for aggregate model analysis, while 20 studies (*n* = 193) allowed for direct pooling analysis. Five-year overall survival for patients in the aggregate model analysis and direct pooled analysis were 72.3% and 83.5%, respectively. In the direct pool analysis group, mean follow-up was 43 months; 157 patients (81%) had a purely endoscopic approach, while 36 (19%) had an endoscopic assisted approach. The most common histology was ONB (32%) followed by sinonasal adenocarcinoma (28%), melanoma (18%), SCCa (14%), SNUC (7%), and adenoid cystic carcinoma (6.7%). While 49% of the tumors were low stage and 28% high stage (unknown in 22%), there was no significant difference in overall survival when stratified by stage. This study concluded that there is strong evidence for the use of endoscopic endonasal resection in sinonasal malignancy with overall survival rates that are comparable, if not higher, than previously reported for open CFR.

Endoscopic Versus Open Approaches for Sinonasal Malignancy: Outcomes

While a direct comparison of outcomes is difficult, several studies have set out to compare endoscopic and open approaches in the management of sinonasal malignancy [13, 16–28, 60, 77–94]. In 2019, Hagemann et al. published a retrospective review on 225 patients undergoing an open craniofacial (oCFR) (45.3%) or endoscopic resection (54.6%) for sinonasal malignancies including SCCa (45%), adenocarcinoma (15%), and malignant melanoma (12%) [20]. Mean OS and DSS were significantly higher in the EEA versus open group (OS 175 vs. 120 months, $p = .024$; DSS 202 vs. 149 months, $p = .036$), as was 5-year OS (76.1% EEA vs. 59.5% oCFR). While histology did not vary significantly between approaches, there was a larger proportion of EEA for T1 tumors and oCFR for T4 tumors ($p = .003$). When stratified according to stage, OS and DSS were similar between the endoscopic and open surgery groups for low-stage tumors (T1/T2) and high-stage tumors (T4). In contrast, there was a significantly higher OS and DSS after endoscopic removal of T3 tumors (mean OS 127 vs. 80 months; 10-year OS 92.3 vs. 18.8%; $p = .038$). Furthermore, there was no difference in OS for patients with skull base, dural or cerebral involvement between the two groups ($p = .752$; .818; .648, respectively). Patients undergoing endoscopic resection had lower risk of major bleeding ($p = .041$) and shorter hospital stay ($p = .001$). This study concluded that endoscopic resection remains an appropriate option for distinct indications with improved outcomes in intermediate-stage tumors, as well as shorter hospital stays and major bleeding events. Similar retrospective studies have found no difference in 5-year overall survival rates when comparing the two approaches; however, EEA has been shown to offer shorter OR times, hospital and ICU stays, as well as intraoperative blood loss [19, 28]. Furthermore, there was no significant difference in the rates of en bloc resection or negative margins [28]. Wood et al. actually found a significantly greater likelihood of residual or recurrent disease at time of last follow-up in patients undergoing oCFR ($p = .029$); however, this possibly reflected more advanced tumor stage or more aggressive pathology at the time of surgery [28]. Overall, these studies provide evidence that an endoscopic approach to select sinonasal malignancies yields decreased hospital stays and operating room times while not compromising survival. Furthermore, EEA has been shown to have improved survival in T3 tumors with trends towards decreased recurrence rates; however, the likelihood of more advanced/aggressive tumors undergoing a CFR complicates these results. Table 6.5 outlines the outcomes of these studies.

In 2011, Higgins et al. published a systematic review and meta-analysis of 226 patients undergoing endoscopic or open resection of sinonasal malignancies [22]. Among low-stage malignancies (T1-T2 or Kadish A-B), the endoscopic and open approaches demonstrated no statistically significant difference in outcomes (5-year OS 87.4% EEA vs. 76.8% oCFR, $p = .351$; 5-year DSS 94.7% vs. 87.7%, $p = .258$; LRC 89.5% vs. 77.2%, $p = .251$). Due to significant heterogeneity between the two groups and variable survival and locoregional control (LRC) rates in the endoscopic cohorts, outcome conclusions on higher stage malignancies were not possible. The authors concluded that endoscopic management of sinonasal malignancies appears to be a promising alternative to open approaches; however, standardization of outcome reporting is needed.

Further support for EEA offering similar survival outcomes to open approaches comes from two large national database studies [23, 26]. Husain et al. (2019) published on 2292 patients within the National Cancer Database undergoing an endoscopic or open approach for sinonasal malignancies between 2010 and 2015 [23]. Patients with adenocarcinoma, adenoid cystic carcinoma, mucosal melanoma, sarcoma, and ONB were more likely to undergo an endoscopic approach compared to those with SCCa. Ethmoid tumors were more likely to undergo an endoscopic approach compared with nasal cavity tumors, whereas maxillary sinus tumors were more likely to undergo an open approach. Patients undergoing EEA had shorter hospital stays (3.13 vs. 5.52 days), with no significant differences in 30-day readmission rates. Five-year OS was not significantly different between the two approaches (59.6% EEA vs. 60.8% CFR, $p = .106$), which held true after controlling for a variety of factors including tumor stage, site, and pathology ($p = .831$). As predicted, adenocarcinoma and ONB had a lower likelihood of mortality compared to SCCa, with MM demonstrating a higher likelihood of mortality. In 2019, Povolotskiy et al. reviewed 1595 patients within the National Cancer Database undergoing definitive surgery with EEA or oCFR between 2004 and 2015, but excluded patients with SCCa. Five-year overall survival was not statistically different between the endoscopic (65.1%) or open (65.4%) cohorts ($p = .59$), but hospital stay was shorter in the endoscopic group. Age greater than 70, AJCC stage IV, tumor size greater than 5 cm, primary site of the ethmoid sinus, and lower income were all significant predictors of mortality. Overall, there is growing body of evidence that endoscopic approaches for the resection of sinonasal malignancy offers comparable, if not superior, outcomes to the traditional open approach.

Table 6.5 Outcomes of endoscopic vs. open CFR resection for sinonasal malignancy

Author	Median follow-up (months)	N (%)	Histology (N/%) SCCa	Adeno	MM	ONB	ACC	SNUC	Other	Stage T1	T2	T3	T4	Results
Hagemann et al. (2019) [20]	*Total*	225	103	34	28	13	10	9	28	36	42	27	100	Significantly improved OS at 5 years (EEA 76.1 vs. CFR 59.5) and 10 years (EEA 69.9 vs. 41.8) Significantly improved DSS (EEA 202 vs. CFR 149 months, $p = .024$)
	EEA 52.4	123 (54.6)	51	16	17	8	7	3	21	25	32	16	33	
	oCFR 45.4	102 (45.3)	52	18	11	5	3	6	7	11	10	11	67	
Higgins et al. (2012) [22]	*Total*	123												Overall survival for entire cohort: 56.5% Significantly improved 5-year overall survival (EEA 88.4 vs. CFR 55.2%), DFS (93.9 vs. 60.8%), and LRC (84.7 vs. 48%%) (No significant difference when stratified by stage)
	EEA 46.5	28	7.1	17.9	3.6	51.8	1.8		17.8	T1-2/ Kadish A-B 78.2%		T3-4/ Kadish C 22.3%		
	oCFR 36	55 (44.7)		21.8		43.6		34.7		21.8%		77.7%		
Wood et al. (2012) [28]	*Total*	*82*	26	6	3	19	11	4	13	13	10	17	42	No significant difference in disease-specific mortality CFR – higher rate of recurrent or residual disease at time of last follow-up ($p = .029$)
	EEA 31	*34*	1	2	1	15	3	2	10	10	8	6	10	
	oCFR 30	*48*	25	4	2	4	8	2	3	3	2	11	32	

EEA endoscopic endonasal approach, *oCFR* open craniofacial resection, *SCCa* squamous cell carcinoma, *Adeno* adenocarcinoma, *MM* mucosal melanoma, *ACC* adenoid cystic carcinoma, *SNUC* sinonasal undifferentiated carcinoma

Endoscopic Approaches to Specific Sinonasal Malignancies: Outcomes

While the previously mentioned studies demonstrate similar survival outcomes between endoscopic and open approaches, they encompass a heterogenous population of varying histologies. Several studies have shown that an endoscopic approach may actually offer improved survival rates in select histological subsets of sinonasal malignancies. In 2009, Devaiah et al. performed a meta-analysis of 361 patients with olfactory neuroblastoma (ONB) treated between 1992 and 2008 [79]. Patients undergoing surgery had more disease-free outcomes ($p < .0001$) and better survival rates ($p < .0001$) than those treated with non-surgical treatment modalities. Both a pure endoscopic approach ($p = .0019$) and endoscopic-assisted approach ($p = .0123$) demonstrated better survival rates than open surgery. Due to studies on open surgical approaches predating endoscopic surgery, they performed a subgroup analysis on articles from 2002 to 2008. The purely endoscopic ($p = .0018$) and endoscopic-assisted group ($p = .0133$) maintained improved survival rates over open approaches. While this study demonstrates promising results with an endoscopic approach to ONB, there was a significant difference in Kadish tumor distribution between the groups with Kadish stage C and D more likely to undergo an open approach. Due to limited data, stratification according to tumor stage was not possible. In a more recent meta-analysis on 609 patients with ONB, Fu et al. found that an endoscopic approach was associated with a significantly better OS and DFS at 5 and 10 years, but was not associated with any difference in locoregional control or metastasis-free survival [80]. On subgroup analysis stratified by advanced Kadish stage (C/D) and Hyams grade (III/IV), the endoscopic cohort maintained significantly improved overall survival rates compared to the open cohort. Furthermore, the endoscopic group had a significantly lower rate of postoperative complications. Similarly, a stage-matched, multi-institutional review of 109 patients with ONB showed that endoscopic resection resulted in improved overall survival in higher stage (Kadish C) tumors [81]. Additionally, the ability to achieve clear surgical margins was significantly improved in those undergoing a purely endoscopic resection (53.1 vs. 84.2%, $p = .001$). These studies demonstrate that an endoscopic resection of ONB allows for complete resection with improved margin status, as well as equivalent or better survival outcomes even with more advanced tumors.

Studies on sinonasal adenocarcinoma have shown that an endoscopic approach offers comparable or improved outcomes, with the possibility of improved morbidity [77, 85–88, 93]. Meccariello et al. (2016) published a meta-analysis of 1826 undergoing endoscopic or open approaches for sinonasal adenocarcinoma [86]. Patients undergoing an endoscopic approach had significantly shorter hospital stays (4.7 vs. 11.5 days, $p < .01$), decreased postoperative complications (6.6 vs. 36.4%, $p < .01$), and lower post-operative mortality ($p = .04$). Overall survival, disease-free survival, and local recurrence-free survival were all improved with an endoscopic approach for T2-T4-staged tumors. Furthermore, multi-variate analysis demonstrated decreased overall survival for advanced T stage and open approaches.

Sinonasal mucosal melanoma (SNM) is one of the most aggressive tumors with a very high propensity to recur and metastasize. Radical wide local resection and systemic control of the disease are crucial as high recurrence rates are thought to be secondary to the multifocal nature of the disease [82]. Wider margins are needed compared to other sinonasal malignancies due to high false negative rates of intraoperative frozen section margins [59]. Studies have found that overall survival is not superior to 50% at 3 years, and between 26.9% and 38.7% at 5 years, indicating poor prognosis despite the modality of treatment [91, 95]. In 2019, Hur et al. performed a meta-analysis on 510 patients undergoing an open or endoscopic resection of sinonasal melanoma [82]. Overall survival was longer in the endoscopic versus open resection group (HR 0.68, 95% CI 0.49–0.095); however, there was no difference in disease-free survival between the two groups. The authors concluded that while tumor resection may be equally effective between the two approaches, the higher morbidity associated with an open approach may be a factor in why the overall survival is longer in patients undergoing an endoscopic resection.

Conclusion

The traditional, gold standard approach for the resection of sinonasal malignancies involves an open craniofacial resection. Over the last three decades, through technological advances and increasing experience, endoscopic approaches have become a viable alternative for select patients with sinonasal malignancies. Studies have demonstrated that in comparison to traditional approaches, endoscopic approaches result in shorter operating room times, lower intraoperative blood loss, decreased rates of postoperative complications, and decreased hospital and ICU stays. The ever-expanding body of evidence demonstrates that endoscopic approaches have decreased perioperative morbidity and mortality, preserved oncologic integrity, with comparable or improved outcomes in carefully selected sinonasal malignancies.

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