

Endoscopic Resection of Sinonasal Cancers

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Abstract Sinonasal malignancies, a rare group of tumors, are characterized by histological heterogeneity and poor survival. As improvements in image-guidance and endoscopic technologies became incorporated into head and neck oncologic and neurosurgical practice, the application of these technologies and techniques to the surgical management of sinonasal malignancy began. Over the past decade, there has been increasing evidence regarding the safety and oncological effectiveness of these techniques. Several institutions have reported their experience with endoscopic surgery and have shown reduced morbidity, better quality of life, and survival outcomes equivalent to those of open surgery in carefully selected patients. Endoscopic cranial base surgery is a rapidly evolving field. We review the literature on oncological outcomes, safety, quality of life, and recent technological advances.

Keywords Sinonasal malignancy · Endoscopic surgery · Skull base surgery · Skull base reconstruction · Head and neck cancer

Introduction

Sinonasal malignancies account for only 3-5 % of head and neck tumors [1, 2]. They are an aggressive and histologically

heterogeneous disease group. Survival remains poor despite advances in treatment over the past 50 years. Ketcham et al. [3] first established the anterior craniofacial resection (ACFR) as the standard of care for sinonasal malignancies in the 1960s. The past decade has witnessed the introduction of endoscopic surgery as a complement to, and more recently at times an alternative to open surgery. Although it was initially met with concerns regarding oncological soundness and faced technical challenges such as adequate reconstruction, there is now increasing acceptance of its safety and oncological effectiveness in carefully selected patients. With endoscopic techniques as part of the surgical armamentarium, tailored surgical strategies can now be devised based on the target lesion, the goals of treatment, and the patient. Endoscopic surgery for sinonasal malignancies is a rapidly evolving field. The growing expertise of surgical teams has paralleled advances in technology and progress in medical and radiation oncology. The role of endoscopic surgery in the multidisciplinary management of sinonasal malignancies is being continually refined. We outline current indications for endoscopic resection of sinonasal malignancy, summarize recent developments, and propose areas for further research.

Anatomical Limits of Endoscopic Endonasal Surgery

Since the advent of endoscopic cranial base surgery, the limit of what is endoscopically resectable has been progressively expanded. Endoscopic resection of the anterior skull base and dura with reconstruction was first described in 2005 [4, 5]. The standard endoscopic endonasal “craniofacial” resection starts with debulking of the intranasal tumor, identifying the attachment of tumor origin, and resection of the sinonasal component. The lamina papyracea, cribriform plate, fovea ethmoidalis, planum sphenoidale, dura, and olfactory bulbs and tracts can be resected depending on the extent of tumor

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involvement. Selected centers are now using the endoscopic technique to resect involved brain parenchyma, although extensive brain involvement remains a relative contraindication to endoscopic surgery alone and in most cases necessitates a combined craniotomy.

In recent years, “extended” transcribiform approaches have been described. “Transpterygoid approaches” provide access to the petrous temporal bone, Meckel’s cave, and middle cranial fossa [6]. “Transclival approaches” allow tumor clearance from the nasopharynx, clivus, and the odontoid, with the lower limit being the nasopalatine line [7]. Further extension of tumors into the oropharynx can be accessed with a combined transnasal and transoral approach. Superolaterally, the endoscopic approach can reach up to the midpoint of the orbit. Tumors extending to the maxillary sinus are cleared via an endoscopic medial maxillectomy or complete medial maxillectomy with resection of the lacrimal duct. Once the maxillary sinus has been opened, further access to the pterygopalatine fossa, parapharyngeal space, and infratemporal fossa is possible [8, 9]. Lateral access may be further improved with the addition of a Caldwell–Luc incision or a septal window that allows binareal access. A purely endoscopic approach is contraindicated where there is involvement of skin and subcutaneous tissue, nasolacrimal sac, anterior table of the frontal sinus, and carotid artery, and extensive dural and brain parenchymal involvement. In such cases, the addition of a transfacial or transcranial approach is warranted.

Oncological Outcomes

Several large studies published over the past decade have reported on the oncological outcomes of open ACFR. An international collaborative study of 1,307 patients treated with ACFR at 17 institutions reported 5-year overall survival (OS), disease-specific survival (DSS) and recurrence-free survival rates of 54, 60, and 53 %, respectively [10]. Howard et al. [11] reported on 259 patients treated by ACFR at a single institution with a mean follow-up of 63 months. The 5-, 10-, and 15-year disease-free survival (DFS) rates were 59, 40, and 33 %, respectively. Survival has improved over the past four decades [12]. In a retrospective medical record review of 282 patients treated at Memorial Sloane-Kettering Cancer Center and Tel Aviv Medical Center between 1973 and 2008, patients operated on after 1996 had better 5-year OS and DSS rates (66 % and 70 %) compared with patients operated on before 1996 (55 % and 57 %). Surgery after 1996 was an independent predictor of outcome on multivariate analysis, despite higher rates of comorbidity, dural and pterygopalatine invasion, and multicompartmental involvement [12].

When endoscopic endonasal surgery was first described for the treatment of sinonasal malignancies, concerns were raised regarding the oncological soundness of the procedure [13]

Criticisms have centered on the inability of the endoscopic approach to perform an en bloc resection [14]. Proponents of the endoscopic technique argue that unless the tumor is small, en bloc resection is rarely achievable with open surgery [15]. Several studies have shown that en bloc resection does not positively impact on oncological outcomes [16, 17]. What is paramount, however, is achieving negative resection margins, regardless of the surgical approach. Multiple studies have demonstrated that a positive resection margin is an independent risk factor for recurrence and reduced survival [10, 12, 16–19]. Open ACFR has reported positive resection margin rates of 15.6–17 % [10, 18]. Endoscopic surgery, with its excellent visualization, has demonstrated a result equivalent to that of open surgery (10–19 %) in selected patients [20, 21•, 22].

The two largest series of recent times have demonstrated endoscopic resection to have oncological results comparable to those of open surgery. Hanna et al. [21•] reported on 120 patients treated at MD Anderson Cancer Center from 1992 to 2007. Seventy-seven percent were treated with an exclusive endoscopic approach (EEA) and 23 % were treated with the craniendoscopic approach (CEA; defined as the transnasal endoscopic approach with the addition of a frontal or subfrontal craniotomy). Sixty-three percent of patients in the EEA group had T1–2 tumor stage, whereas 95 % of patients in the CEA group had T3–4 disease stage ($P < 0.01$). Positive margins were reported in 15 % of patients. Fifty percent of patients received postoperative radiation therapy or chemotherapy and radiation therapy. With a mean follow-up of 37 months, the local, regional, and distant recurrence rates were 15, 6, and 5 %, respectively. The 5- and 10-year DSS rates were 87 and 80 %, respectively. Disease recurrence and survival did not significantly differ between the EEA and CEA groups. Hanna et al. emphasized the role of appropriate adjuvant or neoadjuvant therapy and treatment by expert multidisciplinary teams in the management of sinonasal malignancies. Nicolai et al. [23•] reported on 184 patients from the University of Brescia and the University of Pavia/Insubria-Varese treated from 1996 to 2006. The overall 5-year DSS rate was 82 %. At the mean follow-up of 34 months, the local, regional, and distant recurrence rates were 15, 1, and 7 %, respectively. Both study cohorts had similar distributions of T staging, adjuvant treatment, and proportion of EEA to CEA (Table 1). However, compared with the MD Anderson Cancer Center group, patients in the European group were older, predominantly male, less likely to have had prior treatment (28 % versus 58 %), and more likely to present with adenocarcinoma (37 % versus 14 %). Irrespective of these differences, the 5-year DSS rate for the two series is comparable to the rates reported in the open ACFR cohorts. Both groups concluded that in well-selected patients, endoscopic resection of sinonasal cancers results in acceptable oncological outcomes.

Table 1 Demographic, pathological, and treatment characteristics of the two largest endoscopic resection series to date

	<i>Hanna 2009</i>	<i>Nicolai 2008</i>
Number of cases, n	120	184
Reporting period	1992-2007	1996-2006
Mean age, years	53	59
Male sex, %	54	64
Surgical approach, %		
Exclusively endoscopic approach (EEA)	77	73
Cranioendoscopic approach (CEA)	23	27
Prior treatment, %		
Yes	58	28
No	42	72
T stage, %		
1	25	28
2	25	14
3	21	18
4	29	28
Histology, %		
Esthesioneuroblastoma	17	12
Adenocarcinoma	14	37
Squamous cell carcinoma	13	14
Melanoma	14	9
Adenoid cystic carcinoma	7	7
Other	29	19
Positive margins, %	15	Not reported
Adjuvant treatment, %	50	46.7
Complications, %	11	9
CSF leak	3	4
Mean follow up, months	37	34
Disease Specific Survival, %		
5 year	87	82
10 year	80	Not reported
Site of Recurrence, %		
Local	15	15
Regional	6	1
Distant	5	7

Esthesioneuroblastoma

Esthesioneuroblastoma is one of the most commonly reported diseases among the sinonasal malignancies. The gold standard treatment has traditionally been ACFR followed by postoperative radiation therapy. In a meta-analysis of 390 patients treated with open ACFR between 1990 and 2000, the 5-year DFS rate was 45 % [24]. MD Anderson Cancer Center recently reported on a cohort of 70 patients, most of whom who received definitive resection were treated with open surgery (42 of 50 patients) [25]. Their median OS was 126.3 months (10.5 years) and their median DSS was 139 months

(11.6 years). Howard et al. [11] reported 5-, 10-, and 15-year DFS rates of 74, 50, and 40 %, respectively, for 56 patients treated at a single institution from 1978 to 2004. The University of Virginia Health System published its experience of 50 patients from 1976 to 2004. Its 5-, 15-, and 20-year DFS rates are 86.5, 82.6, and 81.2 %, respectively [14, 26].

Since the advent of endoscopic endonasal surgery, several small series have reported 3- to 5-year DFS rates of between 89 and 100 % [23, 27–30]. In a meta-analysis of 23 articles with 361 patients comparing endoscopic with open surgery, endoscopic surgery was associated with better survival (10-year OS rate of 90 % versus 65 % for open resection) [31]. However, most of the open surgery patients had Kadish C or D disease and there were more cases of long-term follow-up for the open surgery group. Hence, the current literature supports the use of endoscopic surgery for early-stage esthesioneuroblastoma.

Squamous Cell Carcinoma

Open surgical resection of squamous cell carcinoma (SCC) has a 5-year OS rate of 43–64 % [10, 18, 32–34]. Published studies on endoscopic resection of SCC consist of small series of between 11 and 25 patients, the largest of which reported a 5-year DSS rate of 61 % [15, 23, 35]. The University of Pittsburgh Medical Center recently presented its experience of 34 patients treated with endoscopic surgery [22]. The cohort consisted of a majority (85 %) of stage T3–4 tumors. Seventy-four percent of patients were treated with the purely endoscopic endonasal approach (EEA) and 26 % were treated with combined transcranial/transfacial and endoscopic endonasal approaches. Twenty-seven patients had definitive resection and seven had debulking surgery. The definitive resection group had 5-year DFS and OS rates of 62 and 78 %, respectively. The positive margin rate was 19 % in the definitive resection group. Survival was comparable with that for open surgery.

Adenocarcinoma

Open ACFR with postoperative radiation therapy is associated with 3- and 5-year OS rates of 72 and 64 %, respectively [36]. In a series of 66 patients treated at MD Anderson Cancer Center from 1993 to 2009, the 5-year OS and DSS rates were 65.9 and 79.1 %, respectively [20]. Most patients were treated with surgery, and 50 % received adjuvant radiation therapy. Twenty-six percent of patients underwent endoscopic resection and 74 % underwent ACFR. For patients undergoing endoscopic resection, 57 % were staged as having T1–2 disease and 43 % were staged as having T3–4 disease. Ninety-one percent of surgical margins were negative. There was no difference in survival between endoscopic and open approaches across all T classifications. The authors of the

study concluded that open procedures did not significantly improve survival compared with endoscopic surgical resections when outcomes were matched for T staging.

Nicolai et al. [37] reported on 76 patients treated from 1985 to 2009. There were 12 endoscopic resections, 17 endoscopic resections with transnasal craniectomy, nine cranioscopic resections, 11 external approaches to the ethmoid, and 18 ACFRs. The 3- and 5-year OS rates were 68.0 and 48.4 %, respectively. The 3-year OS rates were 92.88 % and an astonishing 33.33 % in patients treated with endoscopic techniques and ACFR, respectively. On multivariate analysis, previous treatment (hazard ratio 3.9, $P=0.01$) and ACFR (hazard ratio 5.16, $P=0.05$) were associated with poorer survival. While acknowledging the inherent bias of the endoscopic technique towards smaller lesions and a later treatment period, Nicolai et al. concluded that the endoscopic technique, in appropriately selected patients, was associated with favorable oncological outcomes and a reduction in the complication rate and hospitalization time.

Morbidity and Complications

Endoscopic surgery avoids craniofacial soft tissue dissection, skeletal disassembly, and brain retraction. Multiple studies have shown endoscopic surgery to be associated with lower morbidity, faster hospital recovery, and decreased hospital stay [21•, 23•, 27, 38, 39]. The two largest endoscopic series of recent years report an overall complication rate of 9–11 % and a mortality rate of 0–1 % [21•, 23•], compared with an overall complication rate of 36.3 % and mortality rate of 4.5 % for open ACFR [18]. The commonest complication was CSF leak (3–4 %), followed by a small percentage of infectious, CNS, and systemic complications. Both studies confirm that the complication rates and length of hospital stay (3.7 days versus 15.4 days) were higher in the CEA group than in the EEA group. The complication rates increased with T4 lesions and larger tumors and if an endoscopic craniectomy was added [39],

CSF Leak and Reconstructive Options

Early reconstructive experience at the University of Pittsburgh Medical Center was associated with CSF leak rates of 20–30 % for endoscopic anterior cranial base defects [40, 41]. The application of a nasoseptal flap placed extradurally has lowered leak rates to 5 % [42]. When there is tumor involvement of the superior nasal septum, the “extended nasoseptal flap” can be harvested from the lower septum and extended onto the floor and lateral wall of the nasal cavity [43]. Other vascularized reconstructive alternatives for the anterior skull base include the minimally invasive pericranial flap [44], the middle turbinate flap for small defects, and the transpterygoid

temporoparietal fascia flap [45, 46]. The inferior turbinate flap, although robust, has limited reach and is best suited to clival defects [47]. Other flaps described in the literature such as the palatal flap [48], the buccinator myomucosal flap [49], and the occipital galeopericranial flap [50] may be considered.

Some investigators have used nonvascularized reconstructive options with favorable results. Gil et al. [51] described a double-layered tensor fascia lata repair with a CSF leak rate of 0.8 %. Histological examination of resected fascia lata in patients who underwent a second operation showed evidence of neovascularization of the fibrous tissue, even without the presence of a vascularized flap. Villaret et al. [52] proposed a three-layer reconstruction with the iliotibial tract. They reported postoperative CSF leak rates of around 4 % [23•, 52].

Vascular Injury

Internal carotid artery (ICA) injury during endoscopic resection of sinonasal malignancy is rare. However, with the ever-expanding indications for endoscopic surgery and the evolution of surgical techniques, resection of tumors near the carotid artery is becoming increasingly common. Gardner et al. [53] described their experience of seven ICA injuries in 2,015 endoscopic endonasal skull base cases over a 13-year period. The mortality rate was 17 % and the average blood loss was 1,600 mL (range 400–4,200 mL). There was one case of ICA injury in 256 sinonasal malignancies. This occurred during resection of a nasopharyngeal carcinoma after prior treatment, resulting in laceration of the ICA at the foramen lacerum. Gardner et al. concluded that the best strategy for managing ICA injury is prevention, “2 surgeon, 3- or 4-hand technique,” anatomical knowledge, preemptive vascular control via a neck incision, careful preoperative assessment of imaging, and planning. Once ICA has occurred, they advocate early endovascular assessment with angiography. They identified neurophysiological monitoring to be a reliable predictor of cerebral hypoperfusion and this can guide the decision to perform intraoperative ICA sacrifice.

Valentine and Wormald [54] developed a sheep model to recreate and train surgeons in the management of ICA injury. A number of hemostatic techniques were tested, including muscle patch treatment (harvested sternocleidomastoid), Floseal (Baxter International, Deerfield, IL, USA), oxidized regenerated cellulose (Surgicel Nu-Knit, Ethicon, West Somerville, NJ, USA), MicroFrance Wormald vascular clamps (Medtronic, Jacksonville, FL, USA), and U-Clip anastomotic sutures (Medtronic) to suture the vascular defect. Muscle patch treatment was effective at achieving vascular control within 10 min, as was use of the MicroFrance Wormald vascular clamp and U-Clips. Other stratagems include active two-surgeon teamwork, the use of two large-bore suctions to direct blood flow away from the endoscope, strategic placement of the endoscope on the contralateral side with respect to

the vascular injury to avoid excess soiling, and use of an endoscope lens-cleaning system.

Quality of Life

The only instrument validated for patients undergoing anterior skull base surgery is the anterior skull base quality-of-life questionnaire [55]. Although specific to patients undergoing extirpation of anterior skull base tumors, it was developed for open surgery [56]. It is a comprehensive multidimensional questionnaire comprising subscale scores for performance, physical function, vitality, pain, specific symptoms (taste, smell, appearance, epiphora, nasal secretions, and visual disturbance), and influence on emotions and a total score. A higher score indicates a better outcome, with a minimum of 1.0 and a maximum of 5.0.

The current available literature supports endoscopic resection having favorable long-term quality-of-life outcomes. Castelnuovo et al. [57] reported on a retrospective series of 153 patients treated with the endoscopic approach for sinonasal malignancies using the anterior skull base quality-of-life questionnaire. They found that quality-of-life scores sharply decreased 1 month after surgery from 4.68 to 4.03. However, the scores recovered to 4.59 over the course of 1 year after treatment. Patients older than 60 years, those who had had postoperative radiation therapy, and those for whom an expanded surgical approach with transnasal craniectomy had been undertaken had lower scores. In a meta-analysis of 273 patients undergoing skull base tumor resection, malignancy and less than 6 months from surgery are associated with worse quality-of-life scores [58]. Patients undergoing endoscopic surgery scored better with regard to physical function and impact on emotions than patients in the open surgery group [58, 59].

Technical Developments

Since the introduction of endoscopic endonasal surgery, specialized operating suites, intraoperative navigational devices, endonasal instrumentation, and Doppler sonography for identifying major vessels have become widely used by skull base surgeons [60]. In the past few years, some centers have introduced the use of microdebriders for fibrous lesions and ultrasonic dissectors as an alternative to the high-speed drill for bone removal [61–64]. Even as high-definition endoscopes have become the norm, depth perception, afforded by the microscope, is lost. The 3D endoscope is a possible alternative but is limited by problems with peripheral image distortions during narrow space exploration, reduced level of sharpness and contrast compared with high-definition 2D endoscopes, and the inability to visualize around corners [65–67].

A localized intraoperative virtual endoscopy image guidance system combines real-time instrument tracking with 3D

virtual endoscopic views, intraoperative image updates, and critical structure proximity alerts [68]. Compared with standard image guidance systems, it was found to reduce scores for mental demand, effort, and frustration in cadaveric studies. Localized intraoperative virtual endoscopy image guidance systems may have a role in technically challenging cases where there are compromised visual landmarks and critical structures are nearby. The system is ready for a clinical trial but one major drawback is the addition of visual and auditory stimuli, which can be unnecessarily distracting.

Robotic surgery is used extensively in head and neck transoral surgery. It offers 3D depth perception, excellent visualization, and 360° rotational arms allowing small, precise, tremor-free movements in enclosed spaces. Several early studies have explored the feasibility of robotic-assisted skull base surgery [69–71]. The main constraint appears to be crowding of instruments in a confined space, but various solutions have been proposed. Hanna et al. [72] reported a robotic transcranial approach to the anterior skull base by introducing instruments through large bilateral anrostomies combined with a transnasal camera. O'Malley and Weinstein [70] used a combined cervical and transoral robotic approach to dissect the median skull base, sella, and parasellar and suprasellar regions of the anterior skull base. Ozer et al. [73] compared transoral, transcervical, transnasal, and transpalatal corridors using cadaveric specimens to assess the optimal route of the camera and instrument placement without using transcervical trocars. They found that a transoral camera provided good instrumentation but visualization over the roof of the nasopharynx and posterior choana was poor. A transnasal camera provided excellent visualization but poor instrumentation. The transpalatal approach was the best compromise but necessitated removal of the posterior aspects of the hard palate.

Dealing with intraoperative bleeding is an important consideration. Preoperative strategies include evaluation for bleeding disorders, appropriate reduction of antiplatelet and anticoagulant medications, and judicious use of preoperative embolization for vascular tumors [74]. Intraoperative measures include control of hypertension, patient positioning in the reverse Trendelenburg position, and use of topical vasoconstrictors and hemostatic agents. Hot water irrigation was originally described for the treatment of epistaxis [75] and is now used routinely in some centers to decrease ooze from sinonasal mucosa. The development of endoscopic bipolar cautery and intranasal CO₂ laser technology [76], and the adaptation of cobaltors for intranasal use can potentially reduce intraoperative blood loss during resection of highly vascular tumors [77, 78].

Areas for Further Research

We have increasing evidence of the oncological soundness and safety of endoscopic resection for appropriately selected

patients. This evidence provides us with a critical understanding of the types of lesions amenable to endoscopic resection. Nevertheless, there are no published studies of followup beyond 10 years and there is a paucity of pathology-specific survival data. The challenge is to define the role of endoscopic surgery within a multidisciplinary oncological strategy that includes rapidly evolving modalities such as proton beam radiation therapy, neoadjuvant chemotherapy, and targeted therapy. Although endoscopic surgery offers better functional and quality-of-life outcomes than open surgery, prospective studies that evaluate and propose solutions to address the impact of the overall treatment strategy, including the effects of adjuvant treatments, are required. Technical limitations in endoscopic skull base surgery include the inability to suture, difficulty accessing around corners, and control of large vessels. The future decade will bring advances in technology that will require thoughtful integration with current practice, balancing innovation, efficacy, and value.

Conclusion

Advances in technique and instrumentation have allowed safe and effective endoscopic resection of tumors in the sinonasal cavity and skull base. Endoscopic surgery offers an oncologically sound alternative to open surgery in selected patients with sinonasal malignancies. It offers the advantages of lower morbidity, faster recovery, and better quality-of-life outcomes. Pathology-specific and long-term follow-up survival data are required to further define the role of endoscopic surgery in the setting of multidisciplinary care.

Compliance with Ethics Guidelines

Conflict of Interest Shirley Y. Su, Michael E. Kupferman, Franco DeMonte, Nicholas B. Levine, Shaan M. Raza, and Ehab Y. Hanna declare that they have no conflict of interest

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

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