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Endonasal endoscopic surgery for sinonasal squamous cell carcinoma from an oncological perspective[☆]

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ABSTRACT

Endonasal endoscopic surgery (EES) has been applied to the management of sinonasal (SN) tumors based on recent advances in endoscopic surgical techniques and technologies over the past three decades. EES has been mainly indicated for benign tumors and less aggressive malignant tumors. Notwithstanding this, EES has been gradually adopted for squamous cell carcinoma (SCC), which is the most common histology among SN malignancies. However, an analysis of the outcomes of EES for patients with SCC is difficult because most articles included SCC a wide range of different tumor histologies. Therefore, we herein review and clarify the current status of EES focusing on SCC from an oncological perspective.

The oncologic outcomes and the ability to achieve a histologically complete resection are similar between endoscopic and open approaches in highly selected patients with SN-SCC. Surgical complications associated with EES are likely similar for SN-SCC compared to other sinonasal malignancies.

The indications for a minimally invasive approach such as EES in the management of patients with SN-SCC should be stricter than those for less aggressive malignant tumors because of the aggressive nature of SCC. Also, it is important to achieve negative surgical margins with EES in patients with SCC. We believe that the indications for EES for SN-SCC are widening due to advances in diagnostic imaging, and endoscopic surgical techniques and technologies.

[☆] This article was written by members and invitees of the International Head and Neck Scientific Group (www.IHNSG.com).

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However, while expanding the indications for EES for SN-SCC we must carefully confirm that the outcomes support this strategy.

1. Introduction

Endonasal endoscopic surgery (EES) has been applied to the management of sinonasal (SN) tumors based on recent advances in endoscopic surgical techniques and technologies over the past three decades [1-3]. It has been mainly employed for benign tumors such as inverted papilloma (IP) and less aggressive malignant tumors such as adenocarcinoma and olfactory neuroblastoma [4-6]. Squamous cell carcinoma (SCC), which is the most common histology among SN malignancies, is aggressive in nature. Therefore, EES is less adopted for patients with SCC, with a traditional open procedure or non-surgical options often preferred. One explanation for this is that there is a perception that SCC must be resected en bloc and with a wide surgical margin due to its aggressive nature. Meanwhile, recent advances in imaging modalities, instruments and endoscopic surgical techniques have enabled us to increasingly adopt EES for SCC in selected cases (Fig. 1). However, the analysis of the usefulness of EES for patients with SCC is difficult because most publications have usually included cohorts with a wide range of histologies [7-10]. Therefore, we herein review and clarify the current status of EES for oncologic endoscopic resection of SCC building on recent literature.

2. Concept of EES for SN-SCC

Previously it was generally agreed that in cancer surgery it was imperative that the tumor be resected en bloc and that cutting into the substance of the tumor should be avoided at all costs [11]. En bloc resection has been traditionally regarded as the ideal form of intervention for patients with SCC of the head and neck cancer and specifically in the nose and sinuses. The advantages of open surgery have been considered to be excellent access and visualization of the surgical site. However, in SN-SCC, en bloc resection is not often achieved

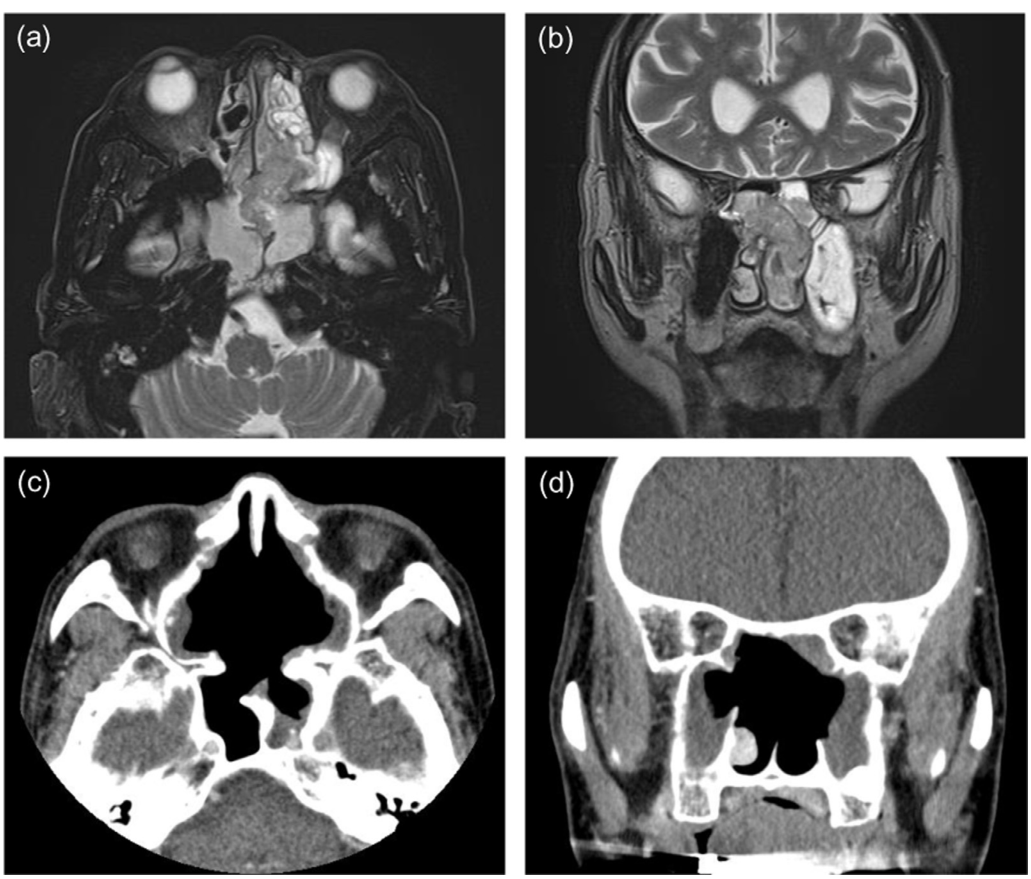

Fig. 1. Preoperative axial and coronal T2-weighted MRI of a patient with a SCC demonstrating a tumor with the epicenter in the left ethmoid sinus classified as T2N0M0 (a and b, respectively). The tumor extended into the right side and the sphenoid sinus. The tumor was removed completely by purely EES and was confirmed to have histologically negative margins. The patient received postoperative radiotherapy. Postoperative axial and coronal CT 10 months after surgery demonstrating no evidence of recurrent tumor (c and d, respectively).

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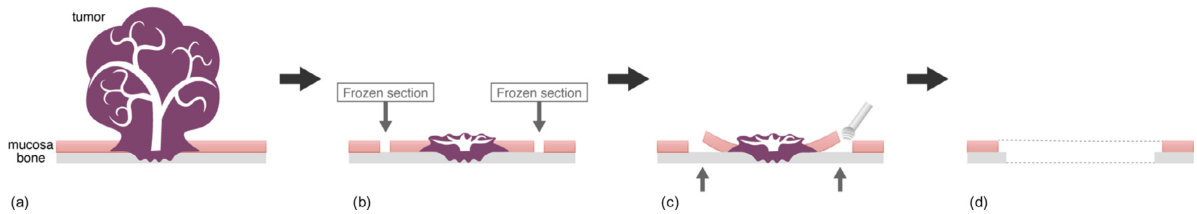

Fig. 2. Surgical concept of the attachment-oriented surgery [21]. The surgery begins with debulking of the tumor with a microdebrider to identify the origin of the tumor (a). A 6–8 point biopsy is taken and frozen sections sent to the pathologist. The mucosal incision is performed with pathologically confirmed tumor-negative margins (b). The tumor attachment site is dissected and excised subperiosteally (c, d). If the underlying bone is eroded, the bone is resected with the tumor.

even by craniofacial resection, and debulking or segmental resection is frequently required. In addition, recent advances in endoscopic instruments have allowed multi-angled and magnified views of the tumor limits, facilitating resection [12]. For other head and neck cancer sites, especially for laryngeal, oropharyngeal, and hypopharyngeal cancers, transoral resection has become popular, due, to a large extent, to the contribution of Steiner, a pioneer of the transoral endoscopic surgery, who reported excellent oncological and functional results for this technique [13-16]. Hinni et al. concluded that piecemeal removal of tumors with three-dimensional margin mapping using an operating microscope or rod telescope is safe from an oncologic perspective and reduces morbidity and the length of hospitalization [17,18]. Under these circumstances, rather than pursuing en bloc resection, it may be feasible to achieve negative margins with good visualization regardless of whether an open or endonasal endoscopic approach is used. In reality, optimum visualization cannot necessarily be achieved without endoscopic assistance, even by an open approach, due to the complexity of the sinonasal anatomy. Due to enhanced visualization, EES is now being increasingly indicated for patients with SN malignancies.

The traditional concept of en bloc resection and a wide surgical margin for SN-SCC could lead to an excessively wide resection [19]. For example, in cancers originating from the ethmoid sinus and in contact with the anterior skull base, there is a trend to choose anterior skull base resection to remove cancer in an en bloc fashion and to ensure a wide surgical margin. However, the cancer might only be in contact with the skull base and not transgress it. In such cases, anterior skull base resection can be excessive. If we accept debulking and segmental resection rather than the traditional concept of en bloc resection, the chance to apply a minimally invasive approach such as EES will be increased. Tumor dissemination around the surgical field and a narrow surgical margin remain concerns for recurrence but have been addressed by previous authors [13-18] in other head and neck areas.

The prerequisites of EES for SN-SCC are the precise identification of the site of origin of the tumor and complete resection of tumor with safe margins. Nakamaru et al. resected the tumor endonasally with reference to “attachment-oriented surgery” and “multilayer centripetal technique,” with slight modifications [20,21]. Attachment-oriented surgery was originally developed for SN-IP and showed good oncological results (Figs. 2 and 3) [22]. Originally, this surgery started with debulking of the tumor using a microdebrider to precisely identify the site of origin, followed by resection of the mucosa far enough from the tumor to ensure safe margins, and finally the tumor attachment site was drilled out with a diamond bur. Frozen sections confirmed the absence of neoplastic cells in the surgical margins. As SN-SCC is more aggressive than SN-IP, Nakamaru et al. set wider surgical margins than for SN-IP and used frozen sections before the mucosa around the tumor was excised. Moreover, they resected eroded bone instead of drilling it down, as drilling of the tumor attachment site may lead to tumor dissemination. The “multilayer centripetal technique” reported by Castelnuovo et al. similarly involved tumor debulking and management of the tumor attachment site through the following 5 steps: (1) reduction of the neoplasm volume; (2) centripetal subperiosteal ethmoidal-nasal removal; (3) removal of bone underlying the tumor (septum, skull base, and lamina papyracea); (4) removal of the dura, olfactory bulb, and periorbita; and (5) skull base duraplasty. This surgical method was applicable for all SN malignant tumors and they have reported excellent results [23]. It is apparent that precise management of the tumor attachment site with tumor debulking would enable complete resection of tumor without reliance on an en bloc method.

Reconstruction of skull base defects to secure cranionasal separation will prevent postoperative complications such as cerebrospinal fluid leakage and meningitis [24]. The flap separating the cranial cavity from the sinonasal tract has to be strong enough to tolerate perioperative radiotherapy, especially for SN-SCC. Harvey et al. reported the intracranial complications in 106 patients who underwent endoscopic skull base reconstruction, mostly with multilayered soft tissue repairs, and found only a 3.8% (4/106) perioperative complication rate [25]. Even though only five patients (4.7%) had received prior irradiation to the head and neck, this factor did not increase the rates of intracranial complications in either the perioperative period or long term. These data indicate that endoscopic skull base repair has become a reliable and robust method for reconstruction of skull base defects, despite removal of bone and meningeal layers. Further, Thorp et al. reported the results of 151 patients who received endoscopic skull base reconstruction using vascularized flaps [26]. Thirty-seven patients received radiotherapy while 114 patients did not undergo radiotherapy as part of the treatment profile. No significant association was found between the perioperative complication rates and radiotherapy ($p = 0.634$). On the other hand, Zanation et al. reported that preoperative radiotherapy tended to be associated with a higher rate of postoperative

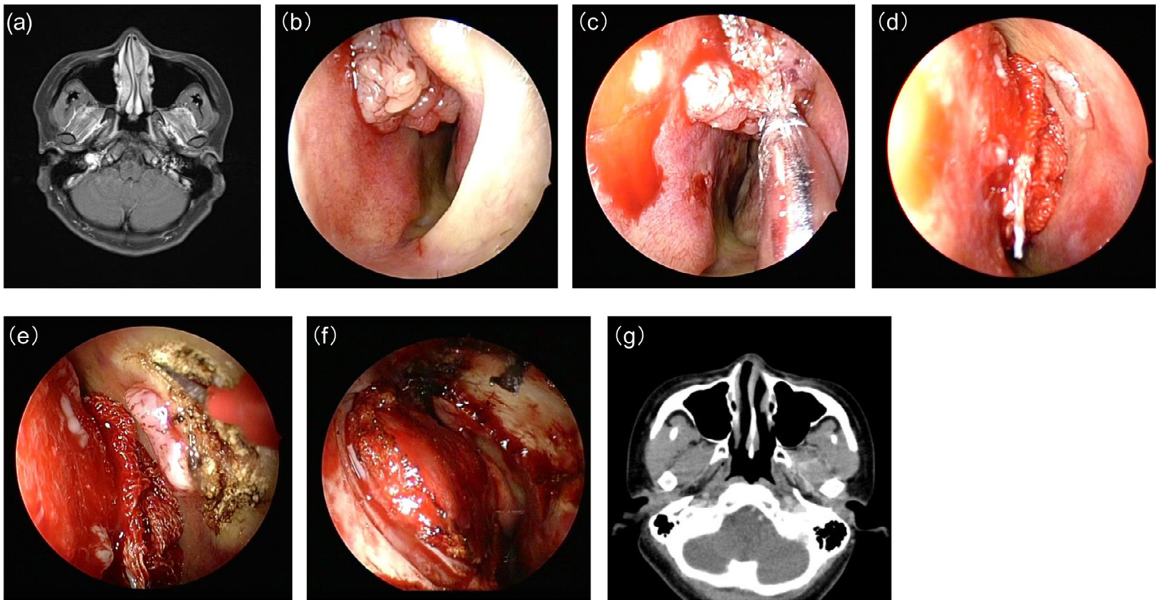

Fig. 3. Magnetic resonance imaging from a patient with SCC in the left nasal cavity is shown (a). Intraoperative photographs from the endonasal endoscopic surgery performed on the patient. Initial view demonstrating a left nasal cavity tumor (b). Endoscopic view during debulking of the tumor using microdebrider to precisely identify the site of origin (c). The tumor was attached to the nasal septum and the agger nasi separately (d). The tumor-attached mucosa of the left agger nasi was resected en bloc with the periosteum (e). The tumor-attached mucosa of the left nasal septum was resected en bloc with margins of 5 mm and the nasal septum cartilage was also resected together to ensure the deep surgical margin, but the mucosa of the nasal septum was preserved (f). Postoperative computed tomography at 14 months of follow up showing no evidence of residual disease (g).

CSF leak in their multivariate analysis of 70 patients undergoing endoscopic extended endonasal approach with primary nasoseptal flap reconstruction ($p = 0.07$) [27]. Although the negative impact of perioperative radiotherapy might not have been proved statistically, we tend to prefer a vascularized flap rather than free grafting for patients with SN-SCC because intracranial complications are potentially life-threatening and lead to long periods of hospitalization. Further study is needed to evaluate whether or not a vascularized flap is really necessary for closure of anterior skull base defects.

3. Treatment outcomes for EES compared to other approaches for SN-SCC

The number of patients with malignant SN-SCC tumors treated at any single center is usually modest and even in larger cohorts the number of SCCs is small, for example only 9 out of 140 (6.4%) sinonasal malignancies were treated endoscopically with curative intent by Lund and Wei [28]. Thus, there have been few reports on the treatment outcomes of patients with SN-SCC other than those occurring in the maxillary sinus. Homma et al. reported 25 consecutive patients with SCC of the nasal cavity and the ethmoid sinus treated between 2000 and 2012 [29]. Four patients were diagnosed with T1, 3 with T2, 4 with T3, 7 with T4a, and 7 with T4b disease. No patient had lymph node metastasis. Twelve patients (48%) were treated with surgery alone or followed by radiotherapy +/- chemotherapy. Of these, 4 underwent exclusively endoscopic surgery. Thirteen (52%) were treated with radiotherapy; 1 with radiotherapy alone, and 4 and 8 with intravenous and intra-arterial chemotherapy, respectively. The 5-year overall survival (OS) and disease-specific survival (DSS) rates calculated by the Kaplan-Meier method were 52.3% and 59.9%, respectively. The 5-year OS rates for T1–3, T4a, and T4b disease were 53.9%, 71.4%, and 29.0%, respectively, while the 5-year DSS rates for T1–3, T4a, and T4b disease were 74.1%, 71.4%, and 29.0%, respectively. In this paper, there is no comparison between results of patients treated with surgery versus radiotherapy.

Michel et al. reported 33 patients with SN-SCC treated between 1995 and 2008 [30]. Tumor locations were maxillary sinus in 16 cases (48.5%), nasal cavity in 9 (27.3%), nasal septum in 6 (18.2%), ethmoid in 1 (3%), and sphenoid in 1 (3%). The tumor was classified as T1 in 6 (18.2%), T2 in 9 (27.3%), T3 in 2 (6.1%), T4a in 9 (27.3%), and T4b in 7 patients (21.2%). Six types of initial treatment were used: surgery alone in 7 cases (21.2%), surgery followed by radiotherapy in 8 (24.2%), surgery followed by concurrent chemoradiotherapy in 3 (9.1%), concurrent chemoradiotherapy in 13 (39.4%), chemotherapy in one (3%), and radiotherapy alone in one (3%; an elderly patient classified as T4aN0M0). As a result, the disease-free survival (DFS) rates at 1 and 5 years were 58.5% and 46.1%, respectively, and the OS were 70.3% and 40%, respectively. Surgery followed by radiotherapy improved OS ($p = 0.005$) and DFS ($p = 0.028$) when compared to other treatment modalities.

Sanghvi et al. examined the incidence and survival of 4994 patients with SN-SCC between 1973 and 2009 using the Surveillance, Epidemiology, and End Result (SEER) database [31]. The 5-, 10-, and 20-year OS rates for 4994 cases of SN-SCC were 53.0%, 44.6%, and 29.4%, respectively. Although, the overall incidence of SN-SCC has been steadily and significantly declining in the past 30 years, survival has not significantly improved in this period.

Table 1. Treatment results of endonasal endoscopic suregry for sinonasal squamous cell carcinoma.

First author (year of publication)	Study design	No. of patient; Stage, Treatment	Follow-up in months; (range)	Treatment results
Lund [32], (2010)	Systematic review	23, T1: 8, T2: 7, T3: 3, T4: 4, Unknown: 1	41.6, (3 - 92)	local recurrence: 6 patients (26.1%); alive without disease: 19 (82.6%); died of disease: 3 (13.0%: [T1: 2; T2: 1]); died of other causes: 1 (4.3%)
de Almeida [33], (2015)	retrospective case series	34, T1: 1, T2: 3, T3: 4, T4a: 11, T4b: 14, N+: none, Purely ESS: 25, EES+open: 9, Definitive resection: 27, Debulking: 7, Adjuvant RT: 24 (71%)	33, (0 - 111)	5-year DFS: 62%, 5-year OS: 78% (among 27 definitive resection), positive margins (19% [5/27 definitive resection]): predictive DFS in a multivariable model
Kilic [35], (2018)	retrospective cohort	1483, ESS: 353 (stage I: 107, II: 51, III: 55, IA: 63, IVB: 31), open: 1130, postoperative RT(+chemo): 53.8% (190/ 353 ESS)		5-year OS: 46.0% (among 353 ESS) vs 56.5% (among 1130 open), $p = 0.953$, positive margins: 21% (negative: 47.9%, unknown: 31.1%), positive margins: poorer OS on multivariate analysis
Nakamaru [21], (2020)	retrospective case series	15, T1: 4, T2: 7, T3:4, N+: none, purely EES: 15, postoperative RT(+chemo): 53.3% (8/15)	26, (7 - 123)	5-year OS: 72.4%, 5-year DSS:79.6%, positive margins: 26.7% (4/15), 5-year DSS: 100% (among 11 negative margins), 37.5% (among 4 positive margins)

Abbreviations: EES: endonasal endoscopic suregry, RT: radiation therapy, DFS: disease-free survival, OS: overall survival, DSS: disease specific survival.

Unfortunately, as can be seen from the above reports, the 5-year OS for SN-SCC ranges from 40 to 53%, and this figure has not changed over the last three decades, despite advances in imaging modalities and treatment regimens [29-31].

Several studies have focused exclusively on endoscopic surgery for SN-SCC (Table 1). According to the European position paper on endoscopic management of tumours of the nose, paranasal sinuses, and skull base published in 2010, only 23 patients underwent purely endoscopic resection among the 150 patients with SN-SCC for whom data are available [32]. This cohort had a preponderance (65.2%) of low stage (T1 to T2) disease at presentation. Local recurrence was noted in 6 patients (26.8%). At last follow-up ranging from 3 to 92 months (mean, 41.6 months), 19 patients (82.6%) were alive without disease. Three patients (two T1 and one T2) died of their disease, including one patient who had distant metastasis to the brain without local recurrence and one patient who died of other causes. De Almeida et al. reported 34 patients with SN-SCC undergoing EES. Of these, 27 had definitive resection and 7 had debulking surgery [33]. Definitive resection was associated with better 5-year DFS and OS rates than was debulking (62% vs. 17%; $p = 0.02$; and 78% vs. 30%; $p = 0.03$).

Shipchandler et al. reported preliminary data for 11 patients with SN-SCC treated by EES in 2005 [34]. All 11 patients were treated with curative intent by endoscopic resection with intraoperative surgical navigation and adjuvant therapies when appropriate. Ten of the 11 patients underwent complete surgical extirpation. One patient presented with cavernous sinus and sellar involvement and was surgically debulked with planned radiation and chemotherapy postoperatively for potential cure. Seven patients had their tumor resected using a solely endoscopic approach and four required bifrontal craniotomy to clear the superior margin. Eight of the 11 patients (73%) received adjuvant therapy. Seven patients (64%) received pre- (2 cases) or postoperative (5) radiotherapy. Four patients (36%) received pre- (1 case) or postoperative (3) chemotherapy, with 3 of these 4 receiving both radiation and chemotherapy. The OS and DFS rates over the mean follow-up period of 31.5 months were both 91%. Although these results are excellent, the follow-up period was too short to provide data regarding the 5-year survival rate.

Nakamaru et al. reported a retrospective analysis of 15 consecutive SN-SCC patients who underwent exclusively EES [21]. The majority of patients had early stage disease, T1 or T2, and there were no cases of stage T4 disease. Eight patients (53%) were treated with surgery alone and 7 (47%) with surgery and postoperative radiotherapy with/without chemotherapy. The 5-year OS, DSS, and local control rates were 72.4%, 79.6%, and 92.9%, respectively. The 5-year DSS rates for T1, T2, and T3 disease were 100% and 75% and 75%, respectively.

A large study based on the National Cancer Database was published in 2018 [35]. They identified a total of 1483 patients (353 patients received EES and 1130 patients underwent open surgery) with SN-SCC. A multivariate logistic regression analysis revealed that a non-academic facility, ethmoid sinus, and stage IVB disease remained significantly associated with EES, suggesting that stage IVB disease is associated with EES independent of anatomic site or facility type. This might be because most stage IVB patients who received EES did so with palliative intent as they are not usually treated with curative intent. Postoperative chemotherapy and/or radiotherapy was performed in 53.8% (190/353) of patients in the EES group and in 51.5% (582/1130) in the open surgery group. Although endoscopic resection was associated with a shorter hospital length of stay, the five-year OS was not significantly different between the 2 approaches ($p = 0.953$; open: 5-year OS, 56.5%; 95% confidence interval, 51.3% to 61.6%; endoscopic: 5-year OS, 46.0%; 95% confidence interval, 33.2% to 58.8%) In the propensity score-matched cohort of 652 patients, there was also no significant difference in OS ($p = 0.850$).

In summary, all of these publications have demonstrated that endoscopic resection is feasible for SN-SCC and has similar oncologic outcome as a traditional open approach.

4. Surgical margins

Regarding surgical margins, in the study by Nakamaru et al., 4 of the 15 patients (27%) showed positive surgical margins [21]. None of the patients with negative surgical margins ($n = 11$) showed recurrence. On the contrary, the 5-year DSS rate of the patients with positive surgical margins was 38% and statistically lower than those with negative surgical margin ($p = 0.0253$). This result suggests that negative surgical margins are important, even in cases treated using the multilayer centripetal technique. Further, their rate of positive surgical margins was equivalent to those of previous studies (21–33%) [35,36]. Robin et al. reported that a positive surgical margin was a poor prognostic factor with a hazard ratio of 1.575 compared to cases with a negative surgical margin [37]. Karligkiotis et al. analyzed 34 patients with IP-derived SCC who had resection with curative intent [38]. In patients with positive margins, the oncologic outcomes were significantly worse. Locoregional control (LRC) and DFS in patients with negative margins was 74% at 5 years compared to 0% in those with positive margins ($p < 0.001$), and the 5-year OS was 93% in those with negative margins compared to 0% in those with positive margins ($p < 0.001$). In a multivariable model, only positive margins were predictive of both poorer LRC ($p = 0.003$) and DFS ($p = 0.003$). Farquhar et al. conducted a propensity score analysis for the comparison of 124 patients with SN tumors who received endoscopic or open resection and indicated no differences in the rate of negative margins between the treatment groups either before or after matching (endoscopic: 67%; open: 68%; adjusted $p = 0.70$) [36]. This study did not indicate that an open approach achieved better negative surgical margins though it had only 28 patients (22.6%) with SCC. As mentioned, it was reported that there was no difference in the rate of positive margins between the endoscopic and open approach groups [35,36], which suggests that the ability to achieve a histologically complete resection was comparable between the two approaches bearing in mind that the ability to ensure negative surgical margins is critical to the management of SN-SCC. Advances in light spectroscopy, endoscopy, imaging, biochemical alteration of tissue, molecular markers and epigenetic alterations, can all be applied to the assessment of surgical margin status [39,40], and these modalities are expected to be available in the near future.

5. Indications for EES for SN-SCC

The oncologic outcomes are similar for EES and open approaches according to previous reports taking into account that appropriate patient selection and thorough margin-negative surgery confers the optimal outcome [41]. As mentioned previously, margin-negative surgery is imperative to achieve a good outcome. Therefore, the indications for EES are based on the expectation that the tumor can be resected by EES with a negative surgical margin.

Nicolai et al. reported their indications for EES for sinonasal malignancies [42]. Patients with extension into the frontal sinus, orbit, lacrimal pathway, bony wall of the maxillary sinus (except the medial wall), pterygopalatine or infratemporal fossa, and erosion of the skull base were excluded from EES. The UK guidelines for sinonasal malignancies also showed similar indications for endoscopic surgery, except for erosion of the skull base [43]. These guidelines for EES include patients with skull base bone erosion and dura or brain involvement medial to the mid orbital roof, and are suitable for less aggressive sinonasal carcinomas.

Nakamaru et al. mentioned that safe indications for EES for patients with SN-SCC were relatively limited disease, such as T1-2 disease, nasal cavity/ethmoid tumors and some T3 disease without bony destruction of the sinus walls [21]. According to the International Consensus Statement on Endoscopic Skull-Base Surgery published in 2019 [41], expert opinion has suggested that the following criteria would indicate that a patient is not an appropriate candidate for endoscopic resection of SN-SCC if the following structures are involved: hard palate, anterior maxillary, inferior maxillary, extensive posterior maxillary, orbital floor, ascending process of the maxilla, nasal bone, anterior table of the frontal sinus, or posterior table of the frontal sinus osseous extension, soft palate extension, extensive pterygopalatine fossa/infratemporal fossa extension, cranial nerve extension to or beyond the respective skull-base foramen, cavernous sinus extension, orbital extension, brain parenchymal extension, or involvement of the soft tissues of the face. This consensus states that so far, oncologic outcomes are similar between endoscopic and open approaches in selected patients with SN-SCC and as expected, inappropriate patient selection may lead to less favorable outcomes. In addition, there is now adequate published evidence of benefit for endoscopic resection of SN-SCC. However, this procedure should be an option only in properly selected patients and with experienced surgeons.

Although high definition imaging modalities are good predictors of tumor invasion into the skull base, it is still very difficult to predict whether a tumor can be resected purely by EES or not. Thus, we should be prepared to be flexible, starting with an endonasal approach, and combining this with a craniotomy and/or an open approach such as lateral rhinotomy when needed. Preparation in advance is necessary for such open approaches when EES is undertaken.

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6. Adjuvant therapy

Robin et al. specifically compared outcomes by treatment modality for SN-SCC using the National Cancer Data Base [37]. Radiotherapy alone (HR, 1.294 [$P = 0.001$]) and chemotherapy alone (HR, 1.834 [$P<0.001$]) were associated with worse OS, but patients treated with adjuvant radiotherapy (HR, 0.658 [$P<0.001$]) and adjuvant chemoradiotherapy (HR, 0.696 [$P = 0.002$]) had improved outcomes compared with patients treated with single-modality surgery. There was no difference in OS between definitive chemoradiotherapy and surgery alone (HR, 1.076; 95% CI, 0.899–1.289 [$P = 0.425$]). This study suggested that treatment outcomes for SN-SCC are influenced by additional treatment, and surgery alone is not sufficient to achieve a good outcome in most situations. Thus, adjuvant therapy, usually postoperative radiotherapy, should be indicated for most patients with advanced disease (stage III-IV) or with a close or positive margin.

7. Surgical complications associated with EES for SN-SCC

Nicolai et al. reported postoperative complications in 134 exclusive EES patients and 50 cranioendoscopic approach (CEA) patients with various types of malignant SN tumors [7]. The mean hospitalization time was 3.7 days (range, 1–10) in the EES group and 15.4 days (range, 10–35) in the CEA group. In the EES group, overall postoperative complications occurred in 8 patients (6%): CSF-leak (4), mucocele (2), frontal stent displacement (1), and meningitis (1). On the other hand, in the CEA group, overall postoperative complications occurred in 8 patients (16%): CSF-leak (4), brain abscess (1), extradural abscess (1), frontal osteomyelitis (1), and ictus cerebri (1). In addition, 2 patients died of brain edema and cerebral hematoma in the early postoperative period in the CEA group. Nicolai et al. concluded that EES was therefore, associated with a lower rate of serious complications, even in cases requiring dura resection.

Similarly, in 140 cases of sinonasal malignancy undergoing endoscopic excision with curative intent and utilizing multi-layered free soft-tissue repair for dural repair, the complications rate was low, comprising three cases (2%) with bleeding in the immediate post-operative period, 3 cases (2%) of cerebrospinal fluid leakage and 8 cases (6%) of epiphora, all successfully treated endoscopically. [28].

Abdelmeguid et al. reported 239 patients who underwent endoscopic resection of SN malignancies with curative intent at the MD Anderson Cancer Center between 1998 and 2018 [10]. 167 (70%) had a purely EES, while 72 (30%) had an endoscopic-assisted approach. Nearly 60% of their study received adjuvant therapy, and 16.3% received induction chemotherapy as part of their treatment. The overall surgical complication rate was 28.8% (69 patients) ranging from minor complications like seroma and sinusitis to major intracranial complications like meningitis and brain infection. Intracranial complications were documented in 34 patients (14.2%), with no significant difference in the rate of the intracranial complications between the purely endoscopic and endoscopic-assisted group ($p = 0.129$). CSF leakage occurred in 14 patients (5.9%), all of whom had a purely EES. In nine patients, the CSF leak was successfully managed conservatively without a need for surgical intervention. Four patients underwent successful endoscopic repair while one patient required additional bifrontal craniotomy and repair of the skull base by pericranial flap. One patient had meningitis that was successfully managed conservatively with antibiotic therapy. Two patients who underwent endoscopic resection with a bifrontal craniotomy experienced delayed infection and frontal lobe abscess that required reopening of the craniotomy and drainage of the abscess. Other complications included epiphora in 20 patients (8.4%), diplopia in 9 patients (3.8%), and brain contusion in 4 patients (1.7%). The CSF leakage rate among purely EES could seem slightly higher but it should be taken into account that they had set wider criteria for EES than in other reports [41,43].

Nakamaru et al. reported no postoperative complications among 15 consecutive SN-SCC patients who underwent exclusively EES [21]. Kılıc et al. reported that hospital stay was significantly shorter in patients with SN-SCC treated with endoscopic resection (endoscopic: 2.50 days; open: 4.67 days; $p < 0.0001$) according to the National Cancer Database [35]. Karligkiotis et al. reported 26 SN-SCC patients managed exclusively with endoscopic resection [38]. Minor postoperative complications occurred in 3 patients (11.5%) after exclusive endoscopic resection: 2 patients presented epistaxis on the first postoperative day, which was managed with bipolar cauterization, and 1 patient experienced epiphora at 6 months after surgery, which required endoscopic dacryocystorhinostomy. Surgical complications associated with EES for SN-SCC are likely similar to those for other sinonasal malignancies although there are few reports focused on SN-SCC treated by purely EES. Overall, securing cranionasal separation for skull base defects is one of the most important procedures to prevent postoperative complications such as CSF leakage and meningitis [24].

8. Conclusion

The indications for EES for SN-SCC, as in other SN cancers, have been widening due to advances in diagnostic imaging systems, high definition endoscopy, surgical navigation, instrumentation, and endoscopic surgical techniques. In addition, the development of highly conformal radiotherapy and more effective antineoplastic drugs might also change the indications for EES for SN-SCC. However, outcomes have to be confirmed when expanding the indications for EES for SN-SCC, which is aggressive in nature and should always be compared to the gold standard of open craniofacial resection. In addition, greater collaboration between centers all over the world is necessary to achieve adequate numbers of patients for study of prognostic factors. And we need to remember that good results for EES for SN-SCC are due not only to the surgery itself but to the development of imaging systems, radiotherapy and antineoplastic drugs. Nevertheless, the indications for EES for SN-SCC will broaden as it is less invasive and provides better cosmetic outcomes than traditional open approaches. To date, the promotion of EES for SN malignancies has been led by rhinologists by the extended application of their technical skills, skills which head and neck surgeons must also acquire leading to the further development of the comprehensive management of SN malignancies including SN-SCC.

Declaration of Competing Interest

We declare that we have no conflicts of interest.

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References

[1] Waitz G, Wigand ME. Results of endoscopic sinus surgery for the treatment of inverted papillomas. Laryngoscope 1992;102:917–22.
[2] Stankiewicz JA, Girgis SJ. Endoscopic surgical treatment of nasal and paranasal sinus inverted papilloma. Otolaryngol Head Neck Surg 1993;109:988–95.
[3] Kamel RH. Transnasal endoscopic medial maxillectomy in inverted papilloma. Laryngoscope 1995;105(8 Pt 1):847–53.
[4] Peng R, Thamboo A, Choby G, Ma Y, Zhou B, Hwang PH. Outcomes of sinonasal inverted papilloma resection by surgical approach: an updated systematic review and meta-analysis. Int Forum Allergy Rhinol 2019;9:573–81.
[5] Meccariello G, Deganello A, Choussy O, Gallo O, Vitali D, De Raucourt D, et al. Endoscopic nasal versus open approach for the management of sinonasal adenocarcinoma: a pooled-analysis of 1826 patients. Head Neck 2016;38(Suppl 1):E2267–74.
[6] Fu TS, Monteiro E, Muhanna N, Goldstein DP, de Almeida JR. Comparison of outcomes for open versus endoscopic approaches for olfactory neuroblastoma: a systematic review and individual participant data meta-analysis. Head Neck 2016;38(Suppl 1):E2306–16.
[7] Nicolai P, Battaglia P, Bignami M, Bolzoni Villaret A, Delù G, et al. Endoscopic surgery for tumors of the sinonasal tract and adjacent skull base: a 10 year experience. Am J Rhinol 2008;22:308–16.
[8] Hanna E, DeMonte F, Ibrahim S, Roberts D, Levine N, Kupferman M. Endoscopic resection of sinonasal cancers with and without craniotomy: oncologic results. Arch Otolaryngol Head Neck Surg 2009;135:1219–34.
[9] Higgins TS, Thorp B, Rawlings BA, Han JK. Outcome results of endoscopic vs craniofacial resection of sinonasal malignancies: a systematic review and pooled-data analysis. Int Forum Allergy Rhinol 2011;1:255–61.
[10] Abdelmeguid AS, Raza SM, Su SY, Kupferman M, Roberts D, DeMonte F, et al. Endoscopic resection of sinonasal malignancies. Head Neck 2020;42:645–52.
[11] Harris AT, Tanyi A, Hart RD, Trites J, Rigby MH, Lancaster J, et al. Transoral laser surgery for laryngeal carcinoma: has Steiner achieved a genuine paradigm shift in oncological surgery? Ann R Coll Surg Engl 2018;100:2–5.
[12] Robinson S, Patel N, Wormald PJ. Endoscopic management of benign tumors extending into the infratemporal fossa: a two-surgeon transnasal approach. Laryngoscope 2005;115:1818–22.
[13] Steiner W. Experience in endoscopic laser surgery of malignant tumours of the upper aero-digestive tract. Adv Otorhinolaryngol 1988;39:135–44.
[14] Steiner W. Results of curative laser microsurgery of laryngeal carcinomas. Am J Otolaryngol 1993;14:116–21.
[15] Steiner W, Ambrosch P, Hess CF, Kron M. Organ preservation by transoral laser microsurgery in piriform sinus carcinoma. Otolaryngol Head Neck Surg 2001;124:58–67.
[16] Weiss BG, Ihler F, Anczykowski MZ, Bertlich M, Kitz J, Steiner W, et al. Transoral laser microsurgery for treatment of oropharyngeal cancer in 368 patients. Head Neck 2019;41:3144–58.
[17] Hinni ML, Salassa JR, Grant DG, Pearson BW, Hayden RE, Martin A, et al. Transoral laser microsurgery for advanced laryngeal cancer. Arch Otolaryngol Head Neck Surg 2007;133:1198–204.
[18] Hinni ML, Zarka MA, Hoxworth JM. Margin mapping in transoral surgery for head and neck cancer. Laryngoscope 2013;123:1190–8.
[19] Robbins KT, Bradford CR, Rodrigo JP, Suárez C, de Bree R, Kowalski LP, et al. Removing the taboo on the surgical violation (cut-through) of cancer. JAMA Otolaryngol Head Neck Surg 2016;142:1010–13.
[20] Landsberg R, Cavel O, Segev Y, Khafif A, Fliss DM. Attachment-oriented endoscopic surgical strategy for sinonasal inverted papilloma. Am J Rhinol 2008;22:629–34.
[21] Nakamaru Y, Suzuki M, Kano S, Mizumachi T, Tsushima N, Suzuki T, et al. The role of endoscopic resection for selected patients with sinonasal squamous cell carcinoma. Auris Nasus Larynx 2020 (in press).
[22] Pagella F, Pusateri A, Giourgos G, Tinelli C, Matti E. Evolution in the treatment of sinonasal inverted papilloma: pedicle-oriented endoscopic surgery. Am J Rhinol Allergy 2014;28:75–81.
[23] Castelnuovo P, Battaglia P, Locatelli D, Delù G, Sberze F, Bignami M. Endonasal micro-endoscopic treatment of malignant tumors of the paranasal sinuses and anterior skull base. Oper Tech Otolaryngol 2006;17:152–67.
[24] Harvey RJ, Parmar P, Sacks R, Zanation AM. Endoscopic skull base reconstruction of large dural defects: a systematic review of published evidence. Laryngoscope 2012;122:452–9.
[25] Harvey RJ, Smith JE, Wise SK, Patel SJ, Frankel BM, Schlosser RJ. Intracranial complications before and after endoscopic skull base reconstruction. Am J Rhinol 2008;22:516–21.
[26] Thorp BD, Sreenath SB, Ebert CS, Zanation AM. Endoscopic skull base reconstruction: a review and clinical case series of 152 vascularized flaps used for surgical skull base defects in the setting of intraoperative cerebrospinal fluid leak. Neurosurg Focus 2014;37:E4.
[27] Zanation AM, Carrau RL, Snyderman CH, Germanwala AV, Gardner PA, Prevedello DM, et al. Nasoseptal flap reconstruction of high flow intraoperative cerebral spinal fluid leaks during endoscopic skull base surgery. Am J Rhinol Allergy 2009;23:518–21.
[28] Lund VJ, Wei WI. Endoscopic surgery for malignant sinonasal tumours: an eighteen year experience. Rhinology 2015;53:204–11.
[29] Homma A, Nakamaru Y, Sakashita T, Onimaru R, Terasaka S, Tsuchiya K, et al. Management for squamous cell carcinoma of the nasal cavity and ethmoid sinus: a single institution experience. Auris Nasus Larynx 2015;42:377–81.
[30] Michel J, Fakhry N, Mancini J, Braustein D, Moreddu E, Giovanni A, et al. Sinonasal squamous cell carcinomas: clinical outcomes and predictive factors. Int J Oral Maxillofac Surg 2014;43:1–6.
[31] Sanghvi S, Khan MN, Patel NR, Yeldandi S, Baredes S, Eloy JA. Epidemiology of sinonasal squamous cell carcinoma: a comprehensive analysis of 4994 patients. Laryngoscope 2014;124:76–83.
[32] Lund VJ, Stammberger H, Nicolai P, Castelnuovo P, Beal T, Beham A, et al. European position paper on endoscopic management of tumours of the nose, paranasal sinuses and skull base. Rhinol Suppl 2010;22:1–143.
[33] de Almeida JR, Su SY, Koutourousiou M, Vaz Guimaraes Filho F, Fernandez Miranda JC, Gardner PA, et al. Endonasal endoscopic surgery for squamous cell carcinoma of the sinonasal cavities and skull base: oncologic outcomes based on treatment strategy and tumor etiology. Head Neck 2015;37:1163–9.
[34] Shipchandler TZ, Batra PS, Citardi MJ, Bolger WE, Lanza DC. Outcomes for endoscopic resection of sinonasal squamous cell carcinoma. Laryngoscope 2005;115:1983–7.
[35] Kilic S, Kilic SS, Baredes S, Chan Woo Park R, Mahmoud O, Suh JD, et al. Comparison of endoscopic and open resection of sinonasal squamous cell carcinoma: a propensity score-matched analysis of 652 patients. Int Forum Allergy Rhinol 2018;8:421–34.
[36] Farquhar D, Kim L, Worrall D, Chiu A, Lee JY, Khalili S, et al. Propensity score analysis of endoscopic and open approaches to malignant paranasal and anterior skull base tumor outcomes. Laryngoscope 2016;126:1724–9.
[37] Robin TP, Jones BL, Gordon OM, Phan A, Abbott D, McDermott JD, et al. A comprehensive comparative analysis of treatment modalities for sinonasal malignancies. Cancer 2017;123:3040–9.

[38] Karligkiotis A, Lepera D, Volpi L, Turri-Zanoni M, Battaglia P, Lombardi D, et al. Survival outcomes after endoscopic resection for sinonasal squamous cell carcinoma arising on inverted papilloma. Head Neck 2016;38:1604–14.
[39] Robbins KT, Triantafyllou A, Suárez C, López F, Hunt JL, Strojan P, et al. Surgical margins in head and neck cancer: intra- and postoperative considerations. Auris Nasus Larynx 2019;46:10–17.
[40] Hart ZP, Nishio N, Krishnan G, Lu G, Zhou Q, Fakurnejad S, et al. Endoscopic fluorescence-guided surgery for sinonasal cancer using an antibody-dye conjugate. Laryngoscope 2020;130:2811–17.
[41] Wang EW, Zanation AM, Gardner PA, Schwartz TH, Eloy JA, Adappa ND, et al. ICAR: endoscopic skull-base surgery. Int Forum Allergy Rhinol 2019;9:S145–365.
[42] Nicolai P, Castelnuovo P, Lombardi D, Battaglia P, Bignami M, Pianta L, et al. Role of endoscopic surgery in the management of selected malignant epithelial neoplasms of the naso-ethmoidal complex. Head Neck 2007;29:1075–82.
[43] Lund VJ, Clarke PM, Swift AC, McGarry GW, Kerawala C, Carnell D. Nose and paranasal sinus tumours: United Kingdom national multidisciplinary guidelines. J Laryngol Otol 2016;130:S111–18.