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REVIEW

The Selective Role of Open and Endoscopic Approaches for Sinonasal Malignant Tumours

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ABSTRACT

Endoscopic endonasal surgery has been demonstrated to be effective in the treatment of selected cases of sinonasal cancers. However, in cases of locally advanced neoplasms, as well as recurrences, the most appropriate approach is still debated. The present review aims to summarize the current state of knowledge on the utility of open approaches to resect sinonasal malignant tumours. Published comparative studies and meta-analyses suggest comparable oncological results with lower morbidity for the endoscopic approaches, but selection biases cannot be excluded. After a critical analysis of the available literature, it can be concluded that endoscopic surgery for selected lesions allows for

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oncologically safe resections with decreased morbidity. However, when endoscopic endonasal surgery is contraindicated and definitive chemoradiotherapy is not appropriate, craniofacial and transfacial approaches remain the best therapeutic option.

Keywords: Craniofacial Resection; Endoscopy; Maxillectomy; Paranasal Sinus Cancer; Sinonasal Malignant Tumours; Skull Base

Key Summary Points

Sinonasal malignancies, in general, are rare tumours with poor prognosis, despite advances in surgical techniques, radiotherapy and systemic therapy.

The therapeutic modality used should be tailored individually according to tumour stage, histology, previous treatments and patient conditions as well as the multidisciplinary team preferences.

Surgery is the mainstay of treatment both in management of the primary tumour and recurrences. Currently, whenever possible, endoscopic approaches should be used in order to minimize the surgical morbidity for the patients.

There appears to be no difference in risk of unfavourable outcomes with endoscopic compared to open approaches in appropriately selected patients.

When endoscopic endonasal surgery is contraindicated and conservative chemoradiotherapy is not appropriate, craniofacial and transfacial approaches still represent an option to consider, despite the non-negligible morbidity. Traditional open surgical approaches have become less destructive, with surgeons disguising the incisions.

INTRODUCTION

The sinonasal cavities represent an anatomical region affected by a variety of tumours with clinical, aetiological, pathological, and genetic features distinct from tumours at other sites of the upper aerodigestive tract [1]. Neither smoking nor alcohol nor human papilloma virus (HPV) is definitively associated with sinonasal cancers [2]. As a result of their insidious symptoms in the early stages, patients are frequently diagnosed with locally advanced disease.

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Based on evidence from a number of retrospective studies, it is commonly accepted that a complete surgical resection, when feasible, often combined with adjuvant therapies [radiotherapy (RT) with or without chemotherapy (ChT)], is the mainstay of treatment of sinonasal malignant tumours (SNMT). The therapeutic modality should be tailored according to tumour stage, histology, previous treatments, patient comorbidities as well as the multidisciplinary team preferences [3, 4]. Numerous improvements in modern imaging have made diagnosis and surgical planning more accurate but imaging can also be misleading. Also, contemporary technical advances in surgical tools, including high-resolution endoscopes, powered instrumentation and neuronavigation, facilitate more extensive and safer tumour resections with reduced risk of neurovascular injuries [5]. However, as a result of close proximity to critical neurovascular structures, variable sinonasal anatomy, challenging reconstruction of the skull base and cosmesis surgical challenges still abound [1, 6].

Once multidisciplinary teams have decided on surgical resection, the choice of open versus endoscopic procedure should be based on the extent of the tumour as well as the patient's general condition. Consensus on contraindications to an exclusive endoscopic approach includes extensive brain or orbital invasion, infiltration of the superficial tissues (skin, nasal bones, and subcutaneous tissue), hard or soft palate invasion, extensive involvement of the frontal sinus, extensive erosion of the anterior, inferior, or lateral bony walls of the maxillary sinus, extensive involvement of the lacrimal duct, and significant extension to the infratemporal fossa, masticatory, and parapharyngeal spaces [7]. It should be noted that a hybrid, combined cranioendoscopic approach may be beneficial in improving surgical resection for selected complex lesions as well as multiportal approaches [8].

Though surgery is generally still the workhorse of the therapeutic armamentarium, histology-driven protocols are now recognized as state-of-the-art for management, which has contributed to the reduction in surgical resection as an upfront treatment strategy, particularly in the case of poorly differentiated neoplasms [9]. On the other hand, the growing experience acquired in endonasal endoscopic surgery has led to its widespread use in the surgical treatment of selected SNMT and the concept of tumour "oriented disassembling" has definitively demonstrated its validity in terms of oncological safety with results comparable to those of en bloc resection [10–14]. However, in interpreting published reports, one needs to be cognizant of the fact that there is significant selection bias in selecting a particular surgical approach. Thus, comparison of various surgical approaches with outcomes would be inappropriate. Further, traditional open surgical approaches, such as maxillectomy, with the standard Weber Fergusson incision, have become less deforming, with surgeons modifying the standard incision respecting the nasal subunits or avoiding the incisions altogether by using facial-degloving approaches, when feasible for selected patients and minimizing morbidity with regional or free flap reconstruction [15, 16].

There is no high-level clinical evidence to guide decision-making and only a few studies have compared open versus endoscopic resections using historical records. Published studies have mostly been single-institution, retrospective studies hampered by limited sample sizes [17–20]. Indirect comparisons lead to the possibility of selection bias in establishing the indication for the type of approach. Tumours of small volume which are accessible without involving critical structures are usually selected for endonasal endoscopic surgery. It is plausible that the improved outcomes seen with endoscopic surgery are a result of this selection bias. The study by Fu et al. [21] illustrates the consequences of heterogeneity in the management of SNMT. As a result of imbalance in the numbers of various groups, their cohort was largely biased toward an open approach (greater than 80%). In addition, the histological diversity of SNMT, which implies different tumours with different biological behaviour, makes comparisons tenuous [22–24]. The purpose of this comprehensive literature review is to present the most current evidence on indications and contraindications for traditional open surgery.

This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

SURGICAL TRENDS

The use of endoscopic techniques is rising, and consequently the utility of open techniques has fallen. Husain et al. [25], in 2019, using the National Cancer Database (NCDB), identified trends and outcomes associated with surgical management of SNMT. They reported that from a total of 10,193 patients with SNMT treated between 2010 and 2015, about 71.9% of patients had an open approach (most of them with T3–T4 tumours) and 28.1% had a purely endoscopic procedure (most of them with T1–T2 tumours). This study included patients treated between 2010 and 2015, so the figures may well be different today. Hence, in a more recent meta-analysis carried out by Lu et al. in 2019 [24], the differences between the percentages of use of both approaches are smaller. They included 900 patients in total where endoscopic and open resections were utilized in 399 (44%) and 501 (56%) cases, respectively. In another systematic review and meta-analysis, Jiang et al. [23] found that out of a sample of 1373 patients, 47.6% were operated on endoscopically (mainly early-stage tumours) and 52.4% by an open approach (mainly advanced-stage tumours). These data seem to confirm the trend towards a more frequent use of endoscopic surgery mostly in early-stage tumours. Nonetheless, open craniofacial or transfacial procedures still find indications in cases of advanced-stage disease. Table 1 shows indications and contraindications of surgical approaches according to the anatomical sites involved. These indications may not be accepted by all head and neck surgeons, as personal experience may affect these general recommendations. In addition, the anatomical characteristics of each patient may influence the type of approach indicated.

ENDOSCOPIC APPROACHES

The development of new endoscopic techniques, as well as the availability of specific instrumentation for the management of challenging regions such as the frontal [26], maxillary sinus [27, 28] and infratemporal fossa [29], and the increase in surgical expertise and skills have progressively reduced the need for external approaches to achieve radical SNMT resection, even for locally advanced cancers. The description of endoscopic approaches and their indications is beyond of the scope of this manuscript.

INDICATIONS FOR OPEN APPROACHES

Infiltration of the dura over the orbital roof or infiltration of the brain parenchyma is usually considered a contraindication to the purely endoscopic approach as craniotomy could provide better control of surgical margins [30]. However, limited dural infiltration has been resected using purely endoscopic techniques, but this needs to be undertaken with caution [31]. This paper underlines that invasion of the dura is a more important factor to be considered than limited brain invasion, as achieving free margins in the dura mater is even more challenging and a frequent site of local failure. This exclusive endoscopic approach was associated with limited morbidity, with few minor complications and no major postoperative problems. However, even Mattavelli et al.'s paper recommended an open approach in case of tumour invasion largely exceeding the rectus gyrus, the medial orbital gyrus, or invading into the sagittal sinus [31].

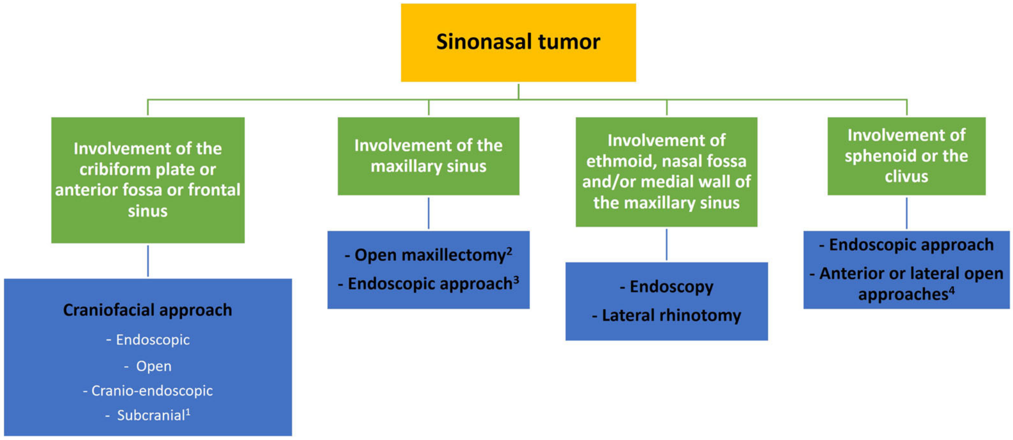
Infiltration of the orbital contents is a poor prognostic factor in terms of local control and survival [32]. Diagnosis can be challenging, and extrinsic compression can be difficult to distinguish from true invasion of orbital contents despite imaging techniques [32, 33]. In a study of 82 patients by Patel et al. [34], the positive predictive value (PPV) of computed tomography (CT) scanning for periorbital involvement from an experienced institution was only 33%, and

Table 1 Indications and contraindications for surgical approaches based on anatomical sites involved

Location	Endoscopic approach	Open approach	Unresectable
Maxillary sinus	Medial maxillary wall and/or orbital floor involvement	Lateral and/or inferior wall involvement Hard and/or soft palate involvement	
Sphenoid sinus	Anterior wall involvement	Planum sphenoidale involvement[a]	Posterior/lateral wall involvement Cavernous sinus involvement Optical chiasm involvement Internal carotid artery involvement
Frontal sinus	Lesions abutting into the sinus Lesions from the lower half of the sinus	Erosion of the anterior or posterior[a] wall Lesions from the upper half of the sinus[a] Extensive involvement of the sinus[a] Skin or subcutaneous tissue involvement Lateral supraorbital attachment in laterally pneumatized sinus[a]	
Nasal bone		Nasal bone involvement	
Orbit	Erosion of the lamina papyracea Invasion of periorbita and/or focal invasion of extraconal periorbital fat	Invasion of the anterior 2/3 orbit Extension beyond mid-plane of orbital roof	Orbital apex involvement
Dura and brain	Limited dural infiltration Olfactory bulb involvement Focal midline brain invasion	Dural infiltration extended laterally over the orbital roofs or posteriorly beyond planum sphenoidale[a] Brain infiltration[a]	Brain infiltration with vascular involvement
Infratemporal and pterygopalatine fossa	Pterygopalatine space involvement Limited infratemporal fossa involvement	Massive infratemporal fossa involvement Parapharyngeal space involvement Masticatory space involvement	Parapharyngeal internal carotid artery involvement
Skin		Facial skin involvement	

[a] A cranioendoscopic approach may be considered

the negative predictive value (NPV) was only 63%. The European Position Paper on Endoscopic Management of Tumours of Nose, Paranasal Sinus and Skull Base [11] noted that while MRI can correctly predict the presence of perineural spread with 95% sensitivity, it can only map the entire extent of spread in around 60% of cases. Orbit management has been discussed by several authors and various classifications have been proposed to establish performance criteria [32, 35–39]. When necessary, surgical removal of the orbital contents can be performed. Orbital exenteration involves removal of the entire contents of the orbit and eyelids whereas the term orbital clearance is used when the eyelids and palpebral conjunctiva are preserved. With respect to orbital invasion, the surgical indications have evolved considerably over time. Initially, invasion of the orbital periosteum was an indication for orbital exenteration. However, since oncological outcomes were similar in cases where the orbit was preserved, indications for orbital exenteration became more limited [37, 40, 41]. Some authors argue that orbital preservation is oncologically safe even in case of periorbital and extraconal fat invasion [42], while others argue that orbital exenteration may improve oncological outcomes of these conditions, considering that postoperative RT does not improve the results of radical surgery while increasing the risk of a post-treatment non-functional eye [43]. Invasion of the extrinsic eye muscles, the orbital apex or the globe seems to be a clear indication for orbital exenteration [39]. However, the lack of precision about the degree of orbital invasion on imaging often does not always allow a consensus for preoperative counselling so frozen sections remain essential for the most accurate intraoperative decision-making process. However, the limitations of intraoperative biopsy must be also considered, as there are contents in the orbit that cannot be sampled without causing damage. Intraoperative assessment of periorbital invasion was only slightly better than imaging, with a PPV of 34% and NPV of 70% [34]. Tumour histology will also influence the decision to undertake orbital exenteration depending on whether the disease is otherwise resectable and patient curable. Castelnuovo et al. [39] have proposed an algorithm which stratifies by grade of orbital invasion, grade of tumour and, in the case of high-grade tumours, the likely response to ChT.



1. A subcranial approach would be performed in case of bilateral frontoethmoidal involvement.
2. In case of orbital involvement, orbital exenteration would be indicated, depending on the degree of involvement. If the infratemporal fossa is affected, an infratemporal maxillectomy should be performed. If the anterior wall of the maxillary sinus is affected, a facial translocation by degloving would be the approach of choice. If the lamina cribrosa or anterior fossa is involved, craniofacial resection would be associated.
3. An endoscopic approach would be indicated in early-staged tumours.
4. The anterior approach of choice would be a facial translocation through degloving. Lateral approaches would be lateral facial translocation and the subtemporal preauricular approach.

Fig. 1 Proposed surgical treatment algorithm according to anatomical location

Induction ChT (mostly combinations of taxanes and platinum) has been considered an option for orbital preservation since the pioneering publication by Hanna et al. [44]. They reported a series of 46 patients with advanced squamous cell carcinoma of the paranasal sinuses that underwent induction ChT followed by surgery and RT or chemoradiotherapy (ChRT) or definitive RT/ChRT. The overall response rate to induction ChT was 67%, and the 2-year overall survival (OS) was 67%. Conservative surgery with orbital preservation was possible in 87% of the patients. These results are superior to some historical series that analysed the combination of surgery and postoperative RT [6, 45, 46].

Finally, although an endoscopic endonasal approach may be a feasible surgical option for the management of selected recurrent SNMT [47], external approaches are the preferred salvage treatment for local recurrences after previous surgery, because local failures often occur in sites no longer manageable with minimally invasive techniques (e.g. orbital content, maxillary sinus floor, critical areas of the skull base). The need to reconstruct with a microvascularised free flap is also an indication for an external approach, especially in case of previous ChRT [15].

Based on all these considerations, a proposed surgical treatment algorithm according to anatomical location is shown in Fig. 1.

SURGICAL STRATEGY ACCORDING TO HISTOLOGY

One of the determining criteria in the election of surgical strategy is the histology of the tumour, given the differential biological behaviour of the diverse SNMT and their different sites of origin. Although not always possible, histological confirmation of the lesion should be carried out prior to selecting a particular therapeutic approach. It is important to properly diagnose newer variants of SNMT that have aggressive biological behaviour with poor prognosis [48].

Squamous cell carcinomas are aggressive tumours usually originating from the nasal fossa or maxillary sinuses [49]. They are aggressive lesions with a tendency to local invasion and perineural spread, so open approaches are usually necessary. Involvement of the sinus walls, infratemporal fossa, masticatory and/or parapharyngeal spaces extension or to the orbit justify the use of open approaches, at least in combination with an initial endonasal delineation of the nasal neoplastic component. Achieving free margins is essential and confirmation of negative histologic margins should be confirmed by frozen section regardless of surgical approach. Endoscopic surgery is still useful in specific cases with limited extension [49–52].

Adenocarcinomas usually originate in the roof of the ethmoid. The mainstay of treatment is surgery with negative margins. In case of poor prognostic features, adjuvant RT may be indicated [53], although the role of RT is much debated. Nicolai et al. [54] could not show benefit for RT after endoscopic surgery whereas Camp et al. [55] did, both looking at reasonable size cohorts with good long-term follow-up. Craniofacial resection (uni- or bilateral) is the standard surgery and can be undertaken by an endoscopic, open, or combined approach [19, 56, 57]. Endoscopic surgical excision has been shown to have comparable oncological results to external approaches with less morbidity [19]. However, external or combined approaches are still indicated on certain occasions. Extensive invasion of the orbit, dura mater, brain, lacrimal system of the nasal bones or soft tissues of the face are still indications for the open approach to be discussed on an individual basis.

Adenoid cystic carcinomas originate in minor salivary glands and are common in the maxillary sinus. Their main characteristic is a tendency for perineural invasion, with frequent extension to the skull base. They are tumours with a poor prognosis despite their slow progression [58]. Both open and endoscopic routes appear to be useful for the treatment of these tumours but endoscopic approach with adjuvant RT offers similar survival with less morbidity to that reported by other studies (including open surgery) [59–62].

Olfactory neuroblastoma or esthesioneuroblastoma develops in the olfactory cleft. Treatment is multimodal, including surgery in combination with postoperative RT [63–67]. For high-grade olfactory neuroblastoma (Hyams 3–4), induction ChT could be considered, followed by ChRT in case of good response [68]. Uni- or bilateral craniofacial resection is the technique of choice. Endoscopic surgery can achieve similar or even better oncological results than open surgery [20, 66, 69]. Endoscopic approaches were also associated with fewer complications than open approaches [21]. Invasion of the maxillary infrastructure and facial structures, the orbital floor lateral to the infraorbital nerve, the intraconal orbital compartment, invasion of the dura mater laterally to the medial plane of the orbit or extensive brain invasion would condition a purely endoscopic approach [70]. An external approach can then be combined to complete such extended resections. Minimal invasion of the frontal lobe does not appear to be a poor prognostic factor for these patients, and endoscopic resection combined with RT could be an effective therapeutic method [71].

Mucosal melanomas are one of the SNMTs with the worst prognosis [72]. They originate most frequently from the lateral nasal wall, followed by the septum and maxillary sinus [72]. Melanomas should be surgically removed whenever possible. RT, or less frequently adjuvant ChT or immunotherapy, may be indicated [73–76]. Endoscopic surgery has been associated with similar oncologic outcomes compared to more invasive surgery [77–79]. Some studies have found better survival and improved local control in patients treated endoscopically compared to those managed by open craniofacial surgery [80, 81], but these results remain controversial and may reflect a selection bias or may be related to the lower morbidity associated with this surgery. Resection with clear margins does not provide a survival benefit in these tumours [75] and, therefore, potentially aggressive procedures such as orbital exenteration, amputation of the nasal pyramid, or maxillectomy should be limited [73]. These indications must therefore be discussed individually, according to the presentation of the tumour and the patient's wishes. Endoscopic procedures, which are associated with less morbidity, can be proposed if they allow complete macroscopic removal [79]. Regardless of surgical approach, these patients remain at high risk for local and distant failure.

Sinonasal undifferentiated (SNUC) and neuroendocrine carcinomas (SNEC) are aggressive malignancies usually diagnosed at a locally advanced stage [82–85]. Surgery alone for resectable well-differentiated SNEC, surgery followed by RT for moderately differentiated tumours, and induction ChT followed by local therapy (surgery or consolidative RT/ChT) for poorly differentiated SNEC may be a reasonable treatment strategy. SNUC are likely best managed by induction ChT with subsequent definitive therapy (surgery versus ChRT) according to initial response. Within the multimodal management necessary for the treatment of these tumours, endoscopic surgery, when deemed feasible, gives good oncological results and with less morbidity [82–86].

Soft tissue sarcomas are rare tumours frequently arising in the maxillary sinus. Tumour resection with wide margins, recommended in other anatomical locations, is frequently not achievable because of the anatomical proximity of the brain and the orbit but it should always be performed when feasible [87]. The recommended wide resection is hardly ever achieved with an endoscopic approach [88].

WHICH OPEN APPROACHES ARE CURRENTLY AVAILABLE?

There are multiple open approaches, and their description is beyond the scope of this review. Nowadays, as a result of the implementation of endoscopic surgery and the technical refinements developed, open approaches can be reduced to two main surgical routes, with some technical variations. The modifications introduced in these approaches are aimed at reducing morbidity and improving cosmesis.

Transfacial Approaches

These surgical procedures expose the bony structure of the midface. They can be used to resect tumours in all sinonasal regions even with a limited extension to the skull base. There are two main types of transfacial surgery: the lateral rhinotomy approach with its variations, and the sublabial approach. They can be combined with a coronal incision for a more extended craniofacial approach or an infratemporal fossa approach. Their indications have significantly decreased in favour of less invasive endoscopic resections.

Lateral rhinotomy [89] primarily provides access to the maxilla, ethmoid, sphenoid, and may also provide access to the frontal sinus and anterior skull base when combined with other incisions. By performing various osteotomies, it is possible to expose the ventral skull base, the infratemporal fossa and to control the internal carotid artery [90]. Lip-splitting incision, which does not seem to be of great advantage, should be avoided whenever possible to avoid cosmetic sequelae.

In the *sublabial approach*, an incision is made at the level of the mucosa of the upper vestibule, directly to the bone, elevating the facial soft tissues and exposing the midfacial bony skeleton. Access is limited, especially to the upper facial territory, but the main advantage is the avoidance of skin incisions. The sublabial approaches are essentially the Rouge-Denker and degloving approaches. In the *Rouge-Denker approach*, the lateral border of the piriform aperture and the lateral nasal wall are resected to gain extended access to the maxillary sinus and ethmoid. The *midfacial degloving approach* [91] allows the anterior aspect of one or both maxillary sinuses to be exposed from one maxillary tuberosity to the other. Through various osteotomies, the ethmoid, sphenoid, and maxillary sinuses can be approached. A disadvantage of this approach is the relatively poor access to the skull base behind the tumour.

Craniofacial Resection

When SNMT extend to the skull base, with or without intracranial invasion, a combined transfacial and coronal approach allows access to the sinonasal part of the tumour and its intracranial component, as well as orbital resection if necessary [92–94]. Craniofacial resection is contraindicated when there is bilateral involvement of the orbital apex, invasion of the optic chiasm, the sella turcica and cavernous sinus or extensive disease in the floor of the anterior fossa or brain, as in these cases the prognosis is extremely poor and non-surgical (palliative) treatment remains the rule rather than the exception [95].

Through a lateral rhinotomy approach, the portion of the tumour involving the nose and paranasal sinuses is resected and the cribriform plate is exposed from below. Subsequently, a frontal craniotomy is performed through a coronal incision, the frontal lobe is retracted, and the floor of the anterior cranial fossa is exposed up to the dorsum of the sella turcica. Transfrontal craniotomy may include resection of the anterior and posterior frontal walls, or a frontal osteoplastic flap may be performed, which decreases the risk of osteomyelitis [90]. To avoid frontal cerebral lobe retraction, a subcranial approach can be used. In this type of approach, the inferior transfrontal osteotomy is performed by including the nasal bones in continuity with the superior orbital rims. This allows access to the base of the skull in the same plane. Although scarring on the face due to the transfacial incision is not prominent, it can be avoided in cases of tumours with moderate intranasal progression by using a midfacial degloving approach instead of lateral rhinotomy or by resection using the intracranial route, through a subfrontal transcranial approach, with or without the aid of an endoscope [10].

After the craniotomy is performed, the frontal lobes are retracted, allowing exposure of the frontal sinus, the floor of the anterior cranial fossa, the roof of both orbits and the sphenoid planum. This manoeuvre allows exposure of the intracranial tumour component and, depending on the degree of dural invasion, dissection is performed extradurally or intradurally, removing the dura mater and, possibly, the invaded brain tissue. The dura must be reconstructed to achieve an airtight seal and avoid cerebrospinal fluid (CSF) leak.

All these different approaches can be extended to other regions depending on the specific tumour extensions. They can be enlarged to involve the orbit and even to allow its exenteration [30], or to complete an anterolateral approach to the skull base [96].

COMPLICATIONS OF OPEN APPROACHES

Open craniofacial surgery is definitively a major head and neck procedure and thus carries potential for considerable postoperative morbidity and mortality. This type of surgery is in fact associated with significant rates of complications [45, 97], ranging between 12% and 47%, with an average mortality of 4% as demonstrated by the systematic review of König et al. [98]. The morbidity associated with open resections and the extent of cranial base defects may also delay adjuvant treatments. These aspects have been receiving growing attention in the last decades and reduced morbidity has been advocated as one of the main advantages of endoscopic resection over external procedures [18]. Meccariello et al. [19] observed that endoscopic and endoscopic-assisted surgery had low rates of major complications (6.6% and 25.9%, respectively) compared to open approaches alone (36.4%; $p < 0.01$). Abdelmeguid et al. [13] reported a complication rate of 29% for endoscopic resections, mainly minor (seroma, sinusitis, etc.) and Lund et al. [99] reported resolvable complications in 11%. However, the different studies directly comparing the complication rates between open and endoscopic approaches did not find any significant difference [20, 100]. Lu et al. [24] observed that, although a reduction in complications has been associated with endoscopic resections, no statistical difference was observed when the comparative studies were pooled overall (with incidences of 18% and 24% in endoscopic and open approaches, respectively). However, it appears evident that endoscopic approach is associated with a significantly shorter hospital stay than open surgery, with average lengths of stay of 3–6 days vs. 6–12 days for open surgery [20, 21, 48, 99–101]. This reduction in hospital stay should be associated with a reduction in costs, but this has yet to be shown with statistical significance, particularly when considering the high costs of state-of-the-art technologies routinely needed for modern endoscopic approaches [13, 102]. The endoscopic approach was also associated with a better postoperative quality of life compared to patients operated on with traditional open techniques [103–106].

In a pivotal study, among 1193 patients who underwent a craniofacial resection, Ganly et al. [45] reported a postoperative mortality rate of 5% and a morbidity rate of 36.3%. The main complications were postoperative CSF leak, pneumocephalus, intracranial infectious and haemorrhagic complications, and frontal lobe syndrome due to frontal lobe retraction. Further ophthalmological complications were observed. Osteoradionecrosis of the frontal flap has also been described after RT. Main factors associated with the development of complications were the presence of medical comorbidities, previous RT, dural and/or brain tumour invasion. It is important to note that the complication rate in open surgery may also increase if free flap reconstruction is required [15]. These data highlight that expanding the surgical field can increase the chances to obtain radical removal of tumours not amenable to endoscopic endonasal resection, but this comes at a cost of increased risk of mortality and morbidity, which should always be discussed preoperatively with the patient, and balanced considering his/her performance status, comorbidities, and expected residual quality of life.

Some authors highlight the specific incidence of CSF leak in the endoscopic vs. open approach [20, 21]. While this represented an issue a few years ago, there have been important technical advances in the reconstruction of skull base defects and, as a consequence, postoperative CSF leak rates have significantly dropped [107]. The use of multilayer techniques with pedicled mucosal flaps and “minimally invasive” pericranial flaps [108] to close the endoscopic dural defects has greatly contributed to the observed decreases of the CSF leak rate, which now come close to those observed after open approaches [109, 110]. This underlines that the ability to perform an adequate reconstruction of the skull base is critical in the indication for endoscopic resection.

COMPARING OUTCOMES OF OPEN AND ENDOSCOPIC APPROACHES REVISITED

The current data are insufficient to draw robust conclusions regarding any potential differences in OS between various resection approaches for SNMT. However, the available evidence suggests at least equivalent survival outcomes between open and endoscopic approaches for patients with similar early-stage tumours. Five-year OS and disease-specific survival (DSS) rates from the largest series reporting on craniofacial resection, which analysed a total of 1307 patients in 2003, were 53.6% and 59.9% for open and endoscopic approaches, respectively [111]. A recent review of patients treated by open craniofacial or transfacial surgery shows similar outcomes, reporting 5-year OS ranging from 46% to 72% (median 54%) and 5-year DSS rates from 46% to 78% (median 60%). These same authors carried out a meta-analysis in which they analysed 2603 patients and the results confirmed a trend with the 5-year OS rate ranging from 46% to 72% (median 54%) and the 5-year DSS rates ranged from 46% to 78% (median 60%) [98]. All these data corroborate the appropriateness of the modern open approaches, but also emphasize that there is still space for improvement of outcomes, considering that only small advancements in survival rates have been observed in the last decades when considering advanced-stage SNMT. These results are in accordance with those observed in meta-analyses of endoscopic approaches. Rawal et al. [112], for example, demonstrated that optimal survival outcomes could also be achieved with an endoscopic approach. A 5-year OS rate of 72.3% was observed, which is comparable and even greater than that from open craniofacial resections. However, one must bear in mind that these are selected patients suitable for endoscopic resection with limited extent or early-stage disease.

Some authors have conducted studies comparing open and endoscopic approaches [19, 22, 24, 48, 101, 113–115]. Higgins et al. [22] conducted a systematic review with a pooled-data analysis to compare outcomes of endoscopic vs. craniofacial resection of SNMT. The 5-year OS was 87.4% (SE ± 5.3) in the endoscopic group vs. 76.8% (SE ± 8.3) for open approaches ($p = 0.351$); DSS was 94.7% (SE ± 3.7) vs. 87.7% (SE ± 6.7; $p = 0.258$); and locoregional control rate was 89.5% (SE ± 5.0) vs. 77.2% (SE ± 10.4; $p = 0.251$). One of the weaknesses of this study is that the number of papers involving endoscopic resection of high-grade tumours remains only moderate. Therefore, the authors concluded that although endoscopic resection is a reasonable alternative to open approaches in the management of early-stage SNMT, open surgery remains an alternative to achieve complete resection in high-grade tumours. Lu et al. [24] conducted a meta-analysis based on comparative studies only to critically evaluate endoscopic vs. open approaches, and to identify and compare clinical outcomes between both approaches in the treatment of SNMT. The results showed that, with respect to various surgical outcomes and recurrence rate, the current literature does not indicate either endoscopic or open approaches as statistically superior. Therefore, until a more sound validation of these associations can be proven, according to these authors, expectations that endoscopic resection for SNMT confers superior surgical outcomes compared to open approaches should be tempered. Meccariello et al. [19] performed a pooled analysis of 1826 patients comparing endoscopic vs. open approach for the management of sinonasal adenocarcinoma. They observed that the incidence of local failure was lower in the endoscopic surgery group as compared with open approach patients (17.8% vs. 38.5%; $p < 0.01$, respectively). However, worse survival was observed in advanced stage tumours with an open approach, which likely represents a selection bias in favour of endoscopic approaches. To control the possible influence of confounding factors, Farquhar et al. [101] utilized a propensity score matching approach to account for disease stage, locoregional spread, and presenting comorbidities, and found that OS outcomes were comparable between both approaches. This highlighted the high likelihood that variations in the reported OS were confounded by those parameters Farquhar et al. accounted for, confirming the decision not to pool the OS data in the case studies. Povolotskiy et al.'s study [115], which included 1595 patients with non-squamous sinonasal carcinomas, found an OS of 65.2% in patients treated by endoscopic surgery and 65.4% in those treated via an external route ($p = 0.59$). Finally, Kılıç et al. [49] using the National Cancer Database analysed all cases of sinonasal squamous cell carcinoma included, dividing them according to the surgical approach adopted: open or endoscopic. A total of 1483 patients were identified, of which 23.8% received an endoscopic and 76.2% an open surgical procedure. The authors found that open surgery was more common in academic centres (62.8% vs. 54.2%; $p = 0.004$), less common for tumours of the ethmoid and sphenoid sinus ($p < 0.0001$), less common for stage IVB tumours, and associated with longer hospital stay (mean 4.67 days vs. 2.50 days; $p < 0.0001$). Five-year OS was not significantly different between the two approaches ($p = 0.953$; open: 5-year OS, 56.5%; 95% confidence interval, 51.3–61.6%; endoscopic: 5-year OS, 46.0%; 95% confidence interval, 33.2–58.8%). Endoscopic surgery appears to be an effective alternative to open surgery, even after taking into account confounding factors that may favour its use. However, the aforementioned meta-analyses cannot exclude important selection biases, such as endoscopic surgery being more frequently chosen for smaller tumours, tumours with different histologies being compared with each other, etc. In addition, as this is highly specialised surgery, pooling and comparing results from surgical teams with different expertise may not be appropriate.

Although almost all survival analysis confirmed the role of pT classification, surgical margins status, dural invasion and orbital apex infiltration as the most important prognostic factors, histological grade also plays an important role. Significant OS difference is found between low- and high-grade cancers [112], and in these high-grade tumours more extensive approaches could be necessary, taking into account the potential morbidity caused by the surgery. However, some studies [49, 116] have observed no differences between the outcomes of open or endoscopic resections in patients with a high-grade tumour.

It is universally accepted that a free-margins resection should be achievable in patients considered suitable for surgery to reduce the risk of recurrence rates and maximize oncologic outcomes. Achieving negative surgical margins seems to be the most important prognostic factor regarding survival, regardless of surgical techniques [98]. However, resection of SNMT with wide margins is not always possible because of the adjacent cranial nerves, orbit, internal carotid artery, or brain. Thus, attempts to remove a tumour with wider surgical margins could cause unacceptable morbidity and would be technically difficult, if not impossible, either by open or endoscopic techniques. Moreover, no evidence suggests that a mutilating approach would substantially increase survival. Radical resection correlates with improved prognosis both for tumours resected through an endoscopic or open approach [17, 98, 111]. Some authors have compared the rate of positive margins between tumours operated by open and those operated by endoscopic surgery, and most have found no difference between these techniques [20, 101, 117]. Endoscopic approaches allow complete resection of tumours in most cases and avoid an excessive resection of healthy tissue. However, some authors criticise piecemeal tumour removal and argue that a significantly higher proportion of gross total resection with negative microscopic margins is obtained when resection is performed in a truly en bloc fashion, as opposed to piecemeal technique [98]. Although piecemeal resection adheres to oncological principles [14], it requires close collaboration with pathologists to ensure accurate analysis of the histological margins [118]. An en bloc unfragmented resection through an open approach in high-grade tumours and in complex locations has the potential to achieve a higher rate of free margins [98], so, in certain cases, open approaches continue to play an important role in skull base surgery. However, it should be acknowledged that removing an en bloc specimen may not always be possible. In conclusion, achieving negative surgical margins is significantly more important than the way a tumour is removed (en bloc vs. piecemeal resection), and it should be the surgical goal regardless of the technique chosen, whenever possible.

Dural and intracranial extension have been recognized as the most adverse prognostic factors in malignant SNMT [119, 120]. Although dural and intracranial resections are possible through an endoscopic approach, open routes allow, in certain cases, safer removal and better control of possible intraoperative complications. Orbital invasion results in a high-risk negative prognostic factor for almost all the survival endpoints, with decreased 5-year OS from 65–55% to 20–30% [107]. In particular, orbital apex infiltration significantly worsens outcomes because a free-margin resection is virtually impossible, regardless of the type of surgery performed [14].

Local recurrence often occurs within 2 years of follow-up and is the main contributor to SNMT mortality, followed by distant failure [111, 121]. Patel et al. [111] reported 3- and 5-year recurrence-free survival (RFS) rates of 50.4% and 45.8%, with a median time to recurrence of 7 months, using open surgery. Recurrence was not significantly different between endoscopic and open approaches with incidences of 42% ($n = 399$) and 50% ($n = 501$), respectively, according to Lu et al. [22]. Dural infiltration and pT classification are factors associated with increased risk of recurrence and systemic dissemination of disease [119]. This was also the case with histological classification, as poorly differentiated tumours or melanomas are more prone to develop distant metastasis [79, 122, 123].

CONCLUSIONS

To provide the best possible care, patients with SNMT should be treated at specialised referral clinical centres for skull base pathology; such centres should include a multidisciplinary team including the key professional figures of otorhinolaryngologists, maxillofacial surgeons, neurosurgeons, plastic and reconstructive surgeons, neuroradiologists, radiation and medical oncologists as well as specialised histopathologists, radiologists, cancer nurses, and prosthodontists. Decision-making is often quite complex and based on multiple factors such as tumour location, extent and stage of disease, histology, orbit and skull base involvement, as well as institutional practice and multidisciplinary board preference.

Progress in multimodal treatment strategies as well as refinements in endoscopic techniques have progressively reduced the role of craniofacial and transfacial resections during the last decades; the latter are still associated with significant rates of perioperative morbidity and significant impact on postoperative quality of life. Moreover, there appears to be no difference in risk of unfavourable outcomes with endoscopic compared to open approaches in appropriately selected patients.

Nevertheless, there is still a role for open surgery which remains an important part of the surgical arsenal of the head and neck surgeon to increase the chances of obtaining radical resection in advanced stage diseases not amenable to exclusive endoscopic approach. Maintaining training and expertise in these techniques may prove an issue in the future.

Open approaches could be also used to treat selected cases of local recurrences involving areas not amenable to salvage endoscopic surgical resection, which are nowadays increasingly observed in view of the growing population of survivors following multidisciplinary treatment strategies.

In conclusion, selected surgical approaches for SNMT are patient- and surgeon-dependent, which argues that both approaches continue to have a place in the management of SNMT.

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