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Endoscopic Resection of Sinonasal Malignancies

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Abstract Malignant tumors of the sinonasal tract are rare, accounting for only 1% of all malignancies. Although they are associated with substantial histological heterogeneity, surgery plays a key role in their management. This review addresses the evolution of current treatments in view of the introduction of endoscopic resection techniques. The absence of facial incisions and osteotomies, decreased hospitalization time, better control of bleeding, improved visualization of tumor borders, and reduced morbidity and mortality rate are the major advantages of endoscopic techniques in comparison to traditional external approaches. The major criticisms focus on oncologic results in view of the short/intermediate follow-up of large series, which have commonly grouped together several histologies that may be associated with different prognoses. Since prospective studies contrasting the results of endoscopic and craniofacial resections are difficult to carry out given the rarity of the disease together with ethical issues, the creation of a large database would favor the analysis of several variables related to the patient, tumor, and treatment on survival performed on a large number of patients.

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Introduction

Sinonasal malignancies are rare, accounting for only 3% to 5% of all head and neck malignant tumors [1, 2]. They are characterized by a significant histological diversity, nonspecific symptoms in the early growth phase frequently mimicking those of rhinosinusitis, and a variable prognosis in relation to histology, site of origin (maxillary sinus, naso-ethmoidal complex and more rarely sphenoid and frontal sinus), and stage. A major advance in the management of sinonasal malignancies was the introduction in the 1960s by Ketcham et al. [3] of craniofacial resection, a combined approach performed by a surgical team including otolaryngologists and neurosurgeons. By including the anterior skull base in the surgical specimen, this intervention has dramatically improved local control of tumors encroaching upon the roof of the ethmoid. However, this approach has been associated with a morbidity and perioperative mortality that is not negligible.

Transnasal endoscopic surgery has revolutionized the treatment of inflammatory diseases and benign tumors of the sinonasal tract. The natural evolution in progressively expanding the indications of endoscopic surgery has been its application to selected cases of malignant tumors. The first reports on its use as a stand-alone procedure or in combination with frontal craniotomy (cranio-endoscopic resection) emerged in the late 1990s [4, 5]. In subsequent years, the publication of several series analyzing small or intermediate cohorts of patients [6–18] enhanced the interest of otolaryngologists towards less invasive methods of treatment. However, this enthusiasm was challenged by the criticism of those who believed that endoscopic surgery, as it did not achieve an en bloc resection, did not adhere to the principles of oncologic surgery. Over the past decade, data from several centers worldwide have demonstrated that endoscopic resection of malignant sinonasal tumors can be extended to include the anterior skull base with acceptable morbidity and outcomes suggesting that this technique can be included among the surgical options available for the management of sinonasal malignant tumors.

In the present review, the criteria and reasons guiding the evolution of the indications for endoscopic surgery will be addressed. Outcome measures in terms of survival and morbidity, pros and cons of the technique, and pending problems are also discussed.

Evolution of Indications

The challenge of approaching malignant tumors of the sinonasal tract with a transnasal endoscopic technique was made feasible not only by the growing expertise of surgeons in this field but also by advances in cross-sectional imaging, which have increased the accuracy of pre-operative diagnosis, together with extraordinary technological developments [19••], which led to the introduction of specialized operating theaters, navigation systems, intraoperative imaging, small ultrasound Doppler probes for major vessel identification, effective hemostatic agents, and specifically designed surgical instruments.

The first experiences were limited to lesions involving the naso-ethmoidal box, but not encroaching upon the anterior skull base. At that time, extension in the frontal sinus, involvement of the lacrimal pathway or of the bony walls of the maxillary sinus (with the exception of the medial one), erosion of the nasal fossa floor, extension into the pterygopalatine or infratemporal fossa, involvement of the orbit, and erosion of the skull base were all considered contraindications for an endoscopic approach [20]. On the other hand, simple contact of the tumor with “high risk” areas, such as the lamina papyracea, the cribriform plate, or the roof of the ethmoid, without radiologic signs of bone erosion and knowledge of the volume of the lesion were not considered contraindications [20].

The subsequent step in the expansion of the indications for endoscopic surgery included the resection of the anterior skull base with the adjacent dura, which can be limited to one side but can also be extended from the frontal sinus to the planum sphenoidale and to both lamina papyracea. This was made possible by the extensive experience acquired in cerebrospinal fluid (CSF) leak repair.

Surgical Technique

Only a few reports on endoscopic surgery for malignancies of the sinonasal tract have specifically focused on surgical technique in relation to the distinct needs of a transnasal approach [21, 22•, 23]. As a general concept, it should be emphasized that the target is radical removal of the lesion with negative margins, as in traditional procedures [19••]. This is rarely achieved through an “en bloc” resection, but more through a progressive disassembling of the lesion, having clearly under view the limits between normal and diseased mucosa.

The intervention typically starts with tumor debulking, which is performed by powered instrumentation or cutting instruments with the intent to define the possible site of origin of the lesion and its relationship with the anterior skull base. These findings, coupled with information coming from preoperative imaging studies can lead to the decision to include or not the anterior skull base and the adjacent dura in the resection and to perform a unilateral or bilateral dissection. On occasion and unexpected to the surgeon a large lesion entirely occupying the nasal fossa may have a small pedicled insertion on an area distant from the skull base without involvement of the adjacent mucosa. The next step includes subperichondral/subperiosteal dissection of the mucosa investing the naso-ethmoidal complex, starting medially along the septum at the level of the insertion of the middle turbinate and laterally along the maxillary line and proceeding posteriorly along the lamina papyracea until the sphenoid sinus is reached. The sphenopalatine artery is identified and coagulated. The dissection is superiorly carried at the level of the fovea ethmoidalis and cribriform plate by cutting the olfactory phyla. Posterior sectioning of the mucosa along the anterior wall of the sphenoid sinus allows release of a mucosal finger glove that incorporates (or includes) the tumor. When the surgical plan includes resection of the entire naso-ethmoidal box, the same step is performed on the contralateral side and the septum is included in the specimen.

In case of tumors abuting or invading the anterior skull base, resection is extended to include as a subsequent layer the dura and the olfactory bulb, unilaterally or bilaterally according to the tumor extent. In the most extensive bilateral resection, the dura is exposed by performing two longitudinal osteotomies with a drill at the junction between the ethmoid roof and lamina papyracea on both sides. These osteotomies are then connected by two transversal osteotomies at the level of planum sphenoidale and at the junction of the posterior wall of the frontal sinus with the ethmoid roof. A rectangular area of dura matching the osteotomies and far enough from tumor borders is resected together with the olfactory bulbs. Frozen sections are obtained from the residual dura and olfactory tracts to assess the completeness of resection [21].

At this point the surgeon is faced with a large defect in the anterior skull base (Fig. 1), which needs to be repaired in order to separate the endocranium from the sinonasal cavities. Although not all authors have described this specific step of the surgical procedure in detail, different materials and techniques have been used in the effort to obtain a water-tight closure of the dural space and minimize postoperative complications. During the early phase of their experience, the Pittsburgh team [21] used a subdural inlay graft of collagen matrix that helped to obliterate the dead space with the recommendation that the graft should extend beyond the dural margins, ideally by 5 to 10 mm. A subsequent inlay graft of acellular dermis was placed in the epidural space or, alternatively, at the nasal side of the defect. This graft was supported by a free abdominal fat graft harvested through a periumbilical incision. After placing Gelfoam against the fat to prevent its accidental dislodgment, the balloon of a 12-F Foley catheter was placed in the nasal cavity to stabilize the plasty and prevent early brain herniation. A rate of CSF leak as high as 30% prompted the group to modify the technique by using a pedicled nasoseptal flap based on the posterior nasoseptal artery [24] as a last layer. The authors considered the introduction of this flap as a major breakthrough for repair of cranial base defects, since it was associated with a significant decrease of postoperative CSF leak at a rate lower than 5% [25]. More recently, other pedicled flaps such as transfrontal pericranial flap [26], transpterygoid temporoparietal fascia flap [27], inferior turbinate flap [28], middle turbinate flap [29], palatal flap [30], and buccinator myo/myomucosal flap [31] have been added to the surgical armamentarium. However, some of these flaps are not viable in sinonasal malignancies either for oncologic reasons or for the sequelae of a previous surgery. Based on the experience in 62 patients, Bolzoni Villaret et al. [32•] advocated the use of a three-layer duraplasty, employing the ilio-tibial tract, which has ideal characteristics in terms of thickness, pliability, and strength. The first intradural layer was oversized 30% larger than the dural defect and split anteriorly on the midline to adjust to the falx cerebri in case of bilateral resection. The second layer, intracranial and extradural, needed to be precisely sized and tacked between the previously undermined dura and the residual anterior skull base. The third extracranial layer had to cover the entire exposed anterior skull base paying particular attention not to interfere with frontal sinus drainage.

Outcome

An extensive review of the pertinent literature on outcomes was the focus of a recent article titled “European Position Paper on Endoscopic Management of Tumours of the Nose, Paranasal Sinuses, and Skull Base” [33]. The major criticisms on the available data concern the short follow-up time, the limited number of patients, and the fact that most series grouped together different histologies. In fact, only a few reports have analyzed data on the outcome in specific histotypes such as adenocarcinoma [34, 35] or olfactory neuroblastoma [36–38], while only two papers collected large cohorts of patients [22•, 39•]. Furthermore, comparison between the results obtained with endoscopic surgery and craniofacial resection, which has been considered for many decades the gold standard in management of malignant tumors abuting the anterior skull base, is hindered by the heterogeneous composition of patient series in terms of histology, stage, and follow-up time.

The two largest series, reporting on 184 [22•] and 120 [39•] patients, were almost concomitantly published (Table 1). The first collected the 10-year experience of two tertiary care Italian centers, while the second summarized the oncologic

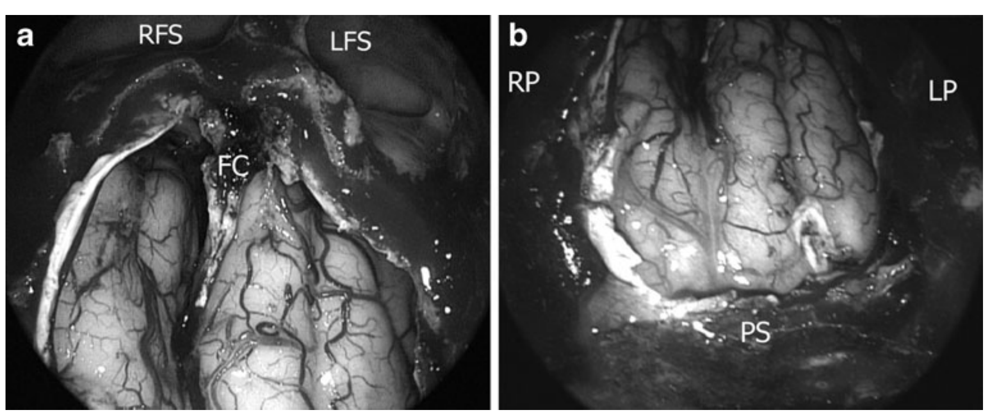

Fig. 1 Intraoperative view with a 45°-angled telescope after endoscopic resection with transnasal craniectomy: a wide defect at the anterior skull base is visible, from frontal sinuses (**a**) to planum sphenoidale (**b**) and latero-laterally from papyracea to papyracea. FC, falx cerebri; LFS, left frontal sinus; LP, left papyracea; PS, planum sphenoidale; RFS, right frontal sinus; RP, right papyracea

Table 1 Summary of 2 major series of patients treated by endoscopic surgery for sinonasal malignancies

	Nicolai et al. [22•]	Hanna et al. [39•]
Cases, *n*	184	120
Type of surgery, *n*		
EER	134	93
CER	50	27
Histology,%		
Adenocarcinoma	37	14
Squamous cell carcinoma	14	13
Olfactory neuroblastoma	12	17
Melanoma	9	14
Sarcoma	5	15
Others	23	27
Complication rate,%	8.7	11
Mean follow-up, *months*	34	37
Recurrence rate,%	23.6	25.8
5-year DSS,%	82	87

CER cranioendoscopic resection; *DSS* disease-specific survival; *EER* exclusive endoscopic resection

results on a cohort of patients treated at the M.D. Anderson Cancer Center in Houston over a 16-year period. Both series included patients where endoscopic surgery was used either alone (72.8% vs 77.5%) or in combination with frontal or subfrontal craniotomy (27.2% vs 22.5%). The distribution of patients in relation to histology reflected the variable prevalence of histologies found in various geographical areas. In the Italian series, adenocarcinoma was the most frequent lesion (37%), while olfactory neuroblastoma was prevalent (17%) in the US experience. With no major differences in the mean follow-up time (34.1 vs 37 months), the 5-year disease-specific survival in the two series for the entire patient cohort was also quite similar: 81.9% vs 87%. Interestingly, Nicolai et al. found a statistically significant difference in 5-year disease-specific survival between patients treated with endoscopic surgery alone compared to those who received cranioendoscopic resection (91.4% vs 58.8%; $P<0.001$), although this observation was not confirmed by Hanna et al. As pointed out by these authors, this variability can reflect different criteria used for patient selection for the different approaches, with the US group being more inclined to reserve an endoscopic approach for patients with relatively earlier disease stage and no or limited skull base invasion. Nicolai et al. performed an analysis of 5-year disease-specific survival by stratifying patients in four groups with comparable biological aggressiveness (epithelial and nonepithelial such as adenocarcinoma, squamous cell carcinoma, and adenoid cystic carcinoma; olfactory neuroblastoma; melanoma; miscellaneous) and found values of 78.6%, 100%, 0%, and 92.4%, respectively. In the group of patients treated with an exclusively endoscopic approach, those with adenocarcinoma had an excellent outcome, with a 5-year disease-specific survival of 94.4%.

Most publications analyzing the efficacy of endoscopic surgery in a specific histology have concentrated on olfactory neuroblastoma. The well-known propensity of this lesion to be associated with late recurrences and therefore with a need for long-term follow-up contributed to mitigate the enthusiasm toward the excellent results achieved by endoscopic surgery, which is commonly used in combination with postoperative radiotherapy. Folbe et al. [38] recently reported the results of a multicenter study performed at two US centers on 23 patients (10.5% were modified Kadish stage A, 58.9% stage B, 26.3% stage C, and 5.3% stage D). All but one patient, who required the association with a transcranial approach to clear a positive margin along the supraorbital dura, had the tumor resected endoscopically. Postoperative radiotherapy was delivered in 16 patients. After a mean follow-up time of 45.2 months, all patients were free of disease at the primary site.

The outcome of endoscopic surgery followed by radiotherapy in adenocarcinoma has been reported by Bogaerts et al. [34] in a series of 44 patients, including one T1, 26 T2, 5 T3, 9 T4a for sphenoid sinus involvement, and 3 T4b for limited dural involvement. Median follow-up, as well as follow-up of patients alive at the end of follow-up, was 36 months. Of note, if the tumor was unilateral no contralateral dissection was undertaken and the resection was rarely extended to include the dural plane. Twelve (27%) patients experienced local recurrence, which was diagnosed within 24 months of primary treatment in 8 cases. Retreatment included a second endoscopic procedure in 9 and craniofacial resection in 3 patients. The 5-year disease-specific survival was 83%, and was not influenced by the occurrence of local recurrence or T stage. In view of the observation of local recurrences in areas that were quite different from the initial presentation, the authors considered the opportunity to include the entire ethmoid labyrinth in the resection. This would be justified by the fact that the exposure to wood dusts which is almost invariably associated with adenocarcinoma renders the mucosa of the naso-ethmoidal complex vulnerable to developing adenocarcinoma foci. Another experience on a small number ($n=12$) of patients with adenocarcinoma (6 T2, 5 T3, and 1 T4) was associated with a 91.6% 5-year disease-free survival after a median follow-up of 30 months [35].

Since a prospective study comparing the results of endoscopic surgery and craniofacial resection is unfeasible due to the rarity of sinonasal tumors as well as for ethical reasons, some authors have attempted to retrospectively compare the two techniques. Eloy et al. [40] analyzed two groups of patients treated at the same institution with either transnasal endoscopic ($n=18$) or craniofacial resection ($n=48$)

for tumors involving the anterior skull base. A statistically significant difference in terms of median hospital stay (3.5 vs 7.0 days) and median operative time (261.5 vs 625.5 min) in favor of endoscopic resections was observed, while the prevalence of perioperative complications was highly similar in the two groups (27.8 vs 25.0%). Since there was no statistically significant difference in overall survival between the two groups, the authors concluded that early and intermediate stage anterior skull base malignancies can be safely and successfully treated with transnasal endoscopic resection. However, there was a quite striking difference in the distribution of tumor local extent and histology, with olfactory neuroblastoma and squamous cell carcinoma being the most frequent histotype in the endoscopic and craniofacial resection group, respectively. Devaiah and Andreoli [41] performed a meta-analysis on 379 patients treated for olfactory neuroblastoma. Although endoscopic surgery yielded statistically significant better survival rates than open surgery, the results must be interpreted with caution based on the differences in follow-up times and Kadish stage distribution between the two groups.

Morbidity and Quality-of-Life Assessment

The absence of facial incisions and osteotomies, decreased hospitalization time, better control of bleeding, improved visualization of tumor borders, and reduced morbidity and mortality rate are commonly cited as the major advantages of endoscopic surgery compared with craniofacial resection. Furthermore, when resection of the skull base is performed transnasally, retraction on the frontal lobes with the ensuing possible complications is avoided. On the other hand, resection of the dura and the consequent need for duraplasty increases the likelihood of CSF leak.

The overall complication rate in the two largest series [22•, 39•], both including patients treated by endoscopic surgery alone or cranioendoscopic resection, was 8.7% and 11%, respectively. Two cases of fatalities in patients with T4b lesions and extensive dural infiltration treated by cranioendoscopic resection occurred in the Italian series, while no deaths were reported in the M.D. Anderson experience. Not unexpectedly, the most frequent major complication in both series was CSF leak with a prevalence of 4.3% [22•] and 3% [39•], respectively. A recent analysis performed by the Italian group on a subset of 62 patients who underwent endoscopic removal of tumor with dural resection showed that the occurrence of CSF leak is clearly related to the learning curve of the surgical team and to the refinement of surgical technique [32•].

Quality of life has been extensively evaluated in patients treated for head and neck cancer, while only a few reports have addressed this issue in patients undergoing endonasal skull base surgery [42, 43]. Although these studies mostly included patients with benign lesions and tumors originating from sites other than the sinonasal tract, the results can be to some extent extrapolated to patients treated for sinonasal malignancies. In one study [42] the evaluation was performed through a sinonasal outcome test (SNOT-22 questionnaire), which provides a symptom score for parameters relating to sinonasal function, and a multidimensional disease-specific questionnaire for anterior skull base neoplasms developed by Gil et al. [44]. The results appear to indicate that there may be a greater disruption of normal sinonasal anatomy and function related to the extensive mucosal denuding which may be higher compared to standard external approaches. However, this morbidity appears to be temporary and symptoms such as nasal crusting and discharge improve within 6 months postoperatively. These conclusions are also supported by the results of a recent prospective study [43], which examined the impact of several variables on nasal crusting and discharge. The authors found that only the latter symptom was influenced by “surgical complexity,” a parameter expressing the extent of the dissection performed.

Open Issues

In general, it can be considered that there are sufficient data in the recent literature supporting the concept that endoscopic surgery can have a reasonable place in the surgical armamentarium for management of sinonasal malignancies. Nonetheless, there are still some controversial points in view of the rarity of these lesions and further clarifications can only be obtained by creating a larger cohort of cases [33]. Longer follow-ups are needed in order to have meaningful information on the outcome of those tumors that can relapse well beyond the usual 5-year period. Stratification of survival data by histology and stage is required to have a better understanding of the impact that these variables have on outcome. The role of adjuvant therapies (radiotherapy, chemotherapy, biological modifiers) also needs to be explored with the intent to identify patients that can benefit from these therapies, thus avoiding an overtreatment in those with a less aggressive disease. Tailoring treatment can be aided by expanding the study of specific biological markers. Prospective quality-of-life evaluation should also be included in the pre and post-treatment assessment of patients.

Conclusions

Treatment of sinonasal malignancies has significantly evolved during the last decades and requires the contribution of a multidisciplinary team. Surgery, which plays a pivotal role in the management of the majority of patients, consists of a large spectrum of different techniques ranging from historical external approaches to modern endoscopic procedures. The surgical team, which for tumors involving the anterior skull base necessarily includes both otolaryngologists and neurosurgeons, should be experienced in all these techniques in order to be able, when required by intraoperative findings, to modify the surgical plan. To optimize outcomes, endoscopic resections should be performed only by surgeons with longstanding experience in the management of inflammatory diseases, benign tumors, and CSF leak repair together with a thorough knowledge of surgical oncologic principles.

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•• Of major importance

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