# Endoscopic Endonasal Surgery for Malignancies of the Anterior Cranial Base

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**Key words**
- Cranio-endoscopic approach
- Craniofacial resection
- Endoscopic endonasal approach
- Sinonasal cancers
- Skull base reconstruction
- Skull base surgery

**Abbreviations and Acronyms**
**ASB**: Anterior skull base
**CER**: Cranio-endoscopic resection
**CSF**: Cerebrospinal fluid
**ER**: Endonasal resection
**MRI**: Magnetic resonance imaging

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■ OBJECTIVE: **Data from several centers worldwide have demonstrated that transnasal endoscopic surgery performed with or without a transcranial approach is capable of achieving radical resection of selected sinonasal malignancies. We report our experience with endoscopic management of sinonasal cancers, with emphasis on naso-ethmoidal malignancies encroaching on the anterior skull base.**

■ METHODS: **Major series reporting results concerning the endoscopic endonasal approach with or without craniectomy for treatment of sinonasal and anterior skull base cancers were reviewed. Preoperative work-up, indications and exclusion criteria, surgical techniques, postoperative management, and adjuvant therapy are reported.**

■ RESULTS: **In the 2 largest series analyzed, the most common malignancies were adenocarcinoma (28%), olfactory neuroblastoma (14.5%), and squamous cell carcinoma (13.5%). The 5-year disease-specific survival rate ranged from 81.9%–87%, with no major differences in the mean follow-up time (34.1 months vs. 37 months).**

■ CONCLUSIONS: **Endoscopic endonasal resection performed with or without a transcranial approach, when properly planned and in expert hands, has an accepted role with precise indications in the surgeon's armamentarium for the treatment of sinonasal and skull base malignancies.**

## INTRODUCTION

The introduction of craniofacial resection by Ketcham et al. in the 1960s (13) was a major advance in the management of sinonasal malignancies. By including the anterior skull base in the surgical specimen, this intervention has dramatically improved local control of tumors invading the roof of the ethmoid (15). However, this approach has been associated with morbidity and perioperative mortality that are not negligible (8, 12).

The growing expertise of skull base teams (neurosurgeons and otorhinolaryngologists) in endoscopic procedures, improved imaging diagnostic systems, and technologic refinement of endoscopic equipment all have contributed to gradual expansion of the indications for an endoscopic approach to resection of selected cases of malignant tumors. The first endoscopic experiences in sinonasal malignancy treatment were published in the late 1990s and were limited to lesions involving the naso-ethmoidal box but not invading the anterior skull base (ASB) (20).

Over the past decade, data from several centers worldwide have demonstrated that the endoscopic resection of malignant sinonasal tumors can be extended to include the dura mater of the ASB (endoscopic resection with transnasal craniectomy), from the posterior wall of the frontal sinus back to the planum sphenoidale and between the orbits (6). The extent of the endoscopic resection can be tailored to specific tumor characteristics (histologic type, site of origin, and proximity to critical areas) preserving uninvolved structures, with reduced functional sequelae as a consequence (16). When the endoscopic endonasal approach is not feasible, owing to an intracranial extension of the tumor, it can be combined with a transcranial approach to obtain better control of the upper margins (4). The present study accurately describes the surgical techniques and emphasizes the evolution of the indications for the endoscopic endonasal approach throughout the years by reviewing the largest series reporting the oncologic outcomes of patients treated for sinonasal and skull base cancer with endoscopic resection or cranio-endoscopic resection (CER).

## MATERIALS AND METHODS

### Preoperative Work-up

The preoperative diagnostic work-up includes magnetic resonance imaging (MRI) with gadolinium enhancement in all cases. In patients with claustrophobia, MRI can be replaced by a computed tomography scan with contrast medium. In very aggressive histologic types (i.e., malignant melanoma), a positron emission tomography scan is performed to rule out systemic dissemination of the disease. All patients scheduled for a purely endoscopic approach must be informed about the possibility of switching to a combined CER intraoperatively, if required.

### Indications and Exclusion Criteria

The endoscopic endonasal approach allows the resection of small-sized to intermediate-sized sinonasal tumors (stage T1–T3) as well as selected T4a–T4b lesions. Based on the site of origin, extension, and histologic type of the tumor, the endoscopic resection can be performed unilaterally (resection extended anteroposteriorly from the posterior wall of the frontal sinus to the planum sphenoidale and laterolaterally from the nasal septum to the lamina papyracea) or bilaterally (resection extended from one lamina papyracea to the opposite one).

Contraindications for an exclusively endoscopic endonasal approach include infiltration of nasal bones and palate, massive involvement of the frontal sinus, massive involvement of the lacrimal pathway or of the bony walls of the maxillary sinus (with the exception of the medial one), extension into the infratemporal fossa, and involvement of the orbit content. Focal contact or suspected infiltration of the tumor with "high-risk" areas, such as the lamina papyracea, the cribriform plate or the roof of the ethmoid, and the dural layer of the anterior cranial fossa, is not considered a contraindication. Concerning ASB involvement and intracranial extension, massive infiltration of the dura mater over the orbital roof or brain parenchyma infiltration, detected in the preoperative or the intraoperative settings, requires combining an endoscopic approach with an external one (CER). At the present time, the only intradural structures that can undergo endoscopic resection are the olfactory bulb and tract.

### Surgical Technique

Although the surgical technique varied slightly among patients according to the site of origin and extent of the lesion, endoscopic endonasal resection (ER) comprised 6 main surgical steps (Figure 1), as follows:

1. Tumor origin identification. The surgical procedure usually starts with disassembling the tumor with powered instrumentation or cutting instruments. The lesion is gradually debulked starting from the core to identify clearly its site of origin. In this phase, it is crucial to preserve the surrounding anatomic structures because these are useful landmarks for orientating the subsequent surgical steps.

2. Surgical target setting. Removal of the posterior two thirds of the nasal septum is performed to gain better exposure of the surgical field and to optimize the endonasal maneuverability of the dedicated instruments, using the 2-nostrils, 4-hands technique (7). In this step, the removal of the rostrum sphenoidale is crucial to expose the posteroinferior margin of the dissection. The septal branches of sphenopalatine arteries are isolated and coagulated to reduce bleeding and improve visibility. The frontal sinus is approached by Draf type IIb sinusotomy in the case of monolateral ER; Draf type III median sinusotomy is performed if the ER involves both sides. The frontal sinusotomy represents the anterosuperior margin of the dissection, allowing precise identification of the beginning of the anterior cranial fossa.

3. Centripetal removal. After the posteroinferior and anterosuperior margins of the resection are exposed, a subperiosteal dissection of the naso-ethmoidal-sphenoidal complex is performed unilaterally or bilaterally (according to the extension of disease) to expose the lateral margins (3). The lamina papyracea is included in the dissection when the tumor is in close proximity or frankly involved in it. When required by the extension of disease, endoscopic medial maxillectomy type III can be performed to obtain good control of the whole maxillary sinus. Nasolacrimal duct exposure and resection, just below the lacrimal sac (Figure 2), is performed during this surgical phase. Superiorly, the dissection is continued in the anteroposterior direction by resecting the olfactory fibers and the basal lamella of the ethmoidal turbinate to mobilize the monoblock. The entire naso-ethmoidal-sphenoidal complex is now isolated and pushed toward the central part of the nasal fossa (centripetal technique) to extract it transorally or through the nasal vestibule. The surgical margins are checked by frozen section, and the dissection is continued if necessary until free margins are obtained.

4. Skull base removal. According to the extension of the disease, endoscopic resection can be extended to include the ASB as well (endoscopic resection with transnasal craniectomy). The ethmoid roof exposure with removal of bony partitions is completed using a drill with a diamond burr. The skull base resection can be performed monolaterally or bilaterally according to the extension of disease and to the particular histologic type of the tumor (Figure 3). The anterior and posterior ethmoidal arteries are exposed, cauterized with bipolar electric forceps, and dissected. The crista galli is carefully detached from the dura mater and removed with blunt instruments, avoiding iatrogenic lesions in the dura mater.

5. Intracranial work. The key point for subsequently performing an optimal skull base reconstruction is to dissect the epidural space properly over the orbital roof laterally, the planum sphenoidale posteriorly, and the posterior wall of the frontal sinus anteriorly before starting resection of the dura mater itself. The dura mater is incised and circumferentially cut with angled scissors or a dedicated scalpel at a safe distance from the suspected area of tumor spread. The falx cerebri is clipped in the anterior portion before its resection to avoid sagittal sinus bleeding; then its posterior portion at the level of the spheno-ethmoidal planum is resected. The arachnoid plane over the intracranial portion of the tumor is dissected and separated from the brain parenchyma. The specimen, including the residual tumor, the ASB, and the overlying dura mater together with one or both of the olfactory bulbs, is removed through the transnasal route. The dural margins are sent for frozen sections (Figure 4).

6. Reconstruction time. The resulting skull base defect is reconstructed by the endoscopic endonasal multilayer technique. Reconstruction is performed preferably using autologous materials.

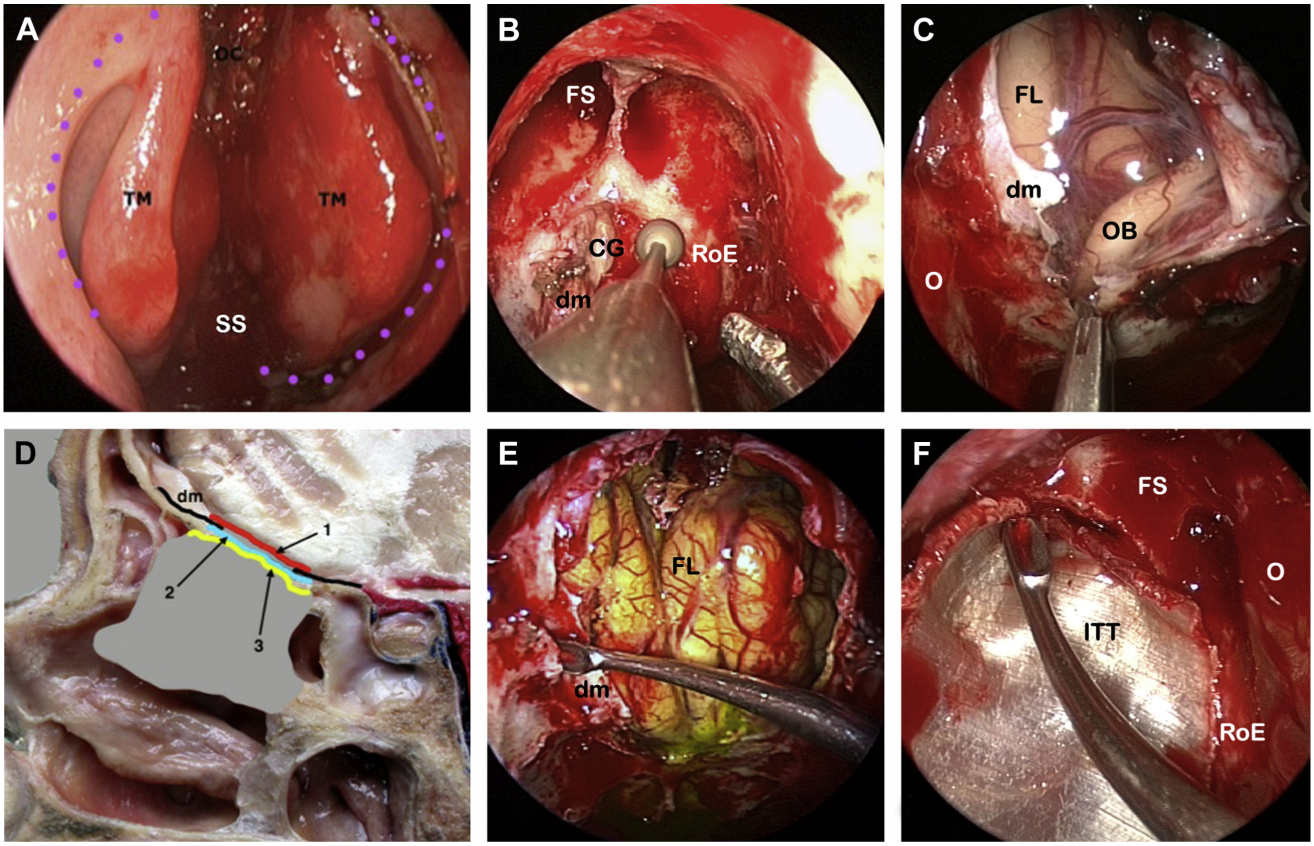


**Figure 1.** Surgical steps of endoscopic endonasal resection. (**A**) Subperiosteal dissection (*dotted lines*) to remove the ethmoidal box. (**B**) Drilling out of the bony ethmoidal roof and removal of the crista galli. (**C**) Transnasal resection of dura mater and olfactory bulb. (**D**) Schematization of the endoscopic endonasal skull base reconstruction according to the multilayer technique. (**E**) Endoscopic view of anterior skull base defect, extended from the posterior wall of the frontal sinus back to the sphenoidal planum and between the orbits. (**F**) Endonasal skull base reconstruction using layers of autologous materials. TM, middle turbinate; SS, sphenoidal sinus; FS, frontal sinus; RoE, roof of ethmoid; CG, crista galli; dm, dura mater; FL, frontal lobe; OB, olfactory bulb; 1, intradural layer; 2, intracranial extradural layer; 3, extracranial layer placed overlay; O, orbit; ITT, iliotibial tract.

In our experience, the fascia lata or the iliotibial tract has the best characteristics in terms of thickness, pliability, and strength (22). For the first intradural layer of duraplasty, the graft has to be at least 30% larger than the dural defect and split anteriorly on the midline to adjust to the falx cerebri in the case of bilateral resection. The second layer, intracranial and extradural, needs to be precisely sized and tacked between the previously undermined dura mater and the residual ASB bone. Pieces of fatty tissue are placed to eliminate the dead space between the second and third layers and to flatten the residual denuded ASB. The third extracranial layer has to cover all the exposed ASB but must not overlap the frontal sinusotomy. The borders of the second and third layers are properly fixed with fibrin glue. In the case of a tumor sparing the nasal septum and without multifocal localizations (e.g., not in the case of intestinal type adenocarcinoma), for the third layer of the skull base reconstruction, it is also possible to use a mucoperiosteum or mucoperichondrium pedicled nasoseptal flap (Hadad-Bassagasteguy flap) (9). Use of this flap facilitates rapid healing of the surgical cavity, especially in patients who require adjuvant irradiation, and results in a sharp decrease in the incidence of postoperative cerebrospinal fluid (CSF) leaks.

At the end of the procedure, in selected cases, a rolled Silastic sheath can be inserted as a stent in the frontal sinusotomy to allow subsequent frontal sinus débridement with no risks for the duraplasty. The surgical cavity is packed for about 48 hours.

For lesions filling the frontal sinus or invading the ASB with intradural extension over the orbital roof or with infiltration of brain parenchyma, the endoscopic endonasal procedure has to be combined with an external approach (CER) (4). This technique makes it possible to surround the lesion completely and remove it as a monoblock, without any interruption in the facial skeleton. The procedure is performed by a surgical team composed of a neurosurgeon and an otorhinolaryngologist and includes 2 simultaneous phases (**Figure 5**), as follows:

1. Endoscopic phase. The procedure starts with disassembling of the

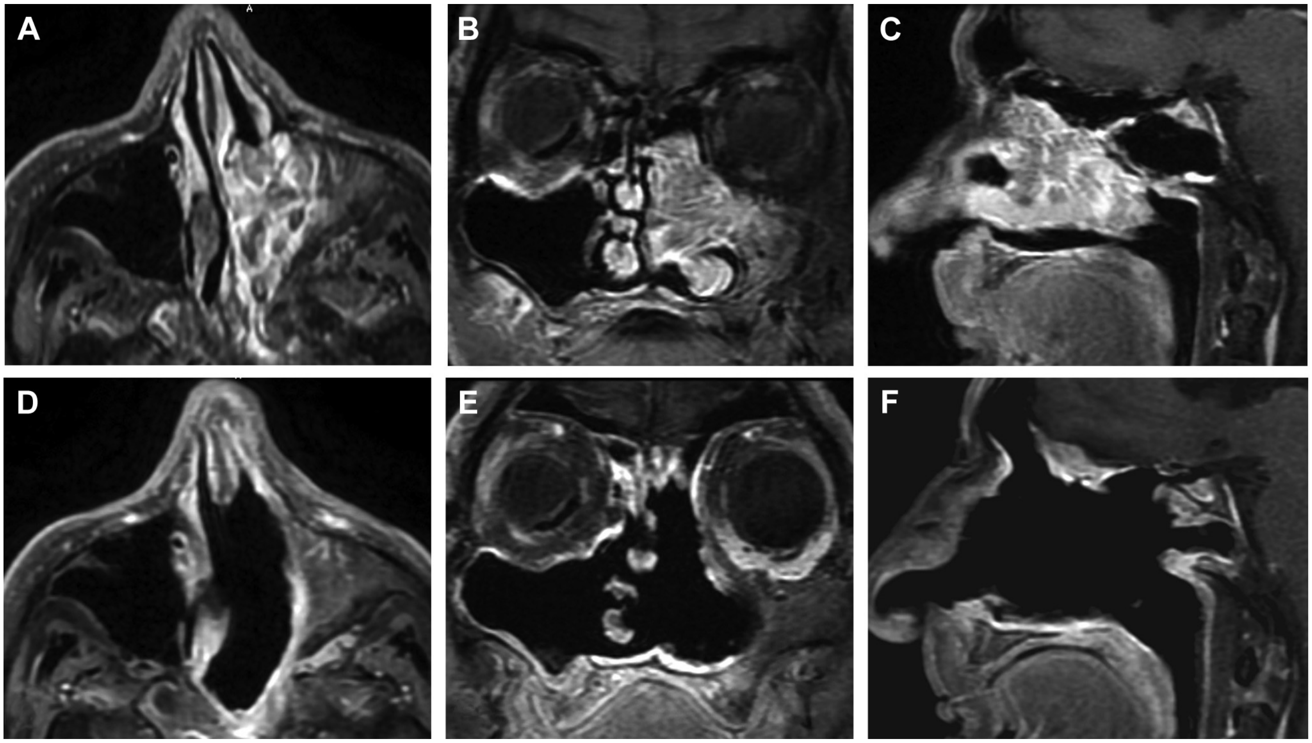


**Figure 2.** Exclusively endoscopic endonasal resection of left maxillary squamous cell carcinoma, arising from inverted papilloma (stage T1N0M0). Preoperative and postoperative contrast-enhanced T1-weighted magnetic resonance imaging scan in axial (**A** and **D**), coronal (**B** and **E**), and sagittal (**C** and **F**) views.

endonasal portion of the tumor plus removal of the nasal septum. Next, dissection of the sphenoidal sinuses, anteroinferior wall, and rostrum is performed, and both sphenopalatine arteries (septal branches) are cauterized. The lateral sections require identification of the lamina papyracea, detached from the periorbit, starting with the anterior margin up to the orbital apex, and then mobilized in a monoblock with the ethmoidal labyrinth. During all this time, correct interaction between the neurosurgeon and otorhinolaryngologist is important as the neurosurgeon cauterizes the ethmoidal arteries from above and helps the otorhinolaryngologist to medialize the lamina papyracea with malleable spatulas. Depending on the size of the tumor, this surgical step may be associated with a medial maxillectomy with nasolacrimal duct exposure and dissection below the lacrimal sac. At the end of the procedure, the endonasal endoscopic approach is especially useful for completing the skull base reconstruction. The endoscope makes it possible to verify the tightness of the pericranium flap and to apply connective tissue in overlay fashion (temporal fascia or fascia lata) to reinforce the ASB reconstruction.

2. Transcranial phase. This phase consists of a subfrontal (or frontal) craniotomy, the size and shape of which depend on the surgical requirements. The craniotomy is carried out a few millimeters above the orbital upper arches to obtain an approach to the frontal skull base as broad and as tangential as possible to reduce as much as possible any excessive retraction of the cerebral parenchyma and avoid excessive kinking of the pericranium flap during the ASB reconstruction. A bony "volet" including the anterior and posterior wall of the frontal sinus is removed. After detaching the bony flap from the dural layer and clipping the sagittal sinus emissaries to control the bleeding, the exposed dura mater is incised, the cerebral falx is dissected, and the intracranial portion of the tumor is carefully resected from the brain parenchyma. With a diamond burr, the superior portion of the frontal-ethmoidal-sphenoidal bony complex is isolated. Finally, the intracranial dissected lesions, together with the ethmoidal box, are extracted transcranially by the 2-physician surgical team cooperating through the different approaches.

The dural defect is rebuilt by suturing the dura mater with the temporal fascia or fascia lata. The ASB defect is reconstructed using a galeoperiosteum flap that is folded over and fixed via button sutures to the remaining sphenoidal border and to the orbital process of the frontal bone (medial edge). In this phase, the simultaneous endoscopic endonasal approach is useful to ensure that the duraplasty grafts are correctly placed, without any dehiscence. The bony flap is put back into place and fixed with titanium plaques and

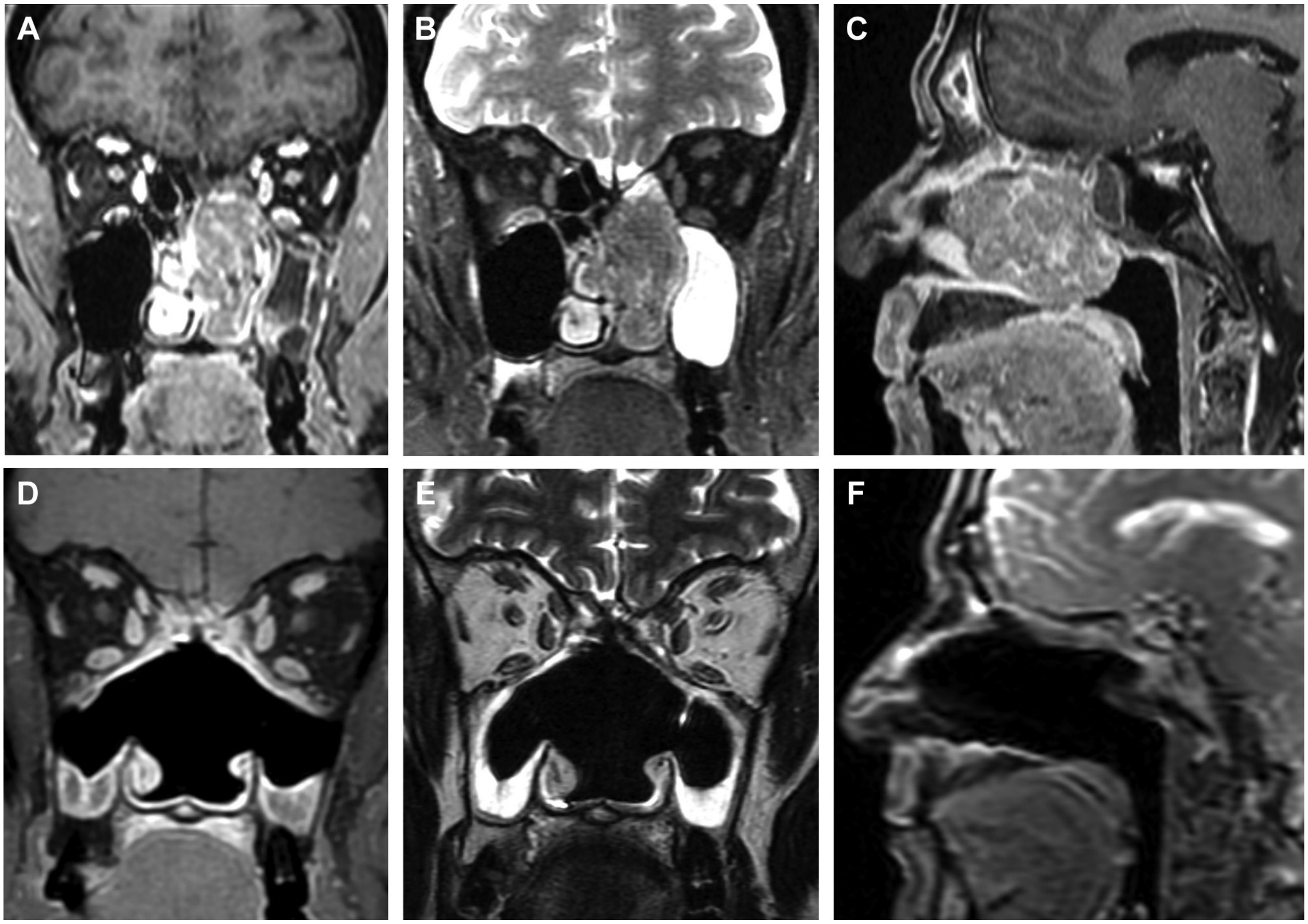


**Figure 3.** Endoscopic resection with transnasal craniectomy of ethmoidal intestinal type adenocarcinoma (stage T3N0M0) in a patient with occupational exposure to wood dusts. Preoperative contrast-enhanced T1-weighted (**A**) and T2-weighted (**B**) magnetic resonance imaging (MRI) scan in coronal view and contrast-enhanced T1-weighted MRI scan in sagittal view (**C**) showed a monolateral lesion without evident skull base involvement. However, the bilateral carcinogenic exposure of the patient and the multifocal spread that characterized the disease forced the endoscopic surgeons to remove the ethmoidal box bilaterally and to perform a transnasal craniectomy to check the dural layer with frozen sections. The patient received adjuvant radiotherapy at the site of the tumor (54 Gy). MRI scan performed 1 year after surgery in coronal (**D** and **E**) and sagittal (**F**) views confirmed radical resection of the disease.

screws. The galeal-skin flap is relocated and fixed with a button suture (**Figure 6**).

### Postoperative Management and Adjuvant Therapy

All patients who undergo skull base reconstruction must undergo a brain computed tomography scan on the first postoperative day to rule out complications and to evaluate the extent of pneumocephalus. Patients must maintain full bed rest in a 30-degree upright position until the third postoperative day. Nasal packing is gradually removed within 48 hours. Intravenous third-generation cephalosporin therapy is started the day before surgery and continued for at least 5 days. Nasal irrigation with saline solution and application of mupirocin ointment twice daily is recommended for at least 1 month.

Postoperative radiotherapy is planned in cases of significant skull base involvement (pT3), intracranial extension and dural infiltration (pT4a-b), close margins to the orbital content or the frontal sinus, and unresectable residual disease (16). All patients with olfactory neuroblastoma received adjuvant radiotherapy (5). Postoperative radiotherapy is indicated in all patients receiving CER as a primary treatment except for patients with mucosal melanoma, in which the role of radiotherapy is unproven (14). Chemotherapy is added to radiotherapy in histologic types with a high risk of systemic dissemination of the disease. All patients have to be followed according to a protocol that includes monthly endoscopic examinations and MRI every 4 months during the first year; endoscopic examination and MRI every 2 and 6 months, respectively, during the second year; and both examinations at 6-month intervals thereafter.

## RESULTS

Most publications analyzing the efficacy of endoscopic surgery in the management of sinonasal cancers have concentrated on a small homogeneous cohort of patients with a specific histology. For this reason,

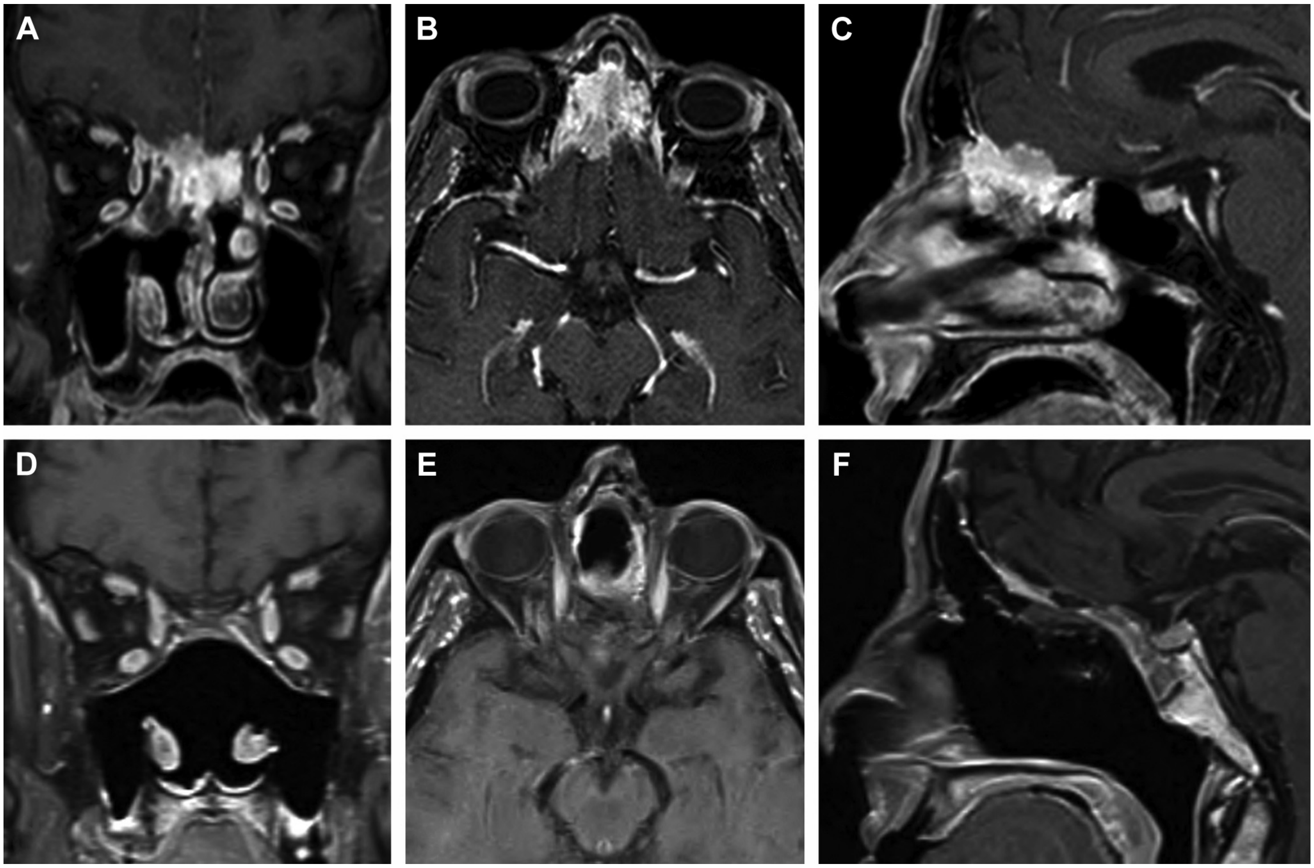


**Figure 4.** A young patient was referred to our tertiary care center for histopathologic diagnosis of olfactory neuroblastoma after endoscopic removal of inflammatory-like ethmoidal neoformations. Contrast-enhanced fat-saturated T1-weighted magnetic resonance imaging scan in coronal (**A**), axial (**B**), and sagittal (**C**) views clearly showed the intracranial persistence of the lesion. The tumor invaded the anterior skull base, passing through the dural layer and compressing the brain without infiltrating it (stage T4bN0M0). Endoscopic resection with transnasal craniectomy was performed, and the olfactory bulbs were resected bilaterally. The patient received adjuvant radiotherapy at the site of the tumor (58 Gy). Magnetic resonance imaging scan performed 1 year after surgery in coronal (**D**), axial (**E**), and sagittal (**F**) views showed radical resection of the lesion.

it seems difficult to analyze results of endoscopic sinus surgery in the management of large cohorts of patients. The 2 largest series, reporting on 184 and 120 patients, respectively, who underwent an endoscopic approach to resect sinonasal and ASB cancer, were published almost concomitantly. The former series collected the data acquired during our 10-year experience in 2 tertiary care Italian centers (17), and the latter summarized the oncologic results in a cohort of patients treated at the M.D. Anderson Cancer Center in Houston, Texas, over a 16-year period (10).

In the Italian experience of 184 patients (17), an ER was performed in 134 (72.8%) cases, and the remaining 50 (27.2%) patients underwent a CER. Overall, 52 (28.3%) patients had failed some form of previous treatment. Definitive histology showed a wide spectrum of histologic types, the most frequent being adenocarcinoma (37%), followed by squamous cell carcinoma (13.6%) and olfactory neuroblastoma (12%). The distribution of tumors in relation to T category was as follows: 52 (28.2%) T1 (49 and 3 in the ER and CER groups, respectively), 26 (14.2%) T2 (25 ER and 1 CER), 32 (17.4%) T3 (20 ER and 12 CER), 17 (9.2%) T4a (9 ER and 8 CER), and 35 (19%) T4b (12 ER and 23 CER). Overall, postoperative complications occurred in 16 (8.7%) patients; the most frequent was CSF leak (8 cases; 4.3%), which required surgical repair in 6 cases, with the remaining 2 controlled by lumbar drainage that was maintained for 5 days. Adjuvant treatment was delivered in 86 (46.7%) patients: 72 patients received radiotherapy alone, 8 patients received chemotherapy, and 6 patients received chemoradiation (5 patients receiving ER and 1 patient receiving CER). Follow-up ranged from 2–123 months (mean, 34.1 months) for the entire patient population. The 5-year disease-specific survival was 81.9% ± 3.9% for the entire patient cohort, varying from 91.4% ± 3.9% for the ER group to 58.8% ± 8.6% for the CER group ($P = 0.0004$). No statistically significant difference in 5-year disease-specific survival was found when comparing patients who had been previously untreated with patients with recurrent tumors ($P = 0.36$).

We assessed more recently the health-related quality of life in a large homogeneous cohort of patients affected by ASB cancers who underwent endoscopic ER (data not published). The data emerging

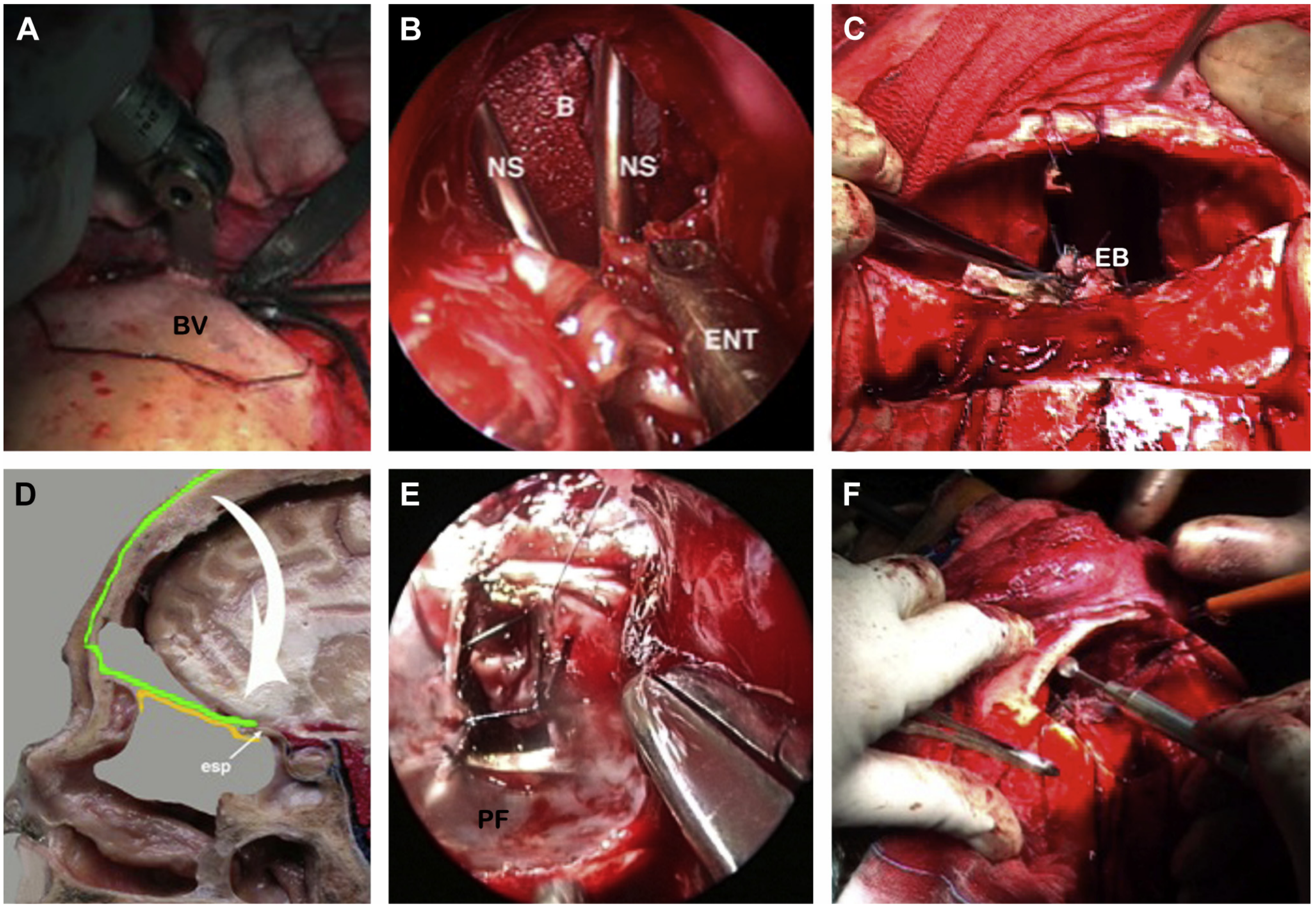


**Figure 5.** Surgical steps of cranio-endoscopic resection. (**A**) Transcranial approach with harvesting of the bony "volet." (**B**) Endoscopic endonasal perspective of the cooperation between the 2-physician surgical team, through the different approaches, during dissection of the tumor. (**C**) Transcranial extraction of the lesion together with the ethmoidal box. (**D**) Schematization of the galeoperiosteum flap rotation to repair the anterior skull base defect. (**E**) The galeoperiosteum flap is fixed by means of sutures to the remaining sphenoidal border and to the orbital process of the frontal bone. The simultaneous endoscopic endonasal perspective is useful in this phase to check the effective seal of the reconstruction. (**F**) Trimming of the border of the bony flap with a diamond burr to put it back in place correctly. BV, bony volet; B, brain; NS, instruments through the transcranial window maneuvered by neurosurgeons; ENT, instruments through the endonasal corridor maneuvered by otolaryngologists; EB, ethmoidal box; esp, spheno-ethmoidal planum; PF, periosteal flap.

from this study are encouraging, showing that patients affected by skull base cancers who undergo endoscopic endonasal surgery report a complete recovery of overall quality of life 1 year after surgery. The variables associated with a worse quality of life were age > 60 years, expanded endoscopic resection associated with transnasal craniectomy, and postoperative radiotherapy.

In the M.D. Anderson Cancer Center experience with 120 patients (10), an ER was performed in 134 (72.8%) patients, and the remaining 50 (27.2%) patients underwent CER. Overall, 52 (28.3%) patients had failed some form of previous treatment. The most common tumor types were olfactory neuroblastoma (17%), sarcoma (15%), adenocarcinoma (14%), melanoma (14%), and squamous cell carcinoma (13%). The primary T stage was evenly distributed across all patients as follows: T1, 25%; T2, 25%; T3, 22%; and T4, 28%. However, T-stage distribution differed significantly between the CER and the ER groups ($P = 0.001$). Approximately two thirds (63%) of patients treated with ER had a lower (T1–T2) disease stage, whereas 95% of patients treated with CER had a higher (T3–T4) disease stage.

The overall surgical complication rate was 11% for the whole group. Postoperative CSF leak occurred in 4 of 120 patients (3.3%) and was not significantly different between the CER (1 of 27) and ER (3 of 93) groups. Of 120 patients, 60 patients (50%) were treated with surgery alone, whereas the other 50% received some form of adjuvant treatment. The 5-year and 10-year disease-specific survival rates were 87% and 80%, respectively. The 5-year and 10-year overall survival rates were 76% and 50%, respectively. There was no statistically significant difference in disease-specific ($P = 0.92$) or overall ($P = 0.79$) survival between the ER and CER groups. Survival was statistically and significantly better for patients who presented with a previously untreated disease than for patients who presented with persistent disease after incomplete surgical resection.

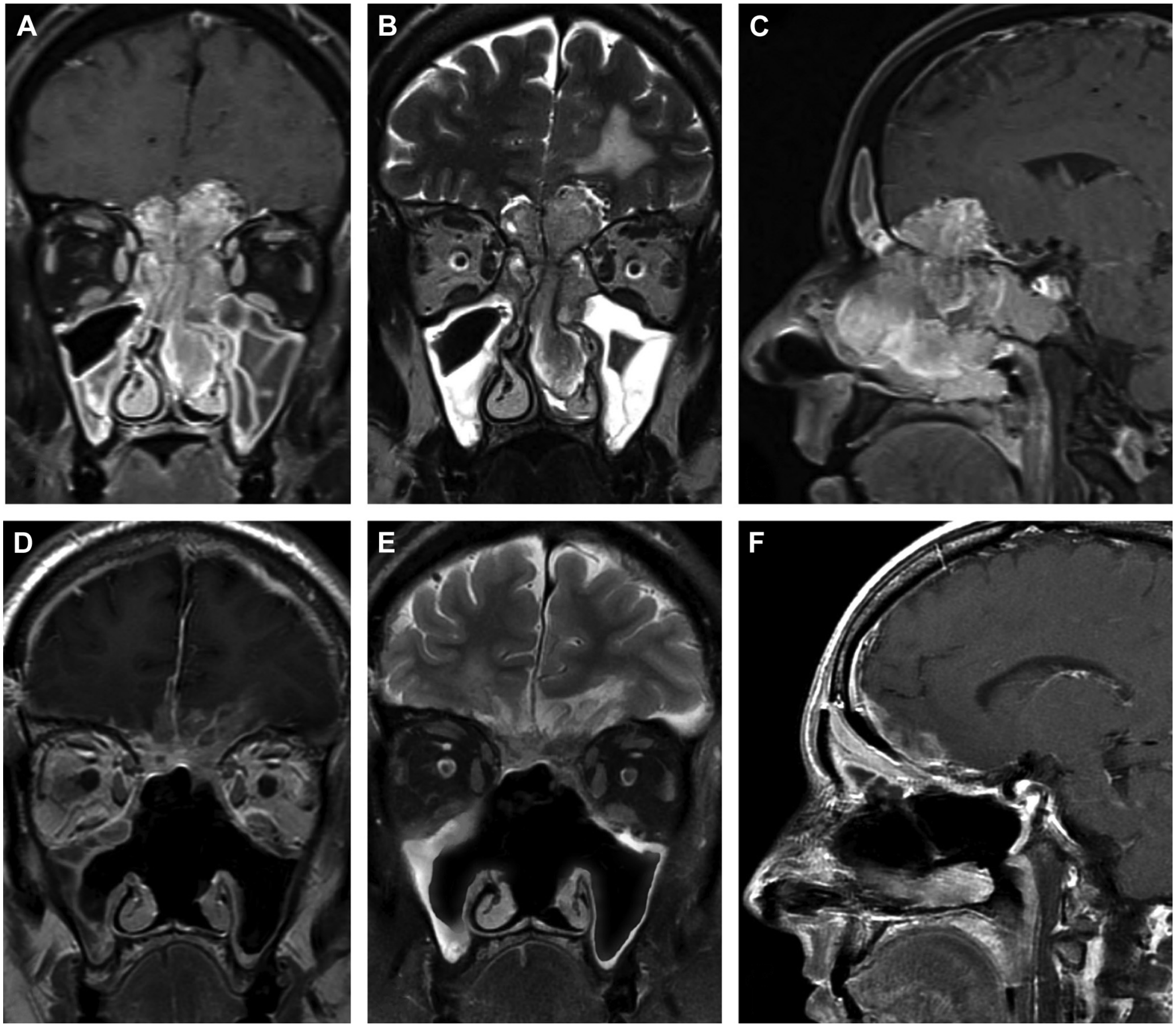


**Figure 6.** Cranio-endoscopic resection of olfactory neuroblastoma (stage T4bN0M0). Contrast-enhanced fat-saturated T1-weighted magnetic resonance imaging (MRI) scan in coronal (**A**) and sagittal (**C**) views showed intracranial extension of the lesion, with perilesional edema in the T2-weighted MRI scan in coronal view (**B**), suggesting infiltration of the brain parenchyma. The patient received postoperative radiotherapy at the site of the tumor (62 Gy). MRI scan performed 1 year after surgery in coronal (**D** and **E**) and sagittal (**F**) views confirmed the radical resection with the multimodal treatment.

## DISCUSSION

Treatment of sinonasal malignancies has significantly evolved in recent decades and requires the contribution of a multidisciplinary team. Surgery, which plays a pivotal role in the management of most patients, comprises a large spectrum of different techniques ranging from traditional external approaches to modern endoscopic procedures. The absence of facial incisions and osteotomies, less postoperative pain, decreased hospitalization time, improved visualization of tumor borders, and reduced morbidity and mortality rates are commonly cited as the major advantages of endoscopic resection compared with the external approach (2). When resection of the skull base is performed transnasally, retraction of the frontal lobes with the ensuing possible complications is avoided. However, as shown in the present series, transnasal resection of the dura mater, with consequent endoscopic duraplasty, increases the likelihood of CSF leak. In the Italian series, the CSF leak rate was 4.3%, and CSF leak represented the most frequent major complication, similar to the M.D. Anderson Cancer Center experience, which reported a CSF leak rate of 3.3% (4 of 120) (10, 17). However, a previous report by the Italian group focusing on skull base reconstruction after endoscopic surgery for malignancies of the sinonasal tract demonstrated that the occurrence of CSF leak is clearly related to the learning curve of the surgical team and to the refinement of the surgical technique, with progressive decrease of this complication over time (23).

Both of these large series analyzed included patients in whom 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 histologic types found in various geographic areas. In the Italian series, adenocarcinoma was the most frequent lesion (37%), whereas olfactory neuroblastoma was prevalent (17%) in the U.S. experience. With no major differences in the mean follow-up time (34.1 months vs. 37 months), the 5-year disease-specific survival in the 2 series for the entire patient cohort was also quite similar: 81.9% vs. 87%. Nicolai et al. (17) found a statistically significant difference in 5-year disease-specific survival between patients treated with endoscopic surgery alone compared with patients treated with CER (91.4% vs. 58.8%; $P < 0.001$), although this observation was not confirmed by Hanna et al. (10). As pointed out by these authors, this variability can reflect the different criteria used for patient selection for the different approaches, with the U.S. group being more inclined to reserve an endoscopic approach for patients with relatively earlier disease stage and no or limited skull base invasion.

Overall, the "gold standard" for skull base procedures is to choose the best surgical corridor to the pathology. It is of paramount importance that the chosen route to the target allow safe and adequate management of the pathology without crossing nerves or other vital structures. The endoscopic endonasal corridor is preferred when it provides the most direct access to the tumor with the least manipulation of neural and vascular structures; if nerves or vessels need to be mobilized to reach the tumor, an alternative approach should be considered. Based on this statement, we believe that every surgical option should be available to the management team and that the surgical choice should be made without any dogmatism.

The choice of a surgical approach depends on patient comorbidities, tumor characteristics, and the level of skill and confidence of the surgeons. The need for an external or combined procedure may be suggested by preoperative imaging studies, but a definite decision can be made only during the surgical procedure itself in a few cases. Consequently, the possibility of switching from an endoscopic to an external procedure must always be discussed with the patient before surgery (19). The surgical team, which for tumors involving the ASB necessarily includes both otolaryngologists and neurosurgeons, should be experienced in all these techniques to be able to perform "multiportal" surgical approaches. To optimize outcomes, endoscopic resections of sinonasal and skull base tumors should be performed only by teams of surgeons with longstanding experience in the endoscopic management of inflammatory diseases and CSF leak repair and a thorough knowledge of the surgical oncologic principles for the management of malignancies.

Although our series as well the other experiences reported in the literature has some limitations (i.e., histologic heterogeneity and limited cohort of cases secondary to the rarity of these lesions), the 5-year overall and disease-specific survival rates seem to indicate that endoscopic surgery, when properly planned and performed by experienced surgeons, may be an effective alternative to standard approaches in the management of selected malignancies of the sinonasal tract. In the surgeon's available armamentarium for the treatment of sinonasal and skull base malignancies, the endoscopic approach has acquired an accepted role with precise indications and should be considered one of the therapeutic options, together with the other surgical approaches and radiochemotherapy, in an oncologic multimodal therapy approach capable of achieving radical and complete treatment of the pathology, while minimizing the morbidity for the patient (11).

However, changes in clinical practice should be rooted in methodologically sound evidence. At the present time, the levels of evidence in endoscopic tumor surgery are mainly level 3 (case series) and level 4 (expert opinion). We will have to reach higher levels of evidence within the next decade. For this purpose, the first step has been setting up a large database of cases with malignant sinonasal and skull base tumors to collect the clinical history of the patient, imaging data, pathologic findings, different types of surgical management, and postoperative treatment (16). A website permits the collection of large series of patients, particularly of rare neoplasms, which would increase our knowledge of the biologic behavior of the tumors. The next step to validate the endoscopic endonasal approach in the management of sinonasal and skull base malignancies will be to perform a collaborative, multicenter, randomized controlled trial with a large cohort of patients, with a precise stratification of the study population in homogeneous groups according to the stage of disease and histologic type. A collaborative multicenter trial is a unique opportunity for an international and interdisciplinary collaboration that would result in benefits for a wide range of patients affected by sinonasal and skull base tumors.

There are still open issues and questions to be answered (18). Longer follow-up times are needed to collect meaningful information on the outcome of tumors that can relapse well beyond the usual 5-year follow-up period. Stratification of survival data by histology and stage is required to gain a better understanding of the impact that these variables have on outcome. The role of adjuvant therapies (radiotherapy, chemotherapy, biologic modifiers) also needs to be explored with the intent of identifying patients who can benefit from these therapies, avoiding overtreatment in patients with less aggressive disease. Tailoring target treatment can be aided by expanding the study of specific biologic markers (21). Prospective quality-of-life evaluation should also be included in the assessment of patients before and after treatment (1).

## CONCLUSIONS

Endoscopic resection of sinonasal malignancies is a technique that is expanding. The role of transnasal endoscopic resection for low-stage (T1-T2 or Kadish A-B) sinonasal malignancies is becoming well established; for advanced-stage lesions with skull base involvement or focal dural infiltration, longer follow-up times and larger case series are needed to validate this approach. In these latter cases, when extensive involvement of the intracranial structures is present, the endoscopic endonasal corridor can be safely combined with a transcranial approach. The encouraging overall and disease-specific survival rates reported in more recently published studies suggest that for well-selected cases and with appropriate use of adjuvant or neoadjuvant therapies, endoscopic ER could produce acceptable oncologic outcomes in the management of sinonasal and ASB cancers.

## REFERENCES


1. Amit M, Abergel A, Fliss DM, Gil Z: The clinical importance of quality-of-life scores in patients with skull base tumors: a meta-analysis and review of the literature. Curr Oncol Rep 14:175-181, 2012.

2. Batra PS: Minimally invasive endoscopic resection of sinonasal and anterior skull base malignant neoplasms. Expert Rev Med Devices 7:781-791, 2010.

3. Castelnuovo P, Battaglia P, Locatelli D, Delù G, Sberze F, Bignami M: Endonasal micro-endoscopic treatment of the malignant tumours of paranasal sinuses and anterior skull base. Oper Tech Otolaryngol 17:152-167, 2006.

4. Castelnuovo PG, Belli E, Bignami M, Battaglia P, Sberze F, Tomei G: Endoscopic nasal and anterior craniotomy resection for malignant nasoethmoid tumours involving the anterior skull base. Skull Base 16:15-18, 2006.

5. Castelnuovo P, Bignami M, Delù G, Battaglia P, Bignardi M, Dallan I: Endonasal endoscopic resection and radiotherapy in olfactory neuroblastoma: our experience. Head Neck 29:845-850, 2007.

6. Castelnuovo P, Dallan I, Battaglia P, Bignami M: Endoscopic endonasal skull base surgery: past, present and future. Eur Arch Otorhinolaryngol 267:649-663, 2010.

7. Castelnuovo P, Pistochini A, Locatelli D: Different surgical approaches to the sellar region: focusing on the "two nostrils four hands technique." Rhinology 44:2-7, 2006.

8. Ganly I, Patel SG, Singh B, Kraus DH, Bridger PG, Cantu G, Cheesman A, De Sa G, Donald P, Fliss DM, Gullane P, Janecka I, Kamata SE, Kowalski LP, Levine PA, Medina Dos Santos LR, Pradhan S, Schramm V, Snyderman C, Wei WI, Shah JP: Craniofacial resection for malignant paranasal sinus tumors: report of an International Collaborative Study. Head Neck 27:575-584, 2005.

9. Hadad G, Bassagasteguy L, Carrau RL, Mataza JC, Kassam A, Snyderman CH, Mintz A: A novel reconstructive technique after endoscopic expanded endonasal approaches: vascular pedicle nasoseptal flap. Laryngoscope 116:1882-1886, 2006.

10. 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 135:1219-1224, 2009.

11. Harvey RJ, Winder M, Parmar P, Lund V: Endoscopic skull base surgery for sinonasal malignancy. Otolaryngol Clin North Am 44:1081-1140, 2011.

12. Ian G, Snehal GP, Bhuvanesh S: Complications of craniofacial resection for malignant tumors of the skull base: report of an International Collaborative Study. Head Neck 27:445-451, 2005.

13. Ketcham AS, Wilkins RH, Van Buren JM, Smith RR: A combined intracranial facial approach to the paranasal sinuses. Am J Surg 106: 698-703, 1963.

14. Lund VJ, Chisholm EJ, Howard DJ, Wei WI: Sinonasal malignant melanoma: an analysis of 115 cases assessing outcomes of surgery, postoperative radiotherapy and endoscopic resection. Rhinology 50:203-210, 2012.

15. Lund VJ, Harrison DFN: Craniofacial resection for tumors of the nasal cavity and paranasal sinuses. Am J Surg 156:187-190, 1988.

16. Lund VJ, Stammberger H, Nicolai P, Castelnuovo P, Beal T, Beham A, Bernal-Sprekelsen M, Braun H, Cappabianca P, Carrau R, Cavallo L, Clarici G, Draf W, Esposito F, Fernandez-Miranda J, Fokkens W, Gardner P, Gellner V, Hellquist H, Hermann P, Hosemann W, Howard D, Jones N, Jorissen M, Kassam A, Kelly D, Kurschel-Lackner S, Leong S, McLaughlin N, Maroldi R, Minovi A, Mokry M, Onerci M, Ong YK, Prevedello D, Saleh H, Sehti DS, Simmen D, Snyderman C, Solares A, Spittle M, Stamm A, Tomazic P, Trimarchi M, Unger F, Wormald PJ, Zanation A: European Rhinologic Society Advisory Board on Endoscopic Techniques in the Management of Nose, Paranasal Sinus and Skull Base Tumours: European position paper on endoscopic management of tumours of the nose, paranasal sinuses and skull base. Rhinol Suppl (22):1-143, 2010.

17. Nicolai P, Battaglia P, Bignami M, Bolzoni Villaret A, Delù G, Khrais T, Lombardi D, Castelnuovo P: Endoscopic surgery for malignant tumours of the sinonasal tract and adjacent skull base: a 10-year experience. Am J Rhinol 22: 308-316, 2008.

18. Nicolai P, Castelnuovo P, Bolzoni Villaret A: Endoscopic resection of sinonasal malignancies. Curr Oncol Rep 13:138-144, 2011.

19. Nicolai P, Castelnuovo P, Lombardi D, Battaglia P, Bignami M, Pianta L, Tomenzoli D: Role of endoscopic surgery in the management of selected malignant epithelial neoplasms of the naso-ethmoidal complex. Head Neck 29:1075-1082, 2007.

20. Stammberger H, Anderhuber W, Walch C, Papaefthymiou G: Possibilities and limitations of endoscopic management of nasal and paranasal sinus malignancies. Acta Otorhinolaryngol Belg 53:199-205, 1999.

21. Turri-Zanoni M, Medicina D, Lombardi D, Ungari M, Balzarini P, Rossini C, Pellegrini W, Battaglia P, Capella C, Castelnuovo P, Palmedo G, Facchetti F, Kutzner H, Nicolai P, Vermi W: Sinonasal mucosal melanoma: molecular profile and therapeutic implications from a series of 32 cases. Head Neck 35:1066-1077, 2013.

22. Villaret AB, Schreiber A, Battaglia P, Bignami M: Endoscopy-assisted iliotibial tract harvesting for skull base reconstruction: feasibility on a cadaveric model. Skull Base 21:185-188, 2011.

23. Villaret AB, Yakirevitch A, Bizzoni A, Bosio R, Bignami M, Pistochini A, Battaglia P, Castelnuovo P, Nicolai P: Endoscopic transnasal craniectomy in the management of selected sinonasal malignancies. Am J Rhinol Allergy 24: 60-65, 2010.


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