

Preservation of olfactory function following endoscopic resection of select malignancies of the nasal vault

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Abstract

Preservation of olfactory function during anterior skull base surgery has been previously described. However, its feasibility during oncological resection remains undefined. The aim of this study was to clarify the feasibility of preserving olfactory function in select patients undergoing oncological anterior skull base resection via endonasal endoscopic approach. This is a retrospective case series study. Postoperatively, all patients underwent a standardized smell identification test (Senonics Inc., Haddon, NJ, USA). From January 2002 to December 2009, we attempted to preserve olfactory function in 9 patients who required an endoscopic resection involving the anterior skull base for treatment of various malignancies presenting unilateral extension. These included: esthesioneuroblastoma (n=6), squamous cell carcinoma (n=1), adenocarcinoma (n=1) and hemangiopericytoma (n=1). In 7 patients, resection included a unilateral endoscopic craniectomy with preservation of the contralateral middle and superior turbinates. Two patients underwent resection of the entire lateral nasal wall and the olfactory epithelium as the superior limit of tumor resection. Six patients received adjuvant radiotherapy. Postoperatively, olfaction was documented in 7 patients (3 normosmic, 4 microsmic). All patients are free of recurrence at the original site at a mean follow-up period of 55.7 months (range 21-101 months). One patient with an esthesioneuroblastoma developed a cervical lymph node recurrence four years after surgery. In selected cases, it is feasible to preserve

olfactory function without apparent compromise of oncological outcomes. The success rate depends largely on the extent of the resection, which, in turn, is dictated, by the extent of the tumor.

Introduction

Surgery remains the mainstay treatment for most sinonasal tumors.¹ Traditionally, the surgical resection is carried out *en bloc* via an open trans-facial and/or transcranial approach. Recent advances in preoperative imaging, intraoperative navigation system, endoscopic instrumentation, and hemostatic materials have made the endoscopic resection of sinonasal tumors a viable alternative to traditional techniques.² Its role in resecting small lesions confined to the nasal cavity is well established. Increasing experience and expertise, have spurred the expansion of endoscopic endonasal approaches beyond the nasal cavity and paranasal sinuses to areas such as the infratemporal fossa, skull base and cranial cavity. Survival rates following endoscopic resection of select sinonasal tumors are comparable to that of open techniques.³⁻⁵

Our initial experience with endoscopic anterior skull base resection was associated with a higher incidence of postoperative cerebrospinal fluid (CSF) leak than that associated with traditional techniques. With the advent of reconstructive techniques using vascular pedicle flaps, our current rate of CSF leak for low flow defects has decreased to less than 5%.⁶⁻⁸

Olfactory function is often neglected when dealing with malignancies of the sinonasal tract and/or anterior skull base. Furthermore, loss of olfaction is considered inevitable and is accepted as sequelae of resecting the nasal vault and the anterior skull base. Patients accept the resulting anosmia. However, it is a permanent deficit that negatively impacts their quality of life. It especially affects those patients who rely on olfaction for their job, such as florists, sommeliers, chefs or perfumers. It is also important from a safety perspective, as anosmic patients may not be alerted to life threatening situations, such as a fire, toxic fumes or chemical spillage.

Others have attempted to preserve olfaction during the resection of anterior skull base tumors using traditional techniques. Spetzler *et al.* first described a technique that preserves the integrity of the cribriform plate with the olfactory nerve roots, dura and mucosa.⁹ This involved an *en bloc* elevation of the olfactory unit from the anterior cranial base and preservation of its attachment to the frontal lobe dura. Three of 4 patients experienced a return of olfaction within eight weeks after surgery. The remaining patient had a more gradual

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recovery, gaining limited olfaction ten months after surgery. Subsequently, others have reported some success with olfaction preservation following open anterior skull base surgeries.¹⁰⁻¹² These reports, however, are fraught by the lack of objective data regarding the use of standardized tests of olfactory function,^{9,10,12} or by the inclusion of a heterogeneous population that included patients affected by trauma, encephaloceles, and benign and malignant tumors.¹³

To our best knowledge, this is the first report addressing preservation of olfactory function following endoscopic endonasal resection of sinonasal malignancies involving the nasal vault and anterior skull base. In this study, we examine the feasibility of preserving the olfactory function in patients undergoing unilateral skull base resection via an endonasal endoscopic approach.

Materials and Methods

We prospectively identified and tested patients presenting malignancies that involve the nasal vault who underwent endoscopic resection with the intent of olfactory preservation, from January 2002 to December 2009 (Institutional Review Board approved database). Evaluation of olfactory function was obtained using a Senonics-40 *scratch and*

sniff test (Sensonics Inc., Haddon, NJ, USA) performed within a period of three months after surgery. For the purpose of our study, we considered the surgery as *olfactory-sparing* if it preserved any part of the olfactory area (mucosa lining the cribriform plate, superior turbinate, superior septum and superior parts of the middle turbinate).¹⁴

All tumors originated at the superior aspect of the sinonasal tract (middle and/or superior turbinates, olfactory cleft, superior septum, ethmoid sinuses); therefore, they directly involved or were immediately adjacent to the anterior skull base and/or olfactory area. An important aspect of our surgical selection criteria is that all these patients had malignancies that involve a single nasal cavity, without contralateral involvement.

Extent of the resection was customized to the extent and histopathology of the disease. Adequacy of the resection was confirmed with intraoperative frozen section analysis and subsequent histopathological and immunohistochemical analyses in all patients.

Patients with tumors that did not directly involve the anterior skull base (*i.e.* arising in the middle turbinate), underwent a total sphenoidectomy with resection of the middle and superior turbinates bone including their attachment to the skull base (conchal plate) and resection of the entire mucoperiosteum of the vault of the nasal cavity. Removal of the lamina papyracea served as the lateral margin of the resection, while the mucoperiosteum of the nasal septum or the contralateral olfactory cleft served as the medial margin. The superior margin was obtained by removing the mucoperiosteum (including olfactory filaments) of the nasal vault/anterior skull base. Patients with tumors that directly involved the mucoperiosteum over the skull base but had a histopathology without propensity for perineural invasion (or evidence of perineural involvement on frozen section analysis) underwent a resection that included the bone of the cribriform plate, fovea ethmoidalis and the perpendicular ethmoid plate of the nasal septum. In patients where the tumor directly eroded the skull base or in those whose tumor showed perineural spread through the cribriform plate (*i.e.* esthesioneuroblastoma), the resection included an ipsilateral endoscopic craniectomy (resection of the anterior skull base from crista galli to planum sphenoidale) including the removal of overlying dura and the ipsilateral olfactory bulb and tract. Two patients had esthesioneuroblastomas that arose from the middle turbinate and their wide resection did not require a craniectomy. Reconstruction of the skull base involved free tissue grafting in the earlier cases or a pedicled vascular flap (Hadad-Bassagasteguy nasoseptal flap or transfrontal pericranial flap; Figure 1) in the most recent

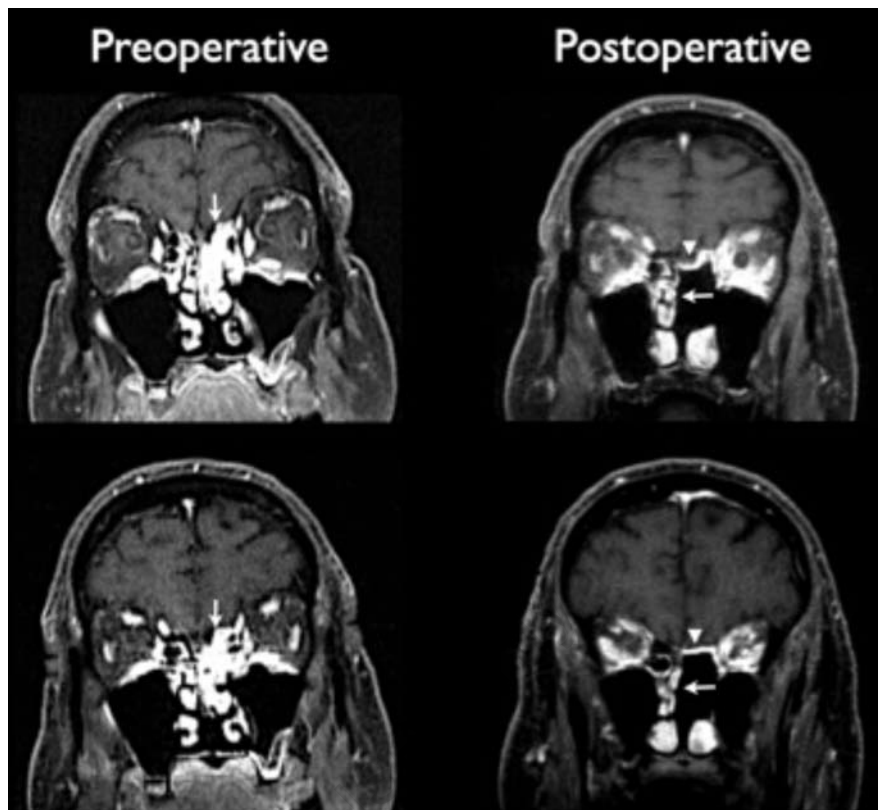


Figure 1. Preoperative and postoperative magnetic resonance coronal images of a patient with a hemangiopericytoma. Vertical arrows in the preoperative images point to the tumor. Arrowheads in the postoperative images point to the nasoseptal flap. Note that the resection extended from the left orbit to the right olfactory cleft preserving the right middle and superior turbinates. This patient had microsmia after surgery.

cases (cases 3, 6, 7, 8 and 9).

According to the extent and histopathology of the tumor, some patients received adjuvant radiotherapy following surgery. All patients continued to be followed with regular endoscopic surveillance and CT/MRI scans. Details such as complication rates, and patients' oncological status were documented.

Results

Table 1 summarizes the pertinent clinical data for our 9 patients; these were 5 men and 4 women with ages ranging from 15 to 73 years at presentation (mean 52 years). Various sinonasal pathologies were encountered, including esthesioneuroblastoma (6 patients), squamous cell carcinoma (one patient), adenocarcinoma (one patient) and malignant hemangiopericytoma (one patient). During this period, we performed an endoscopic anterior skull base resection for 15 esthesioneuroblastomas (ENB), 5 melanomas, 3 adenocarcinomas, one malignant hemangiopericytoma (HPC), 2 chondrosarcomas, 3 sinonasal undifferentiated carcinomas, one Ewing's sarcoma

and 3 squamous cell carcinoma. Only 9 of 33 (27%) patients met the criteria for endoscopic endonasal resection surgery that would attempt to preserve olfactory function (unilateral disease). The remaining group required a bilateral resection of the nasal vault and/or skull base; thus, the resection included all olfactory epithelium and nerves. This group of 24 patients was not tested using a standardized test; however, all had subjective anosmia.

Of the 9 patients with olfaction preservation, 2 patients underwent a resection that included the skull base mucosa (*i.e.* olfactory epithelium) as the superior limit (patients 1 and 5). In 7 patients, the resection involved a unilateral endoscopic craniectomy with preservation of the contralateral middle and superior turbinate. Three of these patients underwent resection of the dura associated to the ipsilateral skull base, as well as resection of the ipsilateral olfactory nerve and bulb (patients 3, 4 and 6). Six patients received adjuvant radiotherapy. The mean follow-up period was 55.7 months (range 22–101 months; median 58.0 months).

Seven patients had some olfactory function postoperatively (3 normosmics and 4 microsmics). One patient had subjective microsmia

preoperatively and remained hyposmic postoperatively. Two of the 3 patients with normosmia had undergone a resection that spared the bone of the anterior skull base. At last follow up, all patients were free of local recurrence. One patient with ENB (case 4) had a nodal recurrence four years after surgery, which was treated with bilateral neck dissections, followed by chemoradiotherapy.

Discussion

Loss of olfaction may follow any endonasal surgery; furthermore, anosmia following a seemingly uneventful endoscopic sinus surgery is not rare. It is postulated that postoperative anosmia may be due to the disruption of the olfactory area, which includes the cribriform plate, superior turbinate, superior septum and parts of the middle turbinate.^{14,15} Most olfactory fibers are concentrated in the area of the cribriform plates and nasal septum. However, they are also present in an area known as the conchal plate.¹⁴ This is an area where the middle, superior and supreme turbinates join and attach to the skull base. Olfactory filaments originating from the olfactory epithelium of the middle and superior turbinates run upwards through the conchal plate, pass through the cribriform plates, and finally enter into the olfactory bulb. Trauma to any of the components of this area may lead to

olfactory dysfunction.

Most olfactory disturbances following endoscopic sinus surgery, however, are temporary. We have encountered this phenomenon following endoscopic pituitary surgery in which most patients who experience postoperative anosmia/hyposmia generally recover their olfaction within three to six months.^{16,17} A recent study by Hart *et al.* also corroborated our experience.¹⁸ These authors studied 57 patients undergoing endoscopic pituitary surgery and reported no significant difference in their preoperative olfactory function and that measured at three months postoperatively using an University of Pennsylvania Smell Identification Test (UPSIT) score.¹⁸

Recovery of olfactory function, however, is exceedingly rare in patients who undergo surgery for malignant tumors of the nasal cavity and paranasal sinuses. Resection with clear margins is of utmost importance in dealing with these tumors; thus, the resection often requires the sacrifice of surrounding structures in order to achieve a complete resection.^{2,19} Use of an endoscopic endonasal technique does not reduce this morbidity, as the principles of surgery and the oncological goal of a complete resection are identical. Resection of the entire anterior skull base including the cribriform plates, olfactory bulbs and nerves will invariably result in permanent anosmia regardless of the approach. An endoscopic resection, however, facilitates a unilateral resection in patients with unilateral neoplasms.

A permanent loss of olfaction may be tolerable; nonetheless, it deprives the patient of two important senses, smell and taste, as taste is significantly affected as a consequence of the loss of olfaction. Efforts to preserve olfaction involve attempting to spare at least some part of the olfactory unit. Spetzler *et al.* described osteotomies around the olfactory unit and resection of the septum more than 1 cm beneath the olfactory plate to elevate the cribriform plate *en bloc* with its associated dura mater during an open craniofacial approach.⁹ This technique, however, only applies to tumors that do not involve the cribriform plate. Similarly, during an endoscopic endonasal resection, only tumors that do not require resection of both cribriform plates may be considered for olfactory preservation.

According to the extent of the tumor, one can attempt to preserve olfaction without compromising the margins of resection; therefore, the first criterion for olfaction preservation requires that the tumor be confined to a single nasal cavity. This allows the preservation of the contralateral olfactory cleft or at the very least the contralateral middle and superior turbinates. Preservation of these structures increases the probability of preserving olfactory function. Browne *et al.* reported a 100% success rate preserving olfaction in patients with unilateral nasal pathology undergoing a modified frontal-subcranial approach for various anterior skull base pathologies.¹³ This was not reproduced in our study. It should be noted,

Table 1. Summary of clinical data.

Patient n.	Age/Sex (years)	Diagnosis	Site of disease	Extent of resection	Adjunctive treatment	Complication	Outcome	Olfaction
1	15/M	ENB	®ethmoid/LP	®sphenoidectomy, MMA, LP, MT, superior nasal vault mucosa	RT	Nil	NED (101 months)	Normosmia
2	68/M	ENB	Prior resection; residual on remnant (L) MT & ethmoid	(L) sphenoidectomy, MMA, MT, (L) CP	Nil	Nil	NED (95 months)	Normosmia
3	57/M	ENB	Prior resection; Residual in (L) ethmoid	(L) endoCrani; posterior septectomy	RT	Nil	NED (27 months)	Hyposmia
4	56/F	ENB	(L) nasal cavity towards CP	(L) endoCrani, septum, crista galli	RT	Nil	Nodal recurrence (87 months)	Anosmia
5	47/F	ENB	®ethmoid, LP	®sphenoidectomy, MMA, LP, MT, superior nasal vault mucosa	RT	Nil	NED (63 months)	Normosmia
6	47/F	ENB	Prior resection; residual at roof of (L) nasal cavity	(L) endoCrani	RT	Nil	NED (29 months)	Hyposmia
7	55/F	SCC	®nasal cavity; attaches to septum & ®olfactory cleft & ®MT	®sphenoidectomy, ®SB, ®MT, septum	RT	Nil	NED (22 months)	Anosmia
8	73/M	HPC	(L) posterior ethmoids, (L) ST, Left posterior SB	(L) sphenoidectomy, (L) MT, (L) SB, posterior septum	Nil	Nil	NED (58 months)	Hyposmia
9	51/M	adenoCA	(L) posterior ethmoid	(L) sphenoidectomy, (L) MT, (L) SB	Nil	Nil	NED (29 months)	Hyposmia

ENB, esthesioneuroblastoma; SCC, squamous cell carcinoma; HPC, hemangiopericytoma; adenoCA, adenocarcinoma; MMA, middle meatal anastomosis; LP, lamina papyracea; MT, middle turbinate; ST, superior turbinate; CP, cribriform plate; SB, skull base; endoCrani, endoscopic craniectomy (includes dura); RT, radiotherapy; NED, no evidence of disease.

however, that Browne *et al.* included only 4 patients with malignant tumors who were mixed with patients presenting benign tumors and patients affected by trauma and meningoencephaloceles.¹³

The second and perhaps the most important criterion is the location of the tumor (site of origin and extent). Tumors located on the lateral aspect of the ethmoid sinus or in the inferior half of the nasal cavity are more favorable for olfactory preservation. Unfortunately, sinonasal tumors commonly occupy the superior half of the nasal cavity. Even tumors that do not involve the skull base may require resection of the mucoperiosteum of the skull base as the superior margin. Disruption of the olfactory unit in these cases is limited; therefore, the probability of olfactory preservation is higher. Tumors that directly involve the skull base may require its resection including the overlying dura and olfactory bulb/tract. These cases rely on the preservation of the contralateral olfactory cleft and/or the middle and superior turbinates.

A third consideration is the tumor histopathology. Benign tumors, as well as low-grade malignancies, are generally better suited for an *olfactory-sparing* technique. Esthesioneuroblastoma, by virtue of its origin from the olfactory roots, usually requires resection of the dura and olfactory bulbs. However, in select cases where the tumor is isolated to a single nasal cavity, one may consider a unilateral endoscopic skull base resection. High-grade tumors such as squamous cell carcinoma (SCC), melanoma or sinonasal undifferentiated carcinoma have more extensive spread and a wide surgical resection is often required to achieve clear margins. Our case of SCC became anosmic despite attempts to preserve olfaction.

Ultimately, the extent of the surgical resection determines the success of olfactory preservation. It follows that the more extensive the resection of the skull base, the lower the probability of olfactory preservation. In our study, the overall preservation rate was 78% (3 normosmic, 4 microsmic). Two patients (cases 1 and 5) who underwent spheo-ethmoidectomies and resection of the skull base mucoperiosteum, and one patient (case 2) with unilateral resection of the anterior skull base, had complete preservation of olfaction. Two patients (cases 8 and 9) who had unilateral resection of the anterior skull base had partial preservation of olfaction. Two of the 3 patients who underwent unilateral endoscopic craniectomies and resection of dura and olfactory bulb (cases 3 and 6) also had partial preservation.

In the 4 patients with postoperative microsmia, the contralateral middle and superior turbinates as well as the olfactory cleft were preserved. Despite the sparing of all these structures, olfactory function was not com-

pletely preserved. We postulate two possible explanations. First, both olfactory clefts must be present to achieve the current definition of normal olfaction (normative data of the standardized test); thus, resecting one cleft increases the olfaction threshold. However, this cannot fully explain why complete preservation was achievable in the first 3 cases where the ipsilateral olfactory cleft mucosa was resected; therefore, there may be an individual variation. Another possibility is that the resection disrupts the contralateral olfactory system or its blood supply. The medial margin of a unilateral cranial base resection is the crista galli and nasal septum. Disruption of these areas can potentially damage the olfactory neuroepithelium along the septum and on the contralateral side resulting in hyposmia/anosmia. The anosmic patient (case 4) following a unilateral cranial base resection underwent a more extensive resection involving the crista galli, which could have disrupted the contralateral olfactory fibers.

Anatomically, preservation of the septum appears to be important for olfactory preservation. Olfactory nerve endings can be identified up to 2 cm below the cribriform plate (range 7-20 mm); therefore, resection of the septum within 2 cm of the cribriform plate can potentially affect olfaction.²⁰ Patient 7 had tumor involving the septum and also underwent extensive resection including both the septum and the ipsilateral skull base. She became anosmic postoperatively. Another possible explanation is that we removed the majority of the olfactory nerve fibers as they are concentrated in the nasal septum and relatively few bundles or nerves are located along the lateral skull base and middle turbinate.²⁰

Other elements are also critical for olfactory function, including preservation of the olfactory neuroepithelium (containing the receptor cells), patency of the nasal cavity and olfactory cleft, and adequate blood supply to the olfactory apparatus (olfactory neuroepithelium, olfactory nerve, and olfactory tract). The olfactory apparatus is supplied by the anterior and posterior ethmoidal arteries and the anterior cerebral artery, all of which anastomose in the area of the cribriform plate. As previously mentioned, surgery in the anterior skull base area can disrupt this blood supply to the cribriform plates resulting in reduced olfaction. This may help to explain why olfaction preservation is difficult and unpredictable.

Similarly, other factors such as age, gender, method of reconstruction (*i.e.* use of the nasoseptal flap), and use of adjunctive therapies may impact the outcome regarding olfactory function. The literature addressing the effects of radiotherapy on olfactory function is sparse. However, both animal models and clinical studies suggest that radiation therapy induces a dose dependent injury on the olfac-

tory apparatus.²¹⁻²⁴ One study followed patients who received radiation for head and neck cancers and found a significant but temporary decrease in olfactory function.²² Others have demonstrated permanent changes in patients who received radiation therapy for nasopharyngeal carcinoma.^{23,24} The latter involves a direct exposure to the radiation and higher doses. We did not find any significant difference among these variables; however, this may be due to the limited number of patients.

We recognize some limitations in our study. In our series, all 9 patients remained without evidence of disease at the local area at a mean follow up of 56 months; although adequate for most types of sinonasal tumors, a longer follow up must be considered for ENB. ENB is known to recur at a mean period of six years after treatment.²⁵ In addition, we recognize several weaknesses regarding the olfactory testing. We used the Sensonics-40 Smell Identification Test (Sensonics Inc., Haddon, NJ, USA). This self-administered test, based on a *scratch and sniff* technique, is the most widely used quantitative olfactory test and is viewed as the standard means for assessing olfactory function in North America.²⁶ It includes 40 microencapsulated odorants that are released by rubbing the microencapsulated strips. The patients' test scores are compared with normative data corrected for age and gender. Based on the test score, the patient can be classified as total anosmia, mild, moderate or severe microsmia and normosmia. However, the evaluation of preoperative olfaction was subjective in most patients. An objective measurement of olfaction prior to surgery may allow a more uniform comparison. In addition, the timing of the test may influence the results. All smell tests were performed within three months of the completion of treatment. It is possible that smell testing at longer follow up would reveal improvement in some of the microsmic patients. Smell identification tests were performed binarily and a no distinction was made between the operated and the contralateral side. Due to the extensive posterior septectomy in many of our patients, the odorants may flow to both sides of the nasal vault regardless of the laterality of the inhalation. However, if it was performed separately, one may be able to detect subtle differences between the two sides. Nonetheless, from the quality of life standpoint, this seems less relevant as long as the airway remains patent in the preserved side. Importantly, the variety in the extent of resection should be taken into consideration. It helps to demonstrate the impact of the extent of the resection. However, the limited number of patients does not allow for a better definition of the impact of multiple other factors that may influence olfaction in this population.

Conclusions

Olfactory preservation is feasible in highly selected patients with sinonasal tumors undergoing endoscopic resection. Postoperative olfaction depends largely on the extent of the resection, which is dictated by the extent of the tumor. Early oncological outcomes appear unaffected in our small series of patients. However, longer follow up is needed for tumors with a tendency toward delayed recurrences, such as esthesioneuroblastomas.

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