



# Expanded Endoscopic Approach for Anterior Skull Base Tumors: Experience of a Multidisciplinary Skull Base Team

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**Abstract:** The aim of this study is to describe the experience of a multidisciplinary skull base team with transnasal endoscopic surgery for anterior cranial base tumors.

A retrospective chart review was conducted on patients who underwent an exclusive expanded transnasal approach to the anterior skull base in the period from December 2014 to November 2015. Data on patient demographics, tumor characteristics, surgical information, imaging, and postoperative complications were collected and analyzed.

From a total of 120 patients with skull base diseases managed by the skull base team, 36 were admitted to this study. The overall complication rate in this series was 16.7%, gross total resection was achieved in 32 cases (88.9%) and postoperative CSF leakage occurred in 5 cases (13.9%).

Our preliminary results confirm that an exclusive endoscopic transnasal approach to the anterior cranial base is a reliable technique with acceptable perioperative morbidity.

**Key Words:** Anterior skull base tumors, endoscopic approach, skull base reconstruction, transnasal resection

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The endoscopic endonasal approach (EEA) is a minimal access technique for the management of midline cranial base pathologies through natural nasal corridors.<sup>1,2</sup> Over the past decades, the EEA was associated with higher rates of cerebrospinal fluid (CSF) leakage than traditional open approaches, due to difficulty in repairing large dural defects.<sup>3</sup> The introduction of the Hadad-Bassagasteguy flap in 2006<sup>4</sup> resulted in a considerable reduction of postoperative CSF leakage rates associated with EEA.<sup>5</sup> The EEA also shows similar rates of gross total resection<sup>3,6</sup> and perioperative mortality<sup>3,7</sup> to open approaches. Furthermore, access through natural corridors avoids complications related to brain retraction and neurovascular manipulation typically required during traditional neurosurgical procedures.<sup>1,6</sup> As a result of these factors, transnasal

endoscopic surgery is actually viewed as a well-established and safe approach, and has expanded its indications to a variety of intra-dural and extra-dural lesions involving the midline cranial base.<sup>2,3,5,7,8</sup>

Along these lines, several authors have analyzed the critical surgical steps and potential predictive factors related to the most common complications of EEA, especially those with regard to CSF leakage, and suggested new operative techniques as a result.<sup>2,3,8–11</sup> Due to the anatomical complexity of the anterior skull base (ASB), an excellent knowledge of nasal corridors, neurovascular structures, and cranial base targets are necessary for successful surgery<sup>12</sup>; collaboration between the otolaryngologist and neurosurgeon is mandatory in all surgical steps, from preoperative planning to skull base reconstruction.<sup>†</sup> Moreover, neoplastic diseases in this anatomical area often show a malignant histopathology, thus making necessary the presence of an oncologist and a radiotherapist. A multidisciplinary approach is therefore essential for the correct management of anterior cranial base pathologies. The aim of this study was to review the experience of the newborn multidisciplinary skull base team at our institution in order to identify potential risk factors of complications related both to surgical issues and to the clinical management of patients. Our results were also compared to the ones reported in literature.

## MATERIALS AND METHODS

We conducted a retrospective study, which included all patients who underwent an exclusive expanded transnasal endoscopic approach to the anterior skull base at Verona University Hospital over a period of 12 months (December 2014 – November 2015). Cases treated with a combined approach (endoscopic plus open craniofacial) were excluded. In addition, only patients managed by members of the skull base team were admitted to the present study. The chart review included patient demographics, pathology, presence or absence of neoadjuvant or adjuvant radiation therapy, preoperative imaging, surgical techniques, intraoperative findings, and complications. All patients were examined until 31 May 2018, thus the minimum follow-up planned for each patient was at least 30 months. Data were recorded in a Microsoft Excel (Redmond, WA) spreadsheet and updated periodically. Statistical significance was assessed using a 2-tailed Fisher exact test. Complications were defined as intraoperative, “early” (arising within 3 months postoperatively) or “delayed” (occurring after 3 months).

## RESULTS

### Patient Demographics

Among a total of 120 patients managed by the skull base team at Verona University Hospital in the period studied, based on inclusion and exclusion criteria, 36 were admitted to this study. Of these, 22 (61.1%) were male and 14 (38.9%) were female. Age at the time of surgery ranged from 21 to 81 years (median 54.9 years). Additional demographic data were collected: smoking was observed in 8 (22.2%) patients, hypertension in 6 (16.7%) patients,

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both dyslipidemia and obesity in 5 patients (13.9%) and diabetes in 4 patients (11.1%).

## Pathology

Surgery was performed for anterior skull base tumors. In the analyzed period 36 cases were treated. Among these neoplastic diseases, 27 (75%) had an intracranial origin and 9 (25%) were derived from the sinonasal tract; sinonasal tumors showed a benign histopathology in 2 cases, while 7 of them were malignant. One of these patients was affected by an RT-induced pleomorphic sarcoma developed after treatment for a giant-cell tumor of the sphenoid bone. Staging for sinonasal malignancies was TIVaNOmO in 3 cases and TIVbNOmO in 4 cases. In 10 cases (27.8%), at presentation, the patients showed a tumor recurrence after failure of previous treatment in other institutes. Specifically, a tumor arising from the sinonasal tract was observed in 4 of these cases: endoscopic resection followed by postoperative radiation therapy (RT) with (1 case) or without (2 cases) concurrent chemotherapy had previously been performed in 4 patients; surgery alone had been performed in 1 patient. In the 6 other patients with recurrent neoplastic disease, an intracranial neoplasm had been previously treated with EEA (3 cases) or traditional craniotomy (3 cases). Tumor characteristics are shown in Supplemental Digital Content 1, Table 1, <http://links.lww.com/SCS/A897>.

## Surgical Data

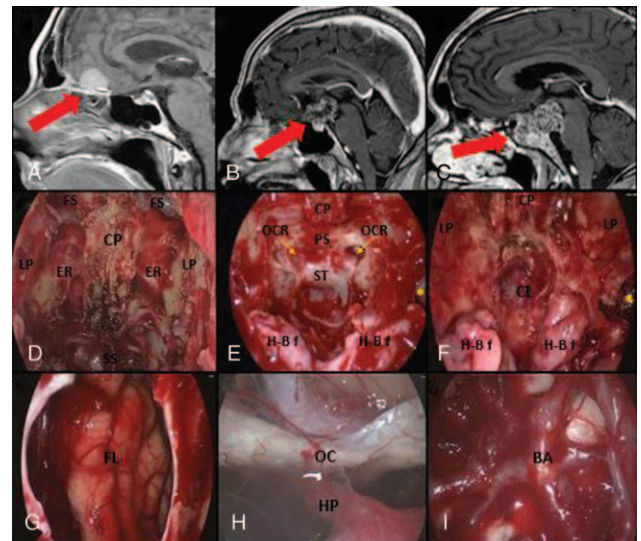
Transnasal resection of malignancies was achieved according to principles described by Castelnuovo et al.<sup>13</sup> The surgical procedure was categorized as follows: nasal corridor and approach to skull base as described by Schwartz et al,<sup>1</sup> extent of resection, type of skull base reconstruction.

## Approach to Skull Base

Based on the location and extent of the tumor, the following corridors and approaches were used: transnasal corridor for a trans-cribriform approach (11 cases; 30.6%), trans-sphenoidal corridor for a trans-sellar (16 cases; 44.4%), transplanum-trans-tuberculum (5 cases; 13.9%) or trans-clival (4 cases; 11.1%) approach. Figure 1 shows 3 different approaches performed in our series depending on tumor location. In all cases, apart from 8 patients in whom tumor recurrence had previously undergone endoscopic surgery, a concomitant trans-ethmoidal corridor was achieved through a complete antero-posterior ethmoidectomy. Partial removal of the nasal septum, already present in 7 patients as a result of previous surgery, was performed in 21 cases to allow dissection maneuvers through both nostrils; in trans-sphenoidal corridors, a concomitant drilling of the sphenoidal rostrum was achieved to optimize visualization of critical landmarks in the sphenoid sinus. In 8 patients showing a significant anterior extension of the neoplasm, an approach to the frontal sinus was performed with the Draf III technique (5 cases) for those requiring bilateral resection, or Draf IIA (2 cases) and Draf IIB (1 case) for those with monolateral extension.

## Extent of Resection

Gross total resection (GTR) was achieved in 88.9% (32 cases) of patients. In the remaining 4 cases (11.1%), GTR was not possible due to the lateral extent of the tumor. In 3 of these (1 giant pituitary adenoma and 2 clival chordomas), the goal of surgery was a decompression without GTR because of the concomitant posterior extension towards the cerebral trunk; these patients were also candidates for postoperative proton therapy. A salvage surgery was performed in the last case, an RT-induced pleomorphic sarcoma, due to the young age (52 years) of the patient.



**FIGURE 1.** Different approaches to the skull base depending on tumor location. Preoperative sagittal MRI demonstrated an olfactory groove meningioma (A), a tuberculum-sellae craniopharyngioma (B), and a clival chordoma with considerable posterior extension (C) treated, respectively, by a trans-cribriform approach (D), a trans-planum trans-tuberculum approach (E), and a trans-clival approach (F). Intraoperative images show intracranial spaces and neurovascular structures after complete tumor resection through trans-cribriform (G), trans-planum trans-tuberculum (H) and trans-clival (I) approaches. BA, basilar artery; CL, clivus; CP, cribriform plate; ER, ethmoidal roof; FL, frontal lobe; FS, frontal sinus; H-B f, Hadad-Bassagasteguy flap; HP, hypophyseal peduncle; LP, lamina papiracea; OC, optic chiasm; OCR, opticocarotid recess OP, planum sphenoidale; PS, planum sphenoidale; ST, sella turcica. The red arrow indicates the trajectory of each approach. The yellow star indicates the posterior wall of maxillary sinus.

## Skull Base Reconstruction

Skull base reconstruction was realized by a multilayer technique, as described by Castelnuovo et al,<sup>13</sup> in 32 patients, while a “gasket-seal” closure<sup>2</sup> was achieved in 4 patients showing large intracranial extension of the tumor. A pedicled vascular flap was harvested in 24 patients (66.7%): single (in 15 cases) or double (in 8 cases) Hadad-Bassagasteguy nasoseptal flap<sup>4</sup> was realized in 23 cases while a middle turbinate flap was achieved in 1 case. Multilayer closure using a combination of intranasal free grafts, fascia lata, and Tutopatch was achieved in 11 patients (30.6%). A galeal flap was harvested in 1 patient (2.8%) with a large anterior defect. A Foley balloon was placed in the nasal cavity in 10 patients (27.8%).

## Complications

We observed a total of 6 complications in 6 of the 36 patients treated, for an overall complication rate of 16.7%. In 1 case, an intraoperative hemorrhage was observed arising from a cavernous sinus. In 5 cases, early postoperative CSF leakage occurred, thus the CSF leakage rate in our series was 13.9%. As shown in Supplemental Digital Content 2, Table 2, <http://links.lww.com/SCS/A898>, in 3 patients, the site of the defect was the sella. No significant difference in CSF leakage rate was found with regard to the location of skull base defects (sella,  $P = 0.6995$ ; clivus,  $P = 0.520$ ; planum,  $P = 1.000$ ). On the other hand, in these 3 cases, a large defect had been created due to the anterior extension of the tumor.

One patient who underwent salvage surgery died 105 days after the operation from a recurrence involving the intracranial spaces: he was a 72-year-old man, previously treated by endoscopic resection plus adjuvant radiotherapy for a sinonasal adenocarcinoma.

Another patient treated for a craniopharyngioma died 76 days after surgery from a cause not related to his disease.

## DISCUSSION

Since its introduction, the transnasal approach has shown similar rates of gross total resection<sup>3,6</sup> and perioperative mortality<sup>3,7</sup> to classical craniofacial approaches. Furthermore, the ventral midline approach through natural corridors avoids complications related to brain retraction and neurovascular manipulation typically required during traditional neurosurgical procedures.<sup>1,6</sup> The main issue with endoscopic resection was the higher risk of postoperative CSF leakage compared with the open approach, due to difficulty in ASB reconstruction, especially when a large defect was created.<sup>3</sup> Thanks to the report on the Hadad-Bassagasteguy flap in 2006<sup>4</sup> the introduction of pedicled intranasal flaps solved this problem leading to a considerable reduction of postoperative CSF leakage rates. Therefore, the transnasal endoscopic approach is actually considered to be a minimally invasive and safe technique and has expanded its application to a variety of intra-dural and extra-dural lesions of the midline cranial base.<sup>2,3,5,7,8,14</sup> From the findings of other authors,<sup>1,13</sup> due to the complexity of this anatomical area, we believe that surgery has to be performed by a surgical team including both otolaryngologists skilled in endoscopic treatment of sinonasal diseases and neurosurgeons experienced with pathologies involving the ASB. Furthermore, considering the malignancies often observed in the ASB, in our opinion, a multidisciplinary approach, also including an oncologist and a radiotherapist, is necessary for their management. For these reasons, a Skull Base Team was created.

Overall, 6 complications were observed among the 36 patients who underwent exclusive endoscopic resection of ASB tumors in our institute. The overall complication rate (16.7%) was consistent with results reported in the literature. In their cohort of 19 patients, Dave et al encountered a total of 16 complications, considering only 2 of these to be major complications directly related to surgical procedures, for a major complication rate of 11%.<sup>14</sup> Batra et al<sup>7</sup> reported 7 major complications in 31 patients (19.4%). In a large Italian series, 184 patients underwent an endoscopic approach for ASB tumors with an overall postoperative complication rate of 8.7%.<sup>15</sup> An exclusive endoscopic resection was performed in just 134 patients (72.8%) while a combined craniendoscopic approach was performed in the remaining 50 (27.2%). Another large review conducted by Hanna et al on 120 patients showed an overall complication rate of 11%.<sup>16</sup>

In several recent studies analyzing ASB tumors, 3 critical issues were considered to be the most relevant outcome measures of endoscopic resection: gross total resection (GTR), recurrence of disease, and postoperative CSF leakage.

Even though preliminary and conditioned by a restricted number of patients, our results are consistent with those reported in the literature. In their large review, Graffeo et al encountered GTR rates of 89.7%, 79.9%, 59%, and 58.8%, respectively for olfactory groove meningioma, tuberculum sellae meningioma, craniopharyngioma, and clival chordoma.<sup>3</sup> In the review conducted by Komotar et al<sup>6</sup> the reported GTR rates were 63.2%, 74.7%, 66.9%, 61%, and 47.2%, respectively for olfactory groove meningioma, tuberculum sellae meningioma, craniopharyngioma, clival chordoma, and giant pituitary adenoma. In order to achieve a complete resection of the tumor, we agree with other authors about the importance of optimal exposure of the surgical field and critical landmarks on the sinonasal side of the skull base. Moreover, a posterior septectomy is useful to optimize dissection by the “2 nostril, 4 hands” technique, thereby allowing better transnasal maneuverability with 2 surgeons working in unison with each other.<sup>13,17</sup> In 4 patients, GTR was not possible. A salvage surgery

was performed in 1 of them affected by an RT-induced pleomorphic sarcoma, due to his young age (52 years). Among the remaining cases (1 giant pituitary adenoma and 2 clival chordomas), the goal of surgery was primarily a decompression because of the concomitant posterior extension of the neoplasm towards the cerebral trunk. In particular, clival chordoma is a locally aggressive tumor and may encase critical neurovascular structures such as the upper cranial nerves, basilar artery or internal carotid arteries.<sup>6,18</sup> Therefore, although many advantages using the endoscopic approach are reported in the literature compared with the classical open approach, its surgical management remains challenging. In a total of 4 cases of clival chordoma encountered in our series, we performed a subtotal resection in 2 patients, leaving small tumoral residuals because of their close bonds with critical vascular structures (internal carotid artery in 1 patient and basilar artery in another). Adjuvant proton therapy was planned for these patients.

Recurrence and disease-free survival are very important issues in evaluating the outcome of endoscopic resections of malignancies.<sup>6,7</sup> In our series, at the time of last follow-up, 33 patients (91.7%) were disease-free, while in 3 cases we observed a recurrence or patient's death as shown in Supplemental Digital Content 3, Table 3, <http://links.lww.com/SCS/A899>. A 56-year-old female patient, affected by a clival chordoma, treated by proton therapy for a small tumoral residual close to the cavernous portion of the left internal carotid artery, showed a recurrence on the left optic nerve after 27 months from the surgery; she underwent transnasal revision surgery and a subtotal removal of the lesion was obtained, leaving a very small tumoral residual. A post-operative MRI has been planned for this patient to plane further decisions. A 72-year-old patient, who failed previous treatment by endoscopic resection with adjuvant radiotherapy for a sinonasal adenocarcinoma, died 105 days after surgery. Another patient died from other causes. These data are limited by the short observational time and we need longer follow-up to yield reliable results.

CSF leakage is considered to be the principal outcome indicator concerning the success of skull base reconstruction. The goal of this surgical step is to reestablish a complete separation of the cranial spaces from the sinonasal cavity, achieving a watertight seal, to avoid potential consequences of CSF leakage such as meningitis or pneumocephalus.<sup>19,20</sup> A variety of reconstructive techniques has been described in the literature, including free grafts, intranasal and extranasal pedicled flaps.<sup>2,4,10,11,19–21</sup> In agreement with other authors, we think that GTR and dead space elimination are critical issues for success. Regarding the type of reconstruction, a multilayered technique gives better results for “surgically created” dural defects and realization of a pedicled intranasal flap is related to a low risk of postoperative CSF leakage.<sup>7,8,9</sup>

In our series, we achieved skull base reconstruction by a multilayered technique in 32 patients and a “gasket-seal” closure technique<sup>2</sup> in 4 patients. The latter was realized in those with a very large dural defect involving the sphenoid boundaries: three cases with a trans-sellar approach with anterior extension of craniectomy to the planum sphenoidale; one case with a trans-clival approach with superior-anterior extension to the sella. The postoperative CSF leakage rate reported in this series (13.9%, five cases) was consistent with results reported in large reviews.<sup>3,8,9</sup> Graffeo et al encountered CSF leak rates of 21.9%, 21.5%, 33.1%, and 16.2%, respectively for olfactory groove meningioma, tuberculum sellae meningioma, craniopharyngioma, and clival chordoma.<sup>3</sup> In the review of Harvey et al the CSF leak rates range from 6.7%, for reconstructions achieved by vascularized intranasal or extranasal flaps, to 15.6% for ASB repairs realized with free grafts.<sup>8</sup> Soudry et al in their large review including 22 studies and 673 patients reported a reconstruction success rate from 67% to 100%.<sup>9</sup> Examining patients showing CSF leakage in our series, we noted 3 large

dural defects through the sella due to anterior extension of the tumor: in 2 cases, reconstruction was achieved by the “gasket-seal” technique and in 1 case by a multilayered technique (Supplemental Digital Content 2, Table 2, <http://links.lww.com/SCS/A898>). Although we respected the main principles in harvesting reconstruction, our experience confirms that the size of the defect remains the most important issue and the most challenging pitfall to solve in cranial base repair.

In patients with a clival defect, during revision surgery, we observed that fat placed to obliterate dead space was not sufficient, thus reinforcing our opinion about the importance of this step during skull base repair. In addition, we would stress the importance of correct postoperative management in preventing CSF leakage. In order to avoid increased intracranial pressure, the patient is confined to bed rest in a supine position for 48 hours after surgery and then moved to a 30-degree position for 1 day before complete mobilization. In addition, we suggest using laxatives to minimize any sudden increase in intracranial pressure during evacuation. After complete mobilization of the patient, a gradual removal of nasal packaging is desirable to prevent postoperative nasal complications such as prolonged nasal crusting or nasal discharge. Regarding this, we agree with other authors that these complications are often underestimated in the literature.<sup>8</sup>

The only intraoperative complication in our series was a hemorrhage arising from a cavernous sinus, observed during removal of a clival chordoma with lateral extension to the parasellar region. We successfully managed this occurrence by a blood transfusion. In our opinion, a preoperative blood unit reserve is mandatory for correct management of this occurrence.

## CONCLUSION

Our preliminary results confirm the expanded endoscopic transnasal approach to anterior cranial base pathologies to be a reliable and safe technique with a low rate of perioperative complications. A multidisciplinary approach with ENT and neurosurgeons working as a team is mandatory in approaching this kind of pathologies. Reconstruction of skull base defect is a critical point and the majority of possible complications can be avoided by a correct reconstructive technique.

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