Endoscopic transnasal craniectomy in the management of selected sinonasal malignancies

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ABSTRACT

Background: *Because of a better understanding of the anatomy from an endoscopic perspective, the acquisition of surgical experience, and concomitant technological advances, endoscopic resection of the anterior skull base (ASB) and overlying dura has now become a reality, opening new possibilities in the management of sinonasal malignancies. Here, the authors review a series of 62 patients, the largest reported to date, who underwent endoscopic transnasal craniectomy (ETC) and endoscopic dural repair for the management of selected sinonasal malignancies. Special emphasis is placed on the surgical technique, technical tricks, choice of materials for endoscopic dural repair, postoperative management, and complications.*

Methods: *From 2004, 62 patients underwent ETC at two referral hospitals, which extended anteroposteriorly from the frontal sinus to planum sphenoidale and laterolaterally from the nasal septum to the lamina papyracea (unilateral resection, n = 28; 45%) or from papyracea to papyracea (bilateral resection, n = 34; 55%). Duraplasty with a three-layer technique was performed using the iliotibial tract and fat tissue.*

Results: *The most frequent histotypes were adenocarcinoma (58%) and olfactory neuroblastoma (22%). Forty-five (73%) patients were previously untreated. The incidence of early (T1–2, Kadish A-B) and advanced (T3–4, Kadish C) tumors was similar. The complication rate was 15%, mostly cerebrospinal fluid leaks (13%). Its prevalence did not correlate with patient age, medical comorbidities, previous treatment, presence of ASB involvement, or whether ETC was mono- or bilateral, but tended to correlate with advanced tumor stage, dural involvement, and the period of treatment. After a mean follow-up of 17.5 months (range, 1–54 months), 58 (94%) patients had no evidence of disease.*

Conclusion: *In correctly selected patients with sinonasal tumors involving the ASB, ETC offers a less invasive alternative than resection by an open approach with an acceptable morbidity.*

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Key words: Craniectomy, duraplasty, endoscopic, reconstruction, sinonasal, surgical technique, transnasal, tumor

Hirschmann pioneered endoscopic nasal examination in 1901,[1] but it took >70 years until Messerklinger began to use endoscopy to treat sinonasal pathology in a minimally invasive fashion, rendering many external approaches obsolete.[2] The gradual broadening of indications from inflammatory diseases of the sinonasal area to neoplastic lesions was a natural and logical evolution.

During the last 10 years, indications for endonasal approaches have expanded as a result of a better understanding of the anatomy from an endoscopic perspective, the acquisition of surgical experience, and concomitant technological advances in instrumentation and image-guided navigation systems. The possibility of achieving an endoscopic resection of the anterior skull base (ASB) and overlying dura with subsequent repair of the defect as first described by Kassam *et al.*[3] has opened new possibilities for management of sinonasal malignancies.

The preliminary experience of our group in the endoscopic management of malignancies of the sinonasal tract began in 1996 at two different University Centers according to a uniform policy in terms of patient selection and surgical techniques and has already been summarized in previous publications.[4–6] This report focuses on a cohort of 62 patients who underwent endoscopic transnasal craniectomy (ETC) and endoscopic dural repair for the management of selected sinonasal malignancies. Special emphasis is placed on the surgical technique, technical details, choice of materials for endoscopic dural repair, postoperative management, and complications.

PATIENTS AND METHODS

Epidemiological and clinical data, surgical reports, pre- and postoperative images, data on adjuvant therapy and complications, and follow-up information of patients with malignant tumors of the sinonasal tract and the adjacent skull base who underwent ETC at the Departments of Otorhinolaryngology of the University of Brescia and Insubria-Varese were retrieved from a database dedicated to neoplasms of the sinonasal tract.[7] All tumors were staged according to the 2002 American Joint Committee on Cancer Staging System,[8] arbitrarily including all histotypes with the exception of olfactory neuroblastoma, which was staged using the Kadish staging system.[9] For statistical analysis, neoplasms staged as T1, T2, or Kadish A-B were classified as early lesions, and those staged as T3, T4, or Kadish C were classified as advanced tumors. ETC was classified as unilateral if the 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 bilateral when it extended from one lamina papyracea to the opposite one. Whenever a lateral tumor extension over the orbital roof or involvement of the anterior wall or lateral portion of the frontal sinus was detected, ETC was considered contraindicated and the endoscopic approach was coupled with subfrontal or frontal craniotomy to gain better exposure of the lesion. All patients were prospectively followed according to a protocol that included monthly endoscopic examinations and MRI every 4 months during the 1st year; endoscopic examination and MRI every 2 and 6 months, respectively, during the 2nd year; and, subsequently, both examinations at 6-month intervals.

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Diagnostic Workup

The preoperative diagnostic workup included MRI with gadolinium enhancement in all cases, apart from patients suffering from claustrophobia who underwent CT with contrast medium. In very aggressive histotypes (*i.e.*, malignant melanoma) a PET scan was obtained to rule out systemic dissemination of the disease. All patients scheduled for ETC were informed about the possibility of switching to a combined cranioendoscopic approach in the presence of an unexpected extensive dural involvement. Informed consent was obtained from all patients.

Exclusion Criteria and Surgical Technique

Contraindications for an endoscopic approach included nasal bones and hard palate infiltration; involvement of the frontal sinus, lacrimal sac, or bony walls of the maxillary sinus (with the exception of the medial one); extension into the pterygopalatine or infratemporal fossa; and involvement of the orbital content. Concerning ASB involvement and intracranial extension, massive infiltration of the ASB and dura or their involvement in close proximity to the lamina papyracea or over the orbital roof detected both in the pre- or intraoperative settings required combining an endoscopic approach with an external one. In contrast, focal contact or suspected infiltration of the ASB or dura of the anterior cranial fossa did not preclude an endoscopic dural resection. At present, the only intradural structures amenable for endoscopic resection are the olfactory bulb and tract.

Fluorescein was routinely injected intrathecally to exclude cerebrospinal fluid (CSF) leak at the end of duraplasty. One milliliter of fluorescein 20% was diluted in 3 mL of bidistilled water, and 1 mL of this solution was further diluted in 9 mL of the patient's CSF and then injected just before surgery.

Although the surgical technique slightly varied in individual patients according to the site of origin and extent of the lesion, ETC included five main surgical steps:

1. The operation was usually started by debulking the tumor with powered instrumentation and/or cutting instruments to more clearly assess the possible site of origin of the lesion.
2. Subperiosteal dissection of the nasoethmoidal–sphenoidal complex was subsequently performed. The frontal sinus was approached by Draf IIb sinusotomy[10] in case of monolateral ETC, whereas Draf III median sinusotomy[10] was performed if the ETC involved both sides. Multiple biopsy specimens from mucosal surgical margins were routinely sent for frozen sections.
3. Completion of the ethmoid roof exposure with removal of the whole mucosa and bony partitions was made using a drill with a diamond burr. The crista galli was carefully detached from the dura and removed. To avoid dura iatrogenic lesions during endoscopic resection of the crista galli, the dura must be carefully detached from the underlying bone by means of blunted instruments. When the tumor was in close proximity or frankly involved the lamina papyracea and the nasal septum, these were included in the dissection.
4. The key point to subsequently perform an optimal skull base reconstruction was to properly dissect the dura over the orbital roof(s) laterally, the planum sphenoidale posteriorly, and the posterior wall of the frontal sinus anteriorly before starting the resection of the dura itself (Fig. 1). The dura was subsequently cauterized with a bipolar, incised and circumferentially cut with angled scissors far enough from the suspected area of tumor spread. The specimen, which included the residual tumor, the mucosa of the olfactory niche(s), the ASB, and the overlying dura together with one or both of the olfactory bulbs, was removed through the nose. The dural margins were verified by frozen sections.
5. Endoscopic duraplasty was performed with a three-layer technique. Reconstruction was preferably performed using autologous material. In our experience, the iliotibial tract (ITT) has the best characteristics in terms of thickness, pliability, and strength. It is a continuation of the fascia lata at the lateral aspect of the thigh extending from the iliac crest to the infracondylar tubercle of the tibia (Gerdy's tubercle), with an average length of 400 mm and average width of 90 mm.[11] Its average thickness at the level of the femoral condyle varies from 2.2 to 1.6 mm in inverse proportion to the patient's age.[12] The ITT was harvested in the middle third of the thigh (10 × 6 cm) together with subcutaneous fat. The wound was closed with double subcutaneous suture to avoid muscle prolapse. For the first, intradural layer of duraplasty the graft 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 ASB. Pieces of fatty tissue were adopted to eliminate the dead space between the second and third layers and to flatten the residual denuded ASB. The third, extracranial layer had to cover all the exposed ASB, but not overlapping the frontal sinusotomy(ies). Each layer was properly fixed with fibrin glue (Fig. 2). At the end of the procedure, the frontal sinus(es) was (are) stented with rolled silastic sheath(s) to allow subsequent frontal sinus debridement with no risks for the duraplasty. The surgical cavity was packed with finger gloves filled with Lyofoam (Seton Health Care Group, Oldham, U.K.).

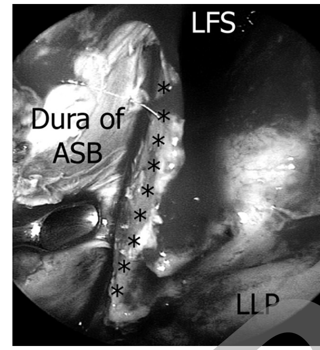

Figure 1. *Left nasal fossa, intraoperative view with a 45° angled telescope: detachment of dura from the anterior skull base (asterisks) with a blunt instrument. LFS = left frontal sinus; LLP = left lamina papyracea.*

Perioperative Management and Adjuvant Therapy

All patients underwent a CT scan of the brain on the 1st postoperative day to rule out complications and evaluate the extent of pneu-

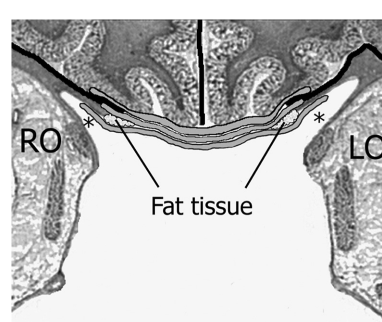

Figure 2. *Schematic illustration of the three-layer duraplasty technique, coronal section at the level of the cribriform plate. RO = right orbit; LO = left orbit; asterisk indicates supraorbital recess.*

mocephalus. Patients were kept on full bed rest in a 30° upright position until the 3rd postoperative day. Nasal packing was gradually removed within 48 hours. A third-generation cephalosporin was started i.v. the day before surgery and continued for at least 5 days. Nasal irrigation with saline solution and application of bacitracin ointment twice daily were recommended for at least 2 months.

Postoperative radiotherapy (RT) was planned in case of significant skull base involvement (pT3), intracranial extension and dural infiltration (Kadish C and pT4a), close margins to the orbital content or the frontal sinus, and in cases of unresectable residual disease.

Statistical Analysis

A commercially available computer software package (SPSS for Windows, Version 10.0.1, 1999; SPSS, Inc., Chicago, IL) was adopted and survival estimates were calculated by the Kaplan-Meier method. The impact of different variables on the prevalence of CSF leak was evaluated by Fisher's exact test. A value of $p < 0.05$ was considered statistically significant.

RESULTS

From April 1996 to December 2008, 190 patients affected by malignant tumors of the sinonasal tract were treated by pure endoscopic resection at two referral University Hospitals. Since 2004, 62 patients of these underwent ETC. The patient population included 18 (29%) women and 44 (71%) men, aged from 25 to 84 years (mean, 61.7 years; median, 65 years). Twenty-nine patients (47%) had at least one significant medical comorbidity. Forty-five patients (73%) presented with a previously untreated tumor and 17 patients (27%) presented with persistent or recurrent disease after previous treatment(s): 14 underwent endoscopic surgery, which was combined with RT in two cases; chemotherapy, RT, and concomitant chemoradiation was delivered in one case each.

Olfactory neuroblastomas accounted for 22% ($n = 13$) of the tumors and were classified as follows: A in two cases (15%), B in six cased (46%), and C in five cases (39%). Table 1 lists the tumor histology and postoperative T staging of other lesions. At presentation, only one patient with melanoma had positive lymph nodes and underwent neck dissection (pN2b).

In 49 cases, tumor arose from the ethmoid; in 4 from the olfactory fissure; in 2 from the sphenoid, superior turbinate, nasal septum and nasal fossa each; and in 1 from the olfactory bulb. According to histopathological examination, ASB was involved by the tumor in 36 (58%) patients and the resected dura was involved in 14 (23%) cases (5 adenocarcinomas, 5 olfactory neuroblastomas, 1 squamous cell carcinoma, 1 adenoid cystic, 1 adenosquamous, and 1 fibrosarcoma). Macroscopic intradural infiltration was intraoperatively recognized in 4 of these 14 patients, confirming in all cases the preoperative MRI finding of suspected intradural extension without brain infiltration

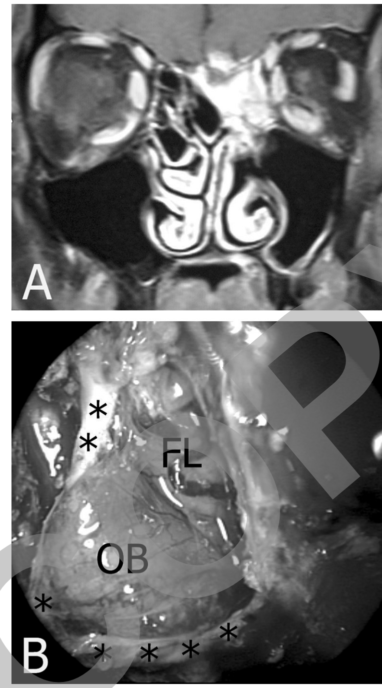

Figure 3. *MRI SE T1 after contrast agent administration on coronal plane: (A) olfactory neuroblastoma of the left nasal fossa with suspected involvement of the olfactory bulb without visible brain edema. (B) left nasal fossa, intraoperative view with a 45° telescope. The olfactory bulb (OB), clinically infiltrated, appears to be in contact with the uninvolved frontal lobe (FL). The asterisks indicate the anterolateral margin of the dura being resected.*

(Fig. 3). Unilateral ETC was performed in 28 (45%) cases and bilateral ETC in 34 (55%) patients.

There were no cases of perioperative mortality and no intraoperative complications. Postoperative complications were observed in nine (14.5%) patients. One (1.5%) case of septic fever was successfully treated with i.v. antibiotic therapy. There were eight (13%) cases of CSF leak, 3 of which required endoscopic surgical revision of duraplasty under local anesthesia (5%); the remaining cases resolved after lumbar drainage placement. Correlation between CSF leak rate and different variables is summarized in Table 2.

The mean hospitalization time was 11 days (range, 5–32 days). Overall, 35 (56%) patients received adjuvant treatment: RT in 32, chemotherapy in 1, and a combination of both in 2. One patient planned for irradiation refused treatment. No patients were lost to follow-up.

Table 1 **Tumor histology and postoperative T staging of the lesions other than olfactory neuroblastoma**

Tumor Histology	No. of Patients	Percent	pT1	pT2	pT3	pT4a	pT4b
Adenocarcinoma	36	58	7	12	9	2	6
Malignant melanoma	3	5	—	2	1	—	—
Adenoid cystic carcinoma	2	3	1	—	—	—	1
Hemangiopericytoma	2	3	1	—	—	1	—
Squamous cell carcinoma	2	3	—	—	1	—	1
Adenosquamous carcinoma	1	1.5	—	—	—	—	1
Fibrosarcoma	1	1.5	—	—	—	—	1
Plasmacytoma	1	1.5	—	—	1	—	—
Extrapleural solitary fibrous tumor	1	1.5	—	1	—	—	—
Total (n)			9	15	12	3	10
Total (%)			18	31	25	6	20

Table 2 **Cerebrospinal fluid (CSF) leak rate in relation to different variables**

Variable (*n*)	CSF Leak Rate (%)	*p* Values
Medical comorbidity		0.13
Yes (29)	7	
No (33)	18	
Previous treatment		0.62
Yes (17)	11.8	
No (45)	13.3	
Stage		0.06
T1, T2, A (27)	3.7	
T3, T4, B, C (35)	20	
ASB involvement		0.26
Yes (36)	17	
No (26)	8	
Dural involvement		0.07
Yes (14)	29	
No (48)	8	
Extent of ETC		0.20
Monolateral (28)	7.1	
Bilateral (34)	17.6	
Institution		0.26
Brescia (26)	7.7	
Varese (36)	16.7	
Period of treatment		0.07
2004–2006 (21)	23.8	
2007–2008 (41)	7.3	

ASB = anterior skull base; ETC = endoscopic transnasal craniectomy.

After a mean follow-up of 20.5 months (range, 4–57 months), 58 (94%) patients had no evidence of disease. The recurrence rate was 6.6%: two patients affected by adenocarcinoma died of unresectable local recurrence 15 and 39 months after ETC. In contrast, two patients affected by malignant melanoma or adenocarcinoma were treated for persistent/recurrent disease by an external approach 2 and 12 months after ETC, respectively, and are deemed free of disease at the time of writing. In two cases an unresectable tumor remnant was irradiated with curative intent. According to the last follow-up imaging, one has persistent disease at the orbital apex and the other has a stable asymptomatic lesion close to the paraclival internal carotid artery. Five-year overall, disease-specific, and recurrence-free survival was 79.6, 80.8, and 85.4%, respectively (Fig. 4).

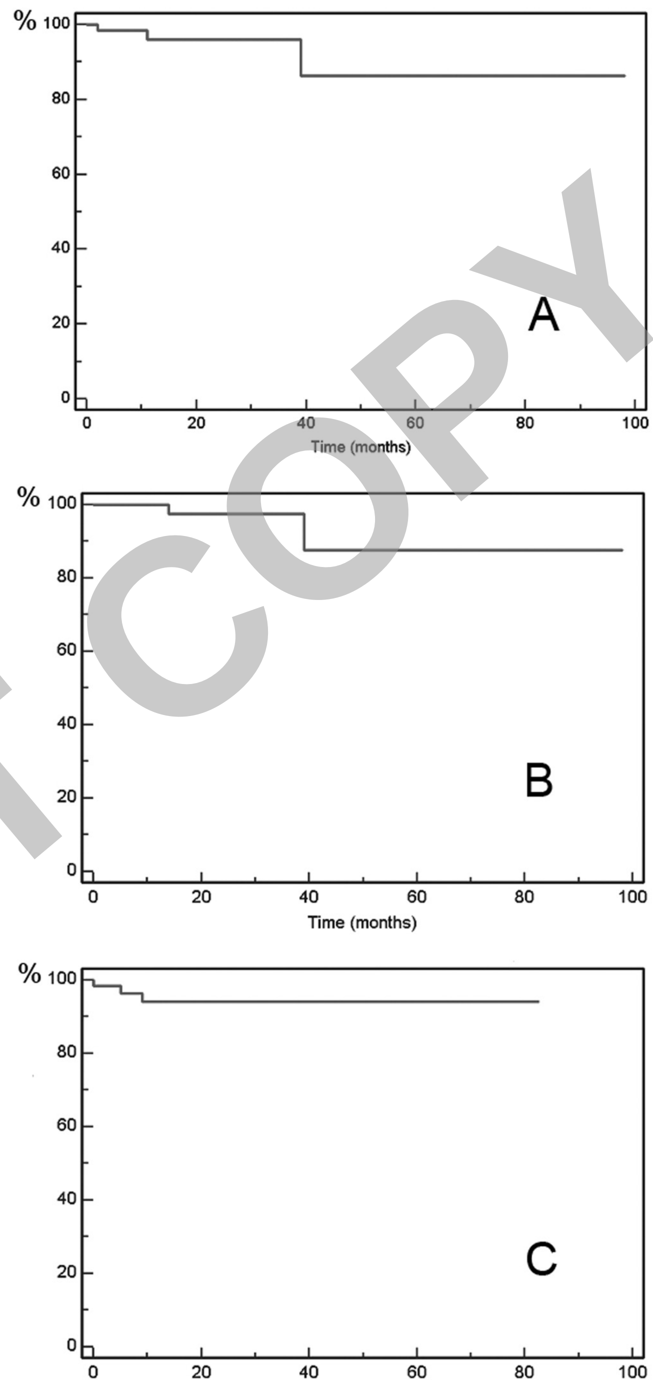

Figure 4. *Five-year (A) overall, (B) disease-specific, and (C) recurrence-free survival Kaplan-Meier curves after ETC.*

DISCUSSION

Malignant tumors of the sinonasal tract are rare, accounting for 3% of all head and neck malignancies. They are characterized by late diagnosis that is related to the silent growth of the lesion during the early phase and by a wide histological heterogeneity.

Traditional open approaches for sinonasal malignancies include lateral rhinotomy, midface degloving, and craniofacial resection (CFR). Proponents of these approaches strongly support prognostic implications of the so called "*en bloc* resection," despite significant morbidity, although a piecemeal removal has not been clinically established to adversely affect either the local recurrence rate or the survival.[13–15] Furthermore, endoscopic surgery offers a number of potential advantages that include less postoperative pain, shorter hospital stay, and a lower complication rate in terms of mortality and morbidity. In addition, endoscopic resection allows precise localization of the tumor origin, which is often surprisingly limited despite a bulky mass filling of the nasal cavity.[16] The extent of the resection can be tailored to specific tumor characteristics (histotype, site of origin, and proximity to critical areas) preserving uninvolved structures with subsequent reduced functional sequelae.

The complications associated with endoscopic skull base reconstruction include persistent CSF leak, intracranial infection, hemorrhage, pneumocephalus, and sinusitis. The complication rate in our series was 14.5%, lower than in previously reported series of exclusively endoscopic resection (20–47%)[17–19] and far lower than the mean rate of CFR in reported series (30–54%).[20,21] As in other published series of ETC,[17–19] there were no fatalities among our patients. In contrast, the mortality rate in CFR has been reported to range from 1.6 to 7.6%.[20,21] These tendencies are supported by the data of Batra *et al.* from a single study comparing CFR (16 patients) and ETC (9 patients) performed at the same institution: while the tumor staging distribution was comparable between two groups, the rates of complications and mortality were lower after minimally invasive endoscopic resection (69% versus 33% and 27% versus 0%, respectively).[15]

The CSF leak rate in our series decreased during the reported period. We can hypothesize that, along with the learning curve, this improvement may be caused by a gradual shift to autologous grafts such as fascia lata, mucoperiosteum, mucoperichondrium, ITT and fat tissue, and a standardized full three-layer reconstruction. Overall, in the present series the CSF leak prevalence was 13%, similar to the reports of Snyderman and Carrau group[17,18] who used collagen matrix (DuraGen), and Batra *et al.*,[15] who used various types of grafts. Harvey *et al.* advocate for pedicled mucosal flaps based on the CSF leak rate of 3.2%.[22] Additionally, the CSF leak rate further decreased to 7.3% in the latter 2 years when ITT and fat tissue were routinely used. As reported in the literature, a higher prevalence of postoperative CSF leak is related to large tumors.[23] Other risk factors include increased intracranial pressure and preoperative CSF leak.[24,25] These data are supported by our findings of a higher prevalence of postoperative CSF leak in patients with advanced tumors and dural involvement. Moreover, ASB involvement and the extent of craniectomy had no influence on CSF leak rate. In the CFR series, the CSF leak rate ranged from 1 to 2.5%[21,26] to 7 to 16%.[27–32] Postoperative meningitis has been reported in 1–9% of CFR cases[21,26–29,31,33] and was never observed in the present series.

In contrast to the findings of Ganly *et al.*[20] in patients treated with CFR, in our series medical comorbidities and previous treatment, particularly RT, were not associated with higher postoperative complication and mortality rates. Given also the relatively low complication rate, ETC might be the preferable solution for patients with high operative risk. On the other hand, the more restricted inclusion criteria for ETC have to be kept in mind and may partially explain the lower complication rate of this approach. Also, the percentage of previously treated patients in our series (27%) was lower than in the series of CFR published by Ganly *et al.*[20] and Howard *et al.*[21] (59 and 51%, respectively).

It can be surmised that the results of an endoscopic approach should be at least similar, if not better, than conventional CFR, at least in the short term, given the selection of patients with less advanced disease. Indeed, 5-year overall, determinate and recurrence-free survival rates in our series were 79.6, 80.%, and 85.4%, respectively. Five-year overall and recurrence-free survival rates for open surgical approaches range from 40 to 65% and 41 to 59%, respectively.[16,20,33] Factors that were recognized to affect survival are involvement of the brain, the lateral wall of sphenoid, and deep involvement of the orbit.[20,32]

These factors are actually contraindications for ETC. Periorbital and dural involvement did not influence the survival after CFR[32] but, on the other hand, do not preclude an exclusively endoscopic approach. The aforementioned factors can explain the relatively high survival rates in the present series but emphasize the difficulty of performing a proper comparison of oncologic results obtained with the two approaches. Moreover, it is difficult to speculate on the long-term results of ETC because of the evidently short follow-up period, and additional studies with larger cohorts of patients are warranted.

CONCLUSION

This largest series of ETC reported to date shows that, in properly selected patients, the method offers a less invasive alternative for radical resection of sinonasal tumors involving the ASB. One of the important prerequisites of success appears to be the use of three-layer ASB reconstruction with ITT and fat tissue allowing for significant reduction of the postoperative CSF leak rate in the last years. The improvements in surgical instrumentation and experience acquired during an 11-year period in endoscopic management of sinonasal malignancies have undoubtedly contributed to expanding the indications for this approach. ETC is a safe procedure with an acceptable complication rate and allows wide resection of the anterior ASB dura, correctly assessing its involvement, and, consequently, better defining the need for adjuvant treatment. The surgeon must be able to switch to an external approach if preoperative planning understages tumor extent.

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