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ORIGINAL ARTICLE

Transnasal endoscopic surgery in selected nasal-ethmoidal cancer with suspected brain invasion: Indications, technique, and outcomes

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Abstract

Background: In nasal-ethmoidal malignancies, brain involvement is associated with dismal prognosis.

Method: Patients undergoing endoscopic resection with transnasal craniectomy and subpial dissection (ERTC-SD) for brain-invading nasal-ethmoidal cancer between 2008 and 2016 were included. Complications were analyzed in all patients, whereas oncological outcomes only in patients with pathological brain invasion. The prognostic impact of previous treatments, brain edema, and histology was assessed. Hospitalization ratio was calculated.

Results: Nineteen patients received ERTC-SD and 11 had pathological-proven brain invasion. Histologies were 6 olfactory neuroblastomas (ONB), 3 neuroendocrine carcinomas, and 2 intestinal-type adenocarcinomas. Mean follow-up was 21.9 months. Three-year overall, local recurrence-free, and distance recurrence-free survivals were 65.5%, 81.8%, and 68.2%, respectively. Overall and distant recurrence-free survivals were significantly better in patients with ONB ($P = 0.032$ and $P = 0.013$, respectively). Hospitalization ratio was 4.1%. Complication rate was 10.5%.

Conclusion: In selected nasal-ethmoidal tumors with brain invasion, ERTC-SD can provide good local control, satisfactory survival, and limited morbidity.

KEYWORDS

brain, endoscopy, ethmoid sinus, nasal cavity, neoplasms

1 | INTRODUCTION

Nasal-ethmoidal cancers are rare and are frequently locally advanced at presentation. They are characterized by a wide variety of histologies, with a remarkable impact on prognosis and treatment strategies.[1,2] Transnasal endoscopic surgery (TES) has progressively become the mainstay of treatment.[3–13] In the last decades, continuous evolution of indications has been observed as the result of increasing surgical expertise and improvements in technology. For instance, transdural extension of the tumor was formerly considered a contraindication to purely endoscopic treatment, whereas several experiences recently demonstrated both the technical feasibility and oncological adequacy of TES in selected cases.[3,8]

Brain involvement is universally recognized as a poor prognosticator.[14–17] Intuitively, survival worsens stepwise when tumor extension progress from bony skull base to dura and brain.[16,18] Brain invasion is generally considered as a contraindication to pure TES. In fact, craniofacial or cranioendoscopic resections provide more effective identification of

the limit between non-invaded brain and tumor together with adequate exposure of involved vessels.

Nevertheless, craniofacial resection is associated with higher morbidity, longer hospitalization, and a non-negligible mortality rate, thus considerably impacting patients' quality of life.[16,19,20] This aspect acquires relevant importance when considering life expectancy of patients. Therefore, the combination of poor prognosis and surgical morbidity has led some surgeons to question the opportunity to embark in surgery, especially in tumors with large brain invasion and/or highly aggressive histology.

In recent years, our two teams progressively introduced the resection of sinonasal cancers with limited brain invasion via a purely transnasal endoscopic procedure (ERTC-SD: endoscopic resection with transnasal craniectomy and subpial dissection) in surgical practice. The rationale to expand the indications for TES was related to three possible purposes: achieve complete resection, reduce morbidity, and improve quality of residual life.

The aim of the present study is to analyze our preliminary experience and explore the technical feasibility of ERTC-SD, associated morbidity, and oncological outcomes. Moreover, we focused on possible parameters for patient selection.

2 | PATIENTS AND METHODS

The institutional database on sinonasal cancers of the Units of Otorhinolaryngology - Head and Neck Surgery of the Universities of Brescia and Insubria-Varese were retrospectively analyzed. Among patients undergoing endoscopic resection with transnasal craniectomy, those who received ERTC-SD with curative intent for a nasal-ethmoidal malignancy between July 2008 and December 2016 were included. All patients were preoperatively studied with contrast-enhanced MRI, biopsy of the lesion, and positron emission tomography (PET) or total body contrast-enhanced CT. Patients with distant metastasis at presentation were excluded. Well-established indications and contraindications to TES for nasal-ethmoidal cancer were followed.[3] In addition, ERTC-SD was performed for tumors with suspected brain invasion extended to gyrus rectus and medial orbital gyrus, without dural extension along the superior sagittal sinus (Figure 1). All patients were informed about the possibility of intraoperative switch to a cranioendoscopic resection (ie, transnasal endoscopic resection with the addition of a transcranial subfrontal approach via bicoronal incision), if required.

Demographics, previous treatment, histology (defined in accordance with 4th edition of WHO Classification of Head and Neck Tumours),[21] TNM classification (8th edition), evidence of brain invasion, edema at preoperative MRI, margin status, duration of hospitalization, postoperative complications, and adjuvant treatments were analyzed. Noteworthy, margin status was considered positive whenever the dural margin of the surgical specimen was at least focally infiltrated, even in case of simultaneous negativity of intraoperative sampling of the same margin.

Oncological outcomes were investigated only in patients with confirmation of brain invasion at pathological examination. Survival estimates for overall survival (OS), disease-specific survival (DSS), recurrence-free survival (RFS), locoregional control (LRC), and distant recurrence-free survival (DRFS) were performed with the Kaplan-Meier method. The impact on oncological outcomes of primary vs recurrent presentation, histology, status of margins, and presence of cerebral edema at preoperative MRI was analyzed with a log-rank test. The "hospitalization ratio" (defined as the ratio between the days of hospitalization and days alive after surgery)[22] was calculated in the subset of patients dead of disease to provide an estimate of the impact of hospitalization on residual life. The volume of the intracranial portion of the tumor was measured on the coronal plane of the most representative MRI sequences using the region of interest function for image analyses of Osirix (Pixmeo SARL, Bernex, Switzerland).

Analysis of complications was performed on all patients receiving ERTC-SD, regardless of histological evidence for brain invasion. The rate of complications of patients having received ERTC-SD was compared with that of patients treated with standard endoscopic resection with transnasal craniectomy without subpial dissection by means of the Fisher's exact test.

2.1 | Surgical technique and postoperative care

Surgical technique for endoscopic resection with transcranial craniectomy has already been described.[3,4,8] Briefly, surgery started with tumor debulking aimed to identify tumor origin and create a working space. Next, the mucosa of the nasal fossa (lateral wall, vault, and septum) was removed together with the ethmoid box following a subperiosteal plane in a centripetal direction toward the insertional site of the tumor. In case of bilateral extension of the tumor, this step was performed in both nasal cavities and the nasal septum was removed. Draf 3 frontal sinusotomy and wide sphenoidotomy were performed. Subsequently, the bony anterior skull base (ethmoid roof, cribriform plate, crista galli, and anterior portion of the planum sphenoidale) was removed and the overlying dura resected together with the olfactory bulbs and tracts (Figure 2A,B). The interface between the intradural portion of the tumor and brain circumvolutions (gyrus rectus and medial orbital gyrus) was inspected with a dissector to identify areas showing tight adhesions suspicious for brain invasion (Figure 2C,D). Medial orbitofrontal vessels crossing the targeted area were carefully cauterized or clipped (Figure 2D). A subpial sharp dissection was performed with the intent to leave a cuff of healthy cerebral parenchyma around the tumor (Figure 2E). The specimen including the infiltrated brain was sent for definitive histological

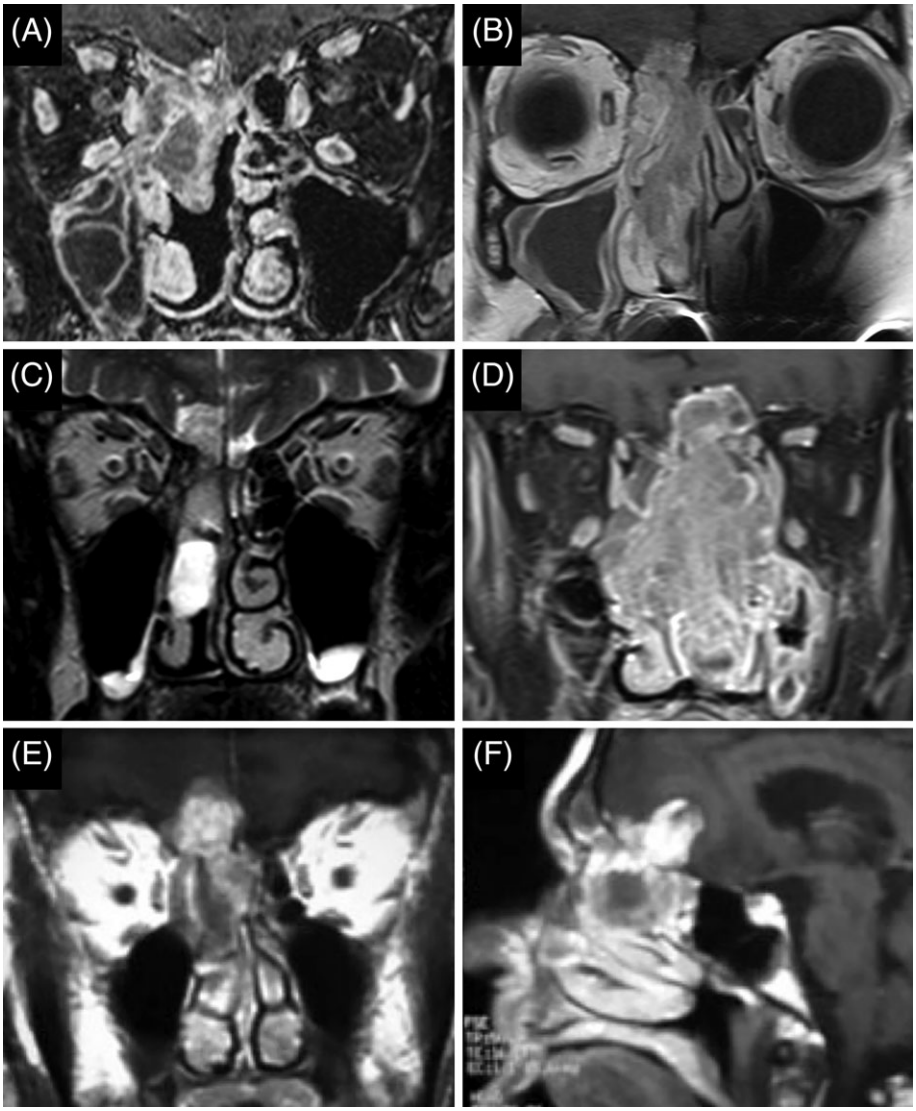

FIGURE 1 Preoperative MRI of patients #1, #4, #6, #9, and #10. A, T1-weighted, contrast-enhanced coronal section with fat saturation of patient #10. B, T1-weighted, contrast-enhanced coronal section of patient #9. C, T2-weighted, coronal section of patient #6. D, T1-weighted, contrast-enhanced coronal section with fat saturation of patient #4. (E,F) T1-weighted coronal and sagittal sections of patient #1

examination. The margin status of the surgical bed and dural boundaries was checked with frozen sections. Hemostasis was achieved with bipolar cauterization. An ultrasonic curette was used at the discretion of the surgeon to extend and regularize the bed of cerebral resection with better control of bleeding, limited thermal damage, and minimal brain manipulation. Finally, an oxidized cellulose-based biodress was carefully laid on the area of brain resection (Figure 2F). Skull base reconstruction was realized with a three-layer duraplasty with the iliotibial tract.[23] The main steps of surgical technique of ERTC-SD are summarized in Supplementary Information Video S1.

Patients were transferred to the intensive-care unit for the first 12-18 hours after surgery, with bed rest and head elevation not exceeding 45° for 48-72 hours. Neurological status was periodically checked; brain non-contrast-enhanced CT was performed on the first postoperative day to exclude severe acute complications (ie, massive pneumocephalus, relevant brain edema, subarachnoid hemorrhage, parenchymal hematoma). Antibiotic crossing the blood–brain barrier and antithrombotic prophylaxis were administered. Patients were discharged when skull base reconstruction was consolidated (no sign of CSF-leak at endoscopic examination) and general conditions were stable.

The oncological follow-up was scheduled as follows: endoscopic examination every 2 months with MRI every 4 months during the first year, endoscopic examination and MRI every 6 months from the second to the fifth year and annually thereafter. A PET or a total body contrast-enhanced CT scan was also performed every 12 months for high-grade tumors.

3 | RESULTS

Of a total of 305 patients undergoing endoscopic resection with transnasal craniectomy for sinonasal cancer in

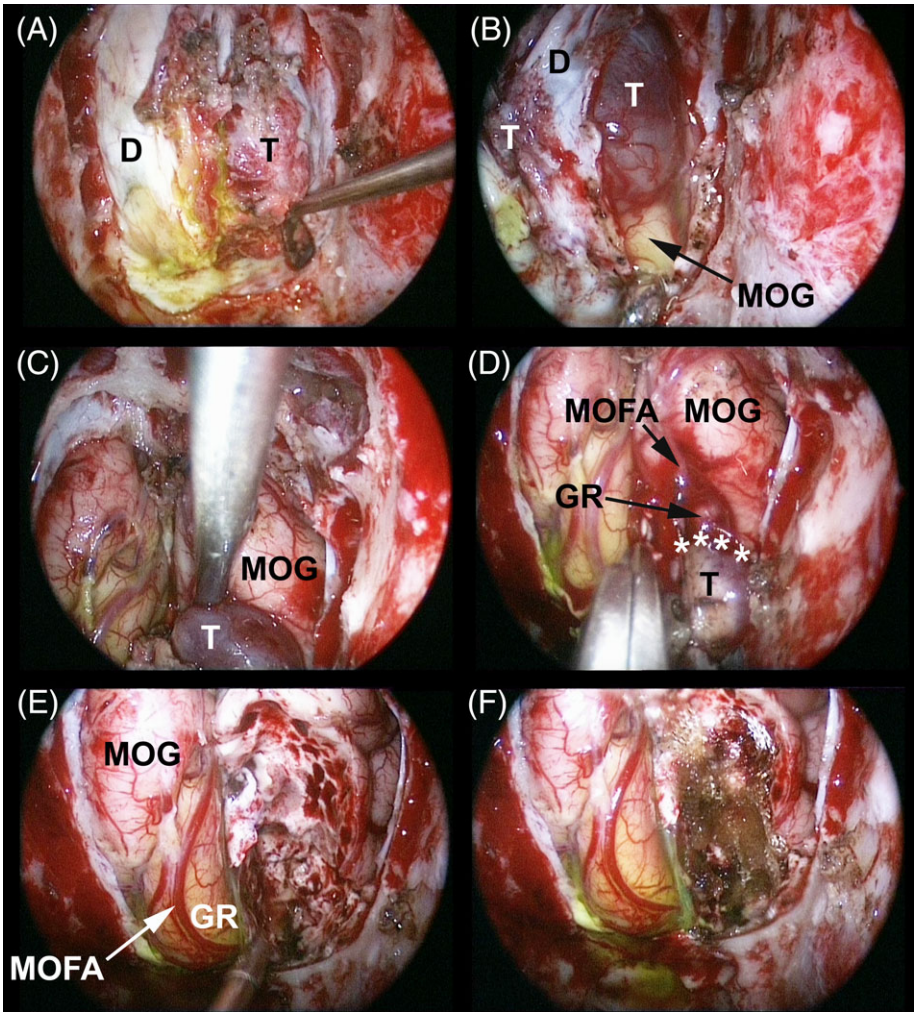

FIGURE 2 Endoscopic resection with transcranial craniectomy and subpial dissection of nasoethmoidal tumors: Surgical technique (patient #5). A, Surgical field after completing bony craniectomy: The dura mater (D) of the midline anterior skull base was completely exposed, demonstrating transdural extension of the tumor (T) at the level of the left olfactory groove. B, View of the transdural growth of the tumor, with a large intradural portion adherent to the medial orbital gyrus (MOG). C, The dissection of the tumor from the brain was started anteriorly, checking for adhesion areas. D, The tumor was progressively detached from the brain surface until a tight adhesion area (white asterisks) was identified between the tumor, gyrus rectus (GR), and medial orbital gyrus. The left medial orbitofrontal artery (MOFA) crossed the adhesion area and was therefore coagulated. E, Subpial dissection of the left gyrus rectus and medial orbital gyrus was performed and the bed of resection was accurately mapped with frozen-section biopsies. F, An oxidized cellulose-based biodress was carefully laid on the area of brain resection [Color figure can be viewed at wileyonlinelibrary.com]

the period from July 2008 to December 2016, 19 (6.2%) underwent ERTC-SD for preoperative or intraoperative evidence of brain invasion. The procedure was never switched to a cranioendoscopic resection. Brain infiltration was confirmed at final histological examination in 11/19 (57.9%) cases, which were included in the oncological analysis.

3.1 | Oncological outcomes

Clinical-pathological features of the 11 patients included in the oncological analysis are summarized in Table 1.

Mean age at diagnosis was 63.5 years (range: 36-79), and male-to-female ratio was 2.7. Four (36.4%) patients received treatment prior to referral to our centers: 2 patients underwent surgery and postoperative radiation therapy, 1 patient induction chemotherapy (with good response) and subsequent chemoradiation, and 1 patient induction chemotherapy with poor response. The latter case was considered a primary tumor because the patient did not receive treatment with curative intent before undergoing ERTC-SD. Therefore, 3 recurrent tumors (27.3%) were included in the series.

Six (54.5%) patients had an olfactory neuroblastoma (ONB) (1 grade I, 4 grade II, and 1 grade III according to Hyams); the remaining histologies were 3 sinonasal neuroendocrine carcinomas (SNEC; 2 small cell and 1 mixed adenoneuroendocrine carcinoma), and 2 intestinal-type adenocarcinomas (ITAC; 1 solid and 1 mucinous signet-ring cell). Given the inclusion criteria, all patients had a pT4b tumor; no nodal or distant metastases were observed at presentation. Brain invasion was suspected at preoperative MRI in all patients except 1 (90.9%) in which it was detected intraoperatively, whereas brain edema was detected only in 3 (27.3%) patients (Figure 1). Mean intracranial tumor volume was 1.81 cm^3 (range: 0.64-4.02 cm^3). Positive margins were

TABLE 1 Main clinical–pathological information on patients who underwent endoscopic resection with transcranial craniectomy and subpial dissection for nasoethmoidal tumors with histologically proven brain invasion

Patient	Sex	Age	Year	Previous treatment	Histology (subgroup)	Brain invasion at preoperative MRI	Brain edema at preoperative MRI	Margin status (location)	Adjuvant treatment	Days of hospitalization (HR)	Recurrence (type; months after treatment)	Management of recurrence	Follow-up duration (months)	Status
#1	M	79	2008	None	SNEC (MANEC)	Present	Present	Negative	IMRT	24 (2.9%)	Yes (bone metastases; 24)	Palliative CHT	27	DOD
#2	M	55	2010	None	ITAC (mucinous, signet-ring)	Present	Absent	Positive (dura)	IMRT	9 (4.2%)	Yes (multiple distant metastases; 7)	BSC	7	DOD
#3	M	73	2011	ER + IMRT	ITAC (solid)	Present	Absent	Positive (dura)	IMRT	15 (0.9%)	Yes (liver metastases; 39)	Surgery	57	AWD
#4	F	79	2011	None	ONB (Hyams II)	Present	Present	Positive (brain)	IMRT	20 (2.6%)	Yes (brain recurrence; 3)	IMRT	25	AWD
#5	M	39	2011	ER + IMRT	ONB (Hyams I)	Present	Absent	Negative	Not performed	11 (0.7%)	None	–	49	NED
#6	M	70	2012	None	ONB (Hyams II)	Absent	Absent	Negative	IMRT	16 (0.9%)	Yes (meningeal metastases; 43)	SRT	60	AWD
#7	M	76	2015	None	ONB (Hyams III)	Present	Present	Negative	IMRT	35 (4.3%)	None	–	27	NED
#8	F	36	2015	None	ONB (Hyams II)	Present	Absent	Positive (dura)	Boost with PBRT on the positive margin and subsequent concomitant IMRT-CHT	9 (1.3%)	None	–	22	NED
#9	F	48	2016	None	ONB (Hyams II)	Present	Absent	Positive (dura)	IMRT	9 (2.3%)	None	–	13	NED
#10	M	71	2016	Induction CHT + concomitant IMRT-RT	SNEC (small cell)	Present	Absent	Positive (dura)	None	8 (5.3%)	Yes (local nasoethmoidal recurrence with massive brain invasion and multiple distant metastases; 2)	Palliative CHT	5	DOD
#11	M	73	2016	Induction CHT	SNEC (small cell)	Present	Absent	Negative	Concomitant IMRT-CHT	18 (4.9%)	None	–	12	NED

Abbreviations: AWD, alive with disease; BSC, best supportive care; CHT, chemotherapy; DOD, dead of disease; ER, endoscopic resection; FESS, functional endoscopic sinus surgery; HR, hospitalization ratio; IMRT, intensity-modulated radiation therapy; ITAC, intestinal-type adenocarcinoma; MANEC, mixed adenoneuroendocrine carcinoma; NED, alive with no evidence of disease; NOS, not otherwise specified; ONB, olfactory neuroblastoma; PBRT, proton-beam radiation therapy; SNEC, Sinonasal neuroendocrine carcinoma; SRT, stereotactic radiation therapy.

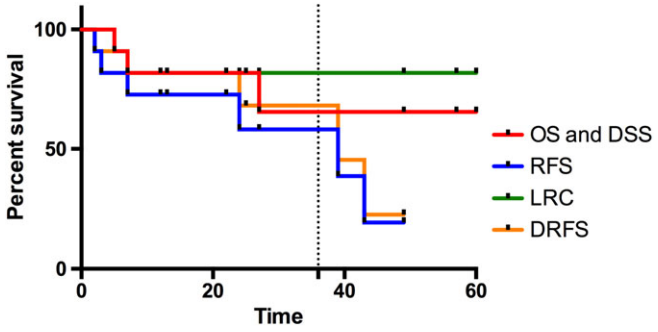

FIGURE 3 The survival plot shows overall survival (OS), disease-specific survival (DSS), recurrence-free survival (RFS), locoregional control (LRC), and distant recurrence-free survival (DRFS) of the 11 patients included in the oncological analysis. The dotted black line shows 3-year survival estimates [Color figure can be viewed at wileyonlinelibrary.com]

reported in 6 (54.5%) cases: in 5 (45.5%) patients there was dura involvement and in 1 (9.1%) brain tissue invasion.

Nine patients (81.8%) underwent adjuvant radiation therapy, including 1 patient who received re-irradiation. The remaining 2 patients had already been irradiated, and were considered not amenable to re-irradiation (patients #5 and #10).

Mean duration of follow-up was 21.9 months (median: 25.0 months; range: 5-60 months). At last examination, patients status was as follows: 5 (45.5%) patients were alive without evidence of disease, 3 (27.3%) alive with disease, and 3 (27.3%) died of disease. Three-year OS and DSS were both 65.5% (Figure 3). Recurrence was observed in 6 (54.5%) cases with the following patterns: 1 (9.1%) local, 4 (36.4%) distant, and 1 (9.1%) both local and distant recurrence. The mean time to recurrence was 22.9 months (median: 23.0 months), ranging from 2 to 43 months. Three-year RFS, LRC, and DRFS were 58.2%, 81.8%, and 68.2%, respectively (Figure 3). Primary vs recurrent presentation, status of margins, and brain edema at preoperative MRI did not significantly influence any outcome. OS, DSS, and DRFS were better in patients with ONB compared to other histologies ($P = .032$, $P = .032$, and $P = .013$, respectively), whereas LRC was not significantly affected by histology (Figure 4).

Mean duration of hospitalization was 15.7 days (8-34 days). Mean hospitalization ratio in patients who died of disease was 4.1%, ranging from 2.9% to 5.3%.

3.2 | Complications and morbidity

Complications were analyzed in the entire series (19 patients). No treatment-associated death occurred. Only 2 (10.5%) minor postoperative complications were seen. On the first postoperative day, a 70-year-old man (not included in Table 1 as brain invasion was not confirmed at final histological examination) developed delirium that was successfully managed with medical therapy. Three weeks after surgery, the same patient was diagnosed with an asymptomatic frontoparietal subdural

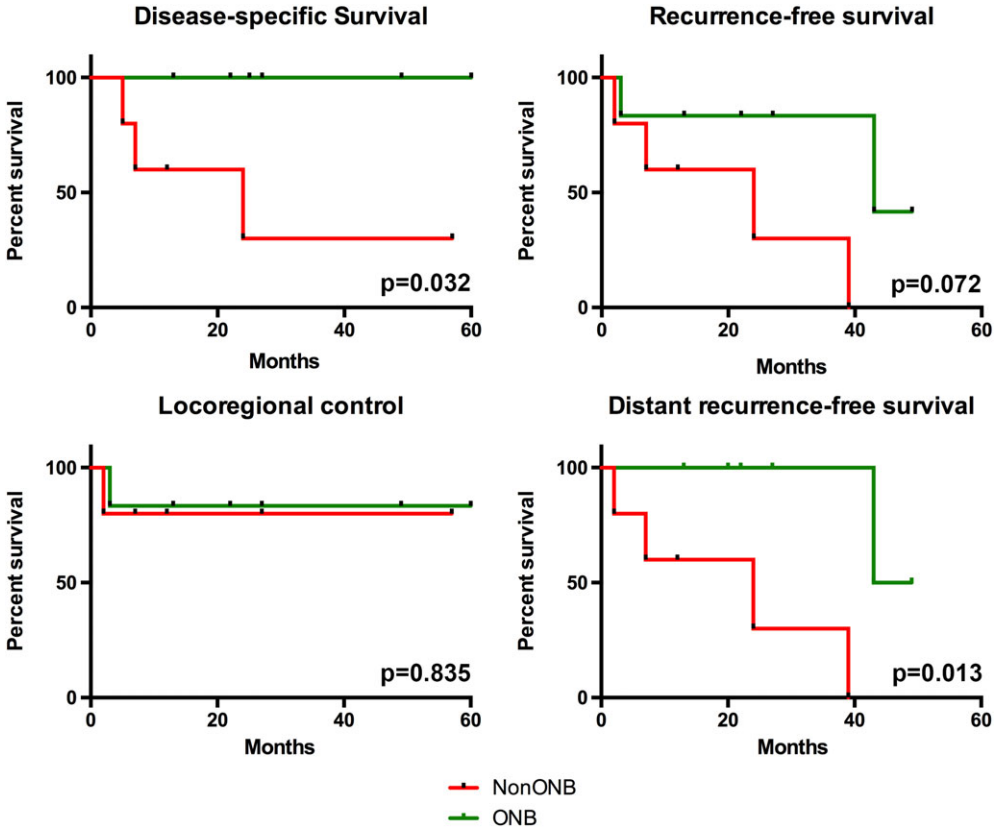

FIGURE 4 Oncological outcomes of olfactory neuroblastoma (ONB) vs non-ONB (NonONB) with brain invasion treated with endoscopic resection with transnasal craniectomy and subpial dissection. Log-rank test *P*-value is reported for each survival plot [Color figure can be viewed at wileyonlinelibrary.com]

hygroma that spontaneously resolved in 2 weeks. In Patient #3, follow-up MRI performed at 8 months after adjuvant treatment showed an asymptomatic frontal mucocele with bone erosion. Successful endoscopic drainage under general anesthesia was performed. The rate of complications of patients having received ERTC-SD did not significantly differ from that of the 286 patients treated with standard endoscopic resection with transnasal craniectomy without subpial dissection at our institutions (10.5% vs 12.5%, respectively).

4 | DISCUSSION

This study analyzes our experience with resection of nasal-ethmoidal tumors with transdural extension and brain invasion via a purely endoscopic transnasal approach on a series of 19 patients. Despite the limited size of the sample, 2 findings are worth highlighting: the very low rate of positive margins in brain tissue and the absence of major complications, permanent disability, or treatment-related deaths. Accordingly, associated short-term morbidity was minimal and the hospitalization ratio low.

The analysis of oncologic outcomes, which was limited to 11 patients who had confirmation of brain invasion at pathologic examination, showed extremely promising results, despite the non-negligible intracranial tumor volume. After a mean follow-up of 21.9 months, 3-year OS and DSS were as high as 65.5%, and RFS was 58.2%. Involvement of the brain is generally recognized as a major negative prognosticator and is associated with extremely poor survival estimates.[16–18] In the international collaborative study on anterior craniofacial resection, brain invasion (identified in 84 patients) doubled the relative risk for recurrence and death. Five-year RFS, DSS, and OS were 20.9%, 29.3%, and 23.2%, respectively.[18] Of note, in our series, 3-year LRC was considerably high (81.8%) and was independent of histology. Accordingly, recurrence rate and survival are mostly impacted by distant metastasis.

Our findings seem to support the oncological validity of the ERTC-SD. Although the rate of positive margins was quite high overall (54.5%), positivity was seen in brain tissue in only one patient (9.1%), whereas in the remainder the dura was involved. Interestingly, in all the cases the dural boundaries of resection were checked with focal sampling and frozen section. This aspect could suggest that tumors with large transcranial extension can display a microscopic dural involvement that goes far beyond the macroscopic limits of the lesion. In these patients, dural resection should be accordingly tailored and possibly a more extended dural mapping with multiple frozen sections should be planned for each dural border. Moreover, brain invasion could be interpreted as a hallmark of high biologic aggressiveness, which necessarily needs adjuvant treatment, whatever the surgical approach. The discrepancy between margin status and local control we observed could be the expression of the efficacy of adjuvant treatments. In this view, ERTC-SD could be favored over classical transcranial approaches because it is associated with shorter hospitalization time and lower morbidity, thus facilitating prompt initiation of adjuvant therapies. Finally, in our series, mortality was almost exclusively caused by distant spread, which is mostly related to histology and biological aggressiveness of the tumor. In view of this finding and the very low incidence of local failure, we can infer that oncological outcomes would not have been remarkably different if a classical craniofacial (or cranioendoscopic) resection had been performed.

The safety profile of ERTC-SD is extremely satisfactory. Notably, the morbidity of the procedure was calculated on the entire cohort of 19 patients having received an ERTC-SD, assuming that the cerebral resection was the preeminent possible cause of complications regardless of actual brain invasion. No permanent disability or treatment-related death was recorded. The complication rate was very low (10.5%) and related to clinical conditions of minor relevance (transient delirium and asymptomatic mucocele). Due to the scarcity of events, no risk factors for complications (ie, prior chemoradiation, age, adjuvant treatments, etc.) could be identified. Of note, a similar complication rate and comparable types of complications were reported by our groups in a retrospective study analyzing morbidity related to skull base reconstruction with iliotibial tract after endoscopic resection with transnasal craniectomy.[24] Apparently, brain resection does not significantly increase the probability of complications.

The comparison with craniofacial resection in terms of safety of the procedure and complication rate is in favor of ERTC-SD. In a retrospective analysis of the international collaborative study on craniofacial resection focusing on complications,[20] the mortality rate was on average as high as 4.7%, and increased to 7.1% in case of brain invasion. Moreover, the overall complication rate was 36.3%, the most frequent being wound dehiscence/infection (19.8%), followed by complications involving the central nervous system (16.2%), and systemic complications (4.8%). Of note, prior radiotherapy and brain invasion were independent risk factors and conferred a 60% and 70% higher probability of postoperative complications, respectively. In particular, brain invasion was associated with risk for complications of the central nervous system that was increased 2-fold in multivariate analysis (32% vs 15%). However, it is worth specifying that data from this paper were collected over a long period (1970-2000), during which adjuvant treatment and patient care substantially improved over time. Moreover, comparison in terms of intracranial tumor volume is not possible due to lack of these data in craniofacial series.

Another advantage of ERTC-SD over the transcranial approach may be the absence of frontal osteotomies in patients who received or are candidate for radiotherapy. In

fact, the possible occurrence of frontal osteoradionecrosis can lead to grievous scenarios requiring major surgery.[25,26]

Noteworthy, 8/19 (42.1%) patients had a suspected brain infiltration at preoperative MRI that was not confirmed at final pathological examination. Consequently, the ERTC-SD allowed a more precise staging of the disease in patients who could otherwise have been addressed to more invasive procedures (ie, cranioendoscopic or craniofacial resection), nonsurgical treatments, or even palliation.

In view of the novelty of ERTC-SD, some surgical considerations should be expressed. The procedure is feasible in clinical practice, but requires high expertise in endoscopic transnasal surgery. We suggest working with a four-hand technique with a 0° endoscope. Although the trajectory of the surgical corridor is unfavorable to control the superior limits of the lesion (ie, the interface between the tumor and brain), the magnification provided by an endoscopic view can help the surgeon to better define resection margins, as demonstrated by the minimal incidence of margin positivity in brain tissue. Great attention should be paid to identify and preventively coagulate major vessels feeding the tumor (or in strict contact with it), because copious hemorrhage in the intracranial compartment is usually difficult to manage via an endoscopic transnasal corridor and might require shifting to an external transcranial approach. Finally, strict collaboration with neurosurgeons is essential in both surgical planning and tumor resection.

Before planning ERTC-SD, several factors should be weighed: tumor extension; tumor biological aggressiveness; histological grade; propensity of histological subtypes to respond to chemoradiotherapy; previous treatments and possibility to deliver adjuvant therapies; and patient performance status. The entity of brain invasion is a key factor in patient selection: involvement of the brain largely beyond gyrus rectus and medial orbital gyrus and tumor spread along sagittal sinus should discourage a purely endoscopic approach.

When the patient is fit and the tumor resectable despite a brain invasion suspected at the preoperative MRI or intraoperatively, ERTC-SD should be always proposed in view of the good control rate achieved in combination with adjuvant therapies. However, the purpose of the procedure can differ substantially according to the realistic probability to cure the disease, and this aspect should be thoroughly discussed in the multidisciplinary team and during patient counseling. In selected cases (ie, Hyams grade I-II ONB, chemoradiosensitive histology, high performance status) treatment has curative intent, or at least can provide a remarkably long survival despite the locally advanced disease. In fact, a high probability of local control can be expected, and even in case of metastatic spread aggressive treatments can be administered (patients #3, #4, #6). Conversely, in case of high grade/aggressive histology (ie, SNEC), poor patient conditions, and/or limited chemo/radiosensitivity the probability to cure the patient or have prolonged survival are very limited (patients #1, #2, #10). In this setting, the procedure can be indicated with the primary aim of improving the quality of residual life (avoid facial disfigurement, recurrent epistaxis, severe headache, etc.) rather than to significantly increase its duration. This possible role of ERTC-SD is further supported by the negligible morbidity and optimal hospitalization ratio observed in patients who eventually died.

The absence of a negative influence of previous treatments should be interpreted cautiously, because it might be biased by the limited number of patients. In fact, several larger series of nasal-ethmoidal tumors reported contrasting results.[12,27] A locally advanced recurrent tumor presents several critical findings (selection of aggressive and chemoradioresistant cellular clones, technical complexity of the resection, decreased spectrum of adjuvant treatments) that should be adequately evaluated when realistically considering the curability of the disease.[22]

5 | CONCLUSION

In nasal-ethmoidal tumors with limited brain invasion detected at preoperative MRI or intraoperatively, ERTC-SD can provide good local control and satisfactory survival. Its safety profile is optimal and associated morbidity is low. Patient selection is essential and should be based on tumor extension and biology, possibility to deliver adjuvant treatments, and patient performance status.

DISCLOSURE OF INTERESTS

Authors have nothing to disclose.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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