Endoscopic Transorbital Approach for Spheno-Orbital Tumors: Case Series and Systematic Review of Literature

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■ BACKGROUND: **Transorbital neuroendoscopic surgery (TONES) comprises a group of approaches with indications expanding from orbital tumors to more complex skull base lesions. We analyzed the role of the endoscopic transorbital approach (eTOA) for spheno-orbital tumors, reporting the results of our clinical series and of a systematic review of the literature.**

■ MATERIALS AND METHODS: **All patients operated on from 2016 to 2022 at our institution for a spheno-orbital tumor through an eTOA were included in a clinical series, and a systematic review of the literature was performed.**

■ RESULTS: **Our series consisted of 22 patients (16 females, mean age 57 ± 13 years). Gross tumor removal was achieved in 8 patients (36.4%) after the eTOA and in 11 (50.0%) after a multistaged strategy combining the eTOA with the endoscopic endonasal approach. Complications included 1 chronic subdural hematoma and 1 permanent extrinsic ocular muscle deficit. Patients were discharged after 2.4 ± 1.3 days. The most common histotype was meningioma (86.4%). Proptosis improved in all cases, visual deficit in 66.6%, and diplopia in 76.9%. These results were confirmed by the review of the 127 cases reported in the literature.**

■ CONCLUSIONS: **Despite its recent introduction, a significant number of spheno-orbital lesions treated with an eTOA are being reported. Its main advantages are favorable patient outcome and optimal cosmetic results, with minimal morbidity and quick recovery. This approach can be combined with other surgical routes or adjuvant therapies for complex tumors. However, it is a technically demanding procedure, requiring specific skills in endoscopic surgery, that should be reserved to dedicated centers.**

INTRODUCTION

Among the various approaches constituting the skull base surgeon's armamentarium, an innovative group, summarized by the term transorbital neuroendoscopic surgery (TONES), has been recently proposed.[1] These approaches are characterized by the use of the orbit as a corridor for selected intraorbital, sinonasal, or even intracranial intradural pathologies and the adoption of the endoscope as the instrument for surgical visualization.[1] The use of the endoscope in skull base surgery dates back to end of the 1990s, when it was adopted as an innovative visualization tool in the transsphenoidal approach.[2] Indeed, it has permitted surgeons to reverse the cone of visualization and illumination given by the microscope, and consequently it has made possible exposure of very large regions of the skull base from small external openings, such as the nasal fossae.[2] The application of this endoscopic endonasal approach (EEA) has progressively

Key words
- Endoscopy
- Meningioma
- Radiotherapy
- Spheno-orbital tumors
- Surgery
- Transorbital approach

Abbreviations and Acronyms
CS: Cavernous sinus
EEA: Endoscopic endonasal approach
eTOA: Endoscopic transorbital approach
GTR: Gross tumor removal
MRI: Magnetic resonance imaging
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
TONES: Transorbital neuroendoscopic surgery

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expanded from pituitary lesions to many other surgical skull base tumors, with the advantage of adopting an extracranial, direct and straightforward corridor and avoiding any brain retraction or manipulation of the main cerebral neurovascular structures.[2,3] However, since the pioneering days of this surgery, it appeared clear that the EEA is mainly a median/paramedian approach, laterally limited mostly by the cranial nerves and major vessels plane, which should not be crossed to avoid direct damage of these structures during instrument insertion and surgical maneuvers.[4]

Following the initial proposal by Moe et al.,[1] the TONES approaches have been developed to overcome such limitations. Indeed, by using a more lateral access, such as the one represented by the orbit, it has been possible to access the skull base laterally to the vascular and cranial nerve plane, e.g., to the optic, oculomotor, and trigeminal nerves.[5-10] Nowadays, the endoscopic transorbital approach (eTOA) is adopted not only for lateral intraorbital or paranasal sinus lesions, but also for middle cranial fossa tumors, such as spheno-orbital neoplasms. These tumors are mostly meningiomas, usually involving many skull base regions, inducing proptosis, diplopia, or visual deficits, which are otherwise approachable exclusively by a transcranial route (i.e., a pterional approach).[5-11] Moreover, with the possibility of expanding the eTOA to the cavernous sinus (CS), Meckel cave, and petrous apex up to the posterior fossa and combining with other EEA or transcranial routes, it can be used by surgeons to manage even complex multicompartmental tumors, such as trigeminal schwannomas, CS, or sphenopetroclival meningiomas.[12-19]

The aim of this study was to analyze our experience with the eTOA for spheno-orbital tumors, considering outcomes and determining advantages, limits, and indications. To support our results, we performed a systematic review of the literature.

MATERIALS AND METHODS

Case Series

Our institutional database of endoscopic skull base procedures was retrospectively reviewed to select all consecutive patients with spheno-orbital tumors operated with an eTOA from 2016 (year of the first case in our center) to September 2022. Inclusion criteria were 1) tumor localization in the spheno-orbital region (Figure 1), 2) both naïve lesions and progressions or recurrences after surgery and/or radiotherapy, 3) adoption of an eTOA (also in association with other approaches in a single or multistaged strategy), and 4) follow-up of at least 6 months. Exclusion criteria were lack of preoperative clinical or neuroradiological information or of clinical data or magnetic resonance imaging (MRI) at follow-up. All patients were treated according to the following protocol.

Patient Management

All patients underwent a preoperative evaluation that included the collection of past medical history. Each patient completed a neurological and a neuro-ophthalmological evaluation, consisting of a physical examination (with particular attention for cranial nerve III, IV, V, and VI deficits), visual acuity and field assessment, optical coherence tomography, and proptosis measurement with the Hertel exophthalmometer. In each case, an MRI scan with gadolinium was performed as well as a computed tomography

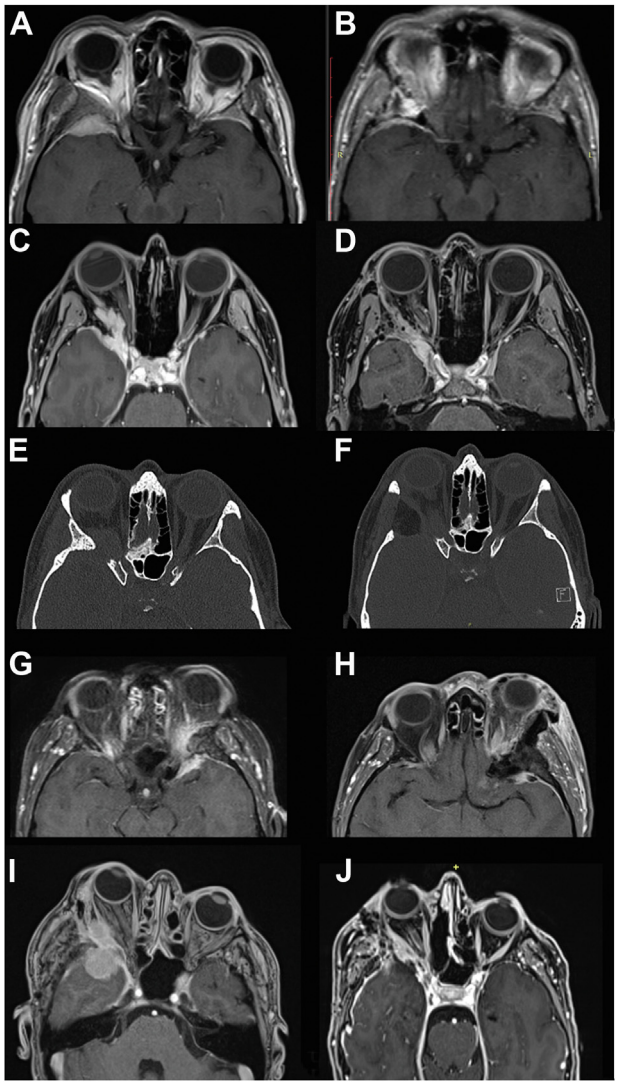

Figure 1. T1-weighted postgadolinium magnetic resonance imaging (MRI) and computed tomography. (**A** and **B**) Preoperative and postoperative MRI of a right en plaque spheno-orbital meningioma with relevant hyperostosis, causing proptosis. The endoscopic transorbital approach(eTOA) permitted the surgeons to achieve a satisfactory orbit decompression, with removal of the hyperostosis and of the fibrous part of the tumor. (**C** and **D**) Preoperative and postoperative MRI of a right spheno-orbital meningioma with significant intraorbital intraconal extension and CS invasion, causing proptosis, diplopia, and visual deficits. Both the intracranial and the intraorbital components of the tumor were removed with the eTOA, while the intracavernous part was left and carefully monitored at follow-up. (**E** and **F**) Preoperative and postoperative computed tomography scan of a right spheno-orbital meningioma. On the postoperative image, the lateral orbit decompression can be appreciated, with sparing of the lateral canthus and the external rim. (**G** and **H**) Preoperative and postoperative MRI of left spheno-orbital meningioma with hyperostosis and significant medial extension toward the superior orbital fissure, causing proptosis and visual deficits. Using the eTOA, it was possible to expose the entire extension of the tumor, decompressing the lateral wall of the orbit and the neural structures. (**I** and **J**) Preoperative and postoperative MRI of a recurrent right spheno-orbital meningioma, already operated on with multiple craniotomies, eTOA, and radiotherapy, with proptosis. The eTOA was repeated without additional morbidity, achieving significant debulking of the tumor and satisfactory orbit decompression with proptosis improvement.

scan with angiography sequences to analyze the tumor location and the presence of hyperostosis.

All surgeries were carried out by a multidisciplinary team of ear, nose, and throat surgeons and neurosurgeons with >10 years of experience in endoscopic surgery according to the following technique. Ultra-short antibiotic prophylaxis was performed with administration of cefazoline at induction of anesthesia, repeated only after 3 hours if surgery lasted more than this time.[20] Patients were awakened and extubated immediately after surgery. Oral feeding and autonomous mobilization were resumed 6 hours after surgery. Corticosteroid and nonsteroidal anti-inflammatory drugs were prescribed for 7–10 days after surgery, then gradually suspended, and ice was kept on the eyelid for the first 6 hours to reduce postoperative palpebral swelling. A computed tomography scan was performed 6 hours after surgery, and an MRI scan with gadolinium was performed within 72 hours. In cases with no complications, patients were discharged from the hospital on postoperative day 2 or 3.

Tumor samples were classified according to the World Health Organization classification of central nervous system tumors criteria.[21] For immunohistochemical analysis, 3-μm-thick serial paraffin sections of each case were processed using an automated immunostainer (Ventana BenchMark AutoStainer; Ventana Medical Systems, Tucson, Arizona, USA).

Suture removal and disinfection of the surgical incision were performed 7 days after surgery and repeated weekly as needed. Patient outcome was assessed by repeating the neurological physical examination and the neuro-ophthalmological evaluations at 3 months and then every 12 months. Proptosis was considered normalized when no significant differences were observed in the exophthalmometer measurement between the 2 eyes and improved when this difference was reduced compared with preoperative values. Other neurological outcomes were considered as normalized or regressed in cases of postoperative full recovery, improved in cases of partial recovery, unchanged or stable if no modifications were observed, or worsened in cases of further neurological deterioration. An MRI scan with gadolinium was performed 3 months after surgery and then periodically depending on the histotype and the adjuvant treatments. The extent of tumor resection was assessed on MRI performed at 3-month follow-up and was defined as gross total resection (GTR) if no tumor remnant was visible, subtotal resection if the residual tumor was <20% of the original mass, and partial tumor removal if the tumor remnant was >20% of the original neoplasm. In cases of evidence of tumor remnant, its location was considered as well as for potential recurrences. At last follow-up, cosmetic outcome was self-evaluated by patients, asking them to score their satisfaction for their esthetic appearance as 1 (very poor), 2 (poor), 3 (neutral), 4 (good), or 5 (excellent). Patients' postoperative quality of life was assessed by the Katz index of independence in activities of daily living at last follow-up (**Table 1**).[22]

Surgical Technique

The patient lies in a supine position, with the head slightly tilted away from the side of the tumor. Surgery is performed under general anesthesia with orotracheal intubation. For the external approach, we use the exoscope (Karl Storz, Tubingen, Germany) to achieve adequate magnification, then we insert the straight endoscope with high-definition cameras for the periorbita dissection (SPIES; Karl Storz). Surgery is performed with the use of neuronavigation (StealthStation S8; Medtronic, Minneapolis, Minnesota, USA), based on preoperative computed tomography angiography and MRI, processed through StealthMerge (Medtronic) software.

Surgery starts with a skin incision in the lateral third of the eyelid at the level of a wrinkle (**Figure 2**). Fibers of the orbicular oculis muscles are dissected to expose the bone margin of the orbital rim up the lateral canthus, paying attention to avoid any damage to the levator palpebrae muscle. Afterward, the periorbita is progressively dissected by the lateral wall of the orbit, then it is covered with a Silastic band and progressively gently retracted (we plan to stop the retraction for 60–120 seconds every 20 minutes). The lateral wall of the orbit is progressively drilled out to increase the working space, arresting at the level of the temporalis muscle (**Figures 1E, F** and **3**).

For hyperostotic tumors, such as meningiomas, the bone part is drilled out as extensively as possible, then the dura of the temporal pole is exposed and largely coagulated. Then, it is incised, and the fibrous part of the tumor is resected with a bimanual microsurgical technique, using the arachnoid as a cleavage plane from the brain tissue when possible (**Figure 4**). For lesions with a significant medial extension or infiltration of the CS and/or Meckel cave, the sagittal crest, an artificial but constant landmark constituted by the medial remnant of the greater sphenoidal wing, marking the lateral border of this superior orbital fissure, is gently removed with a Kerrison rongeur to avoid heating or direct injury to the cranial nerves.[23] After subsequent cutting of the orbitomeningeal band, the medial

Table 1. Criteria for Definition of the Level of Functional Patient Outcome

Level	Functional Outcome
1	Complete autonomy in daily activities and social and work/school tasks
2	Partial autonomy in daily activities and social and work/school tasks
3	Occasional external support necessary for daily life and impossibility to fulfill any social and work/school tasks, i.e., a semidependence condition
4	Daily life absolutely dependent on continuous external support, i.e., a condition of absolute dependence

Adapted from Katz S, Ford AB, Moskiwitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychological function. JAMA. 1963;21:914-919.[22]

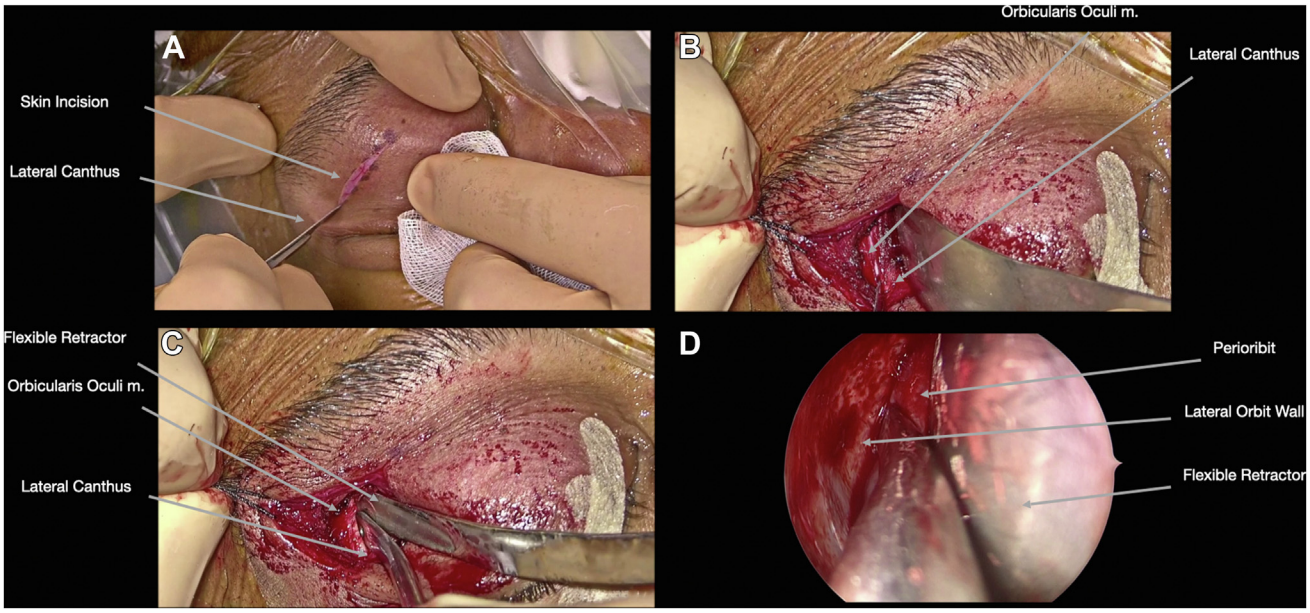

Figure 2. Incision phase. Intraoperative exoscopic and endoscopic (0°) images. (**A**) Before skin incision, it is important to identify the main anatomical landmarks, constituted by the lateral canthus and the supraorbital notch. The incision should be lateral to the notch, to avoid any damage to the neurovascular bundle and to the levator palpebrae, as close as possible to the superolateral orbital rim. (**B**) Immediately after skin incision, it is relevant to identify the fibers of the orbicularis oculi muscle, which have a tangential or longitudinal direction (conversely, levator palpebrae fibers are vertically directed). The dissection of these fibers permits the surgeons to identify the superolateral orbital rim. (**C**) The bone of the lateral canthus and of the surrounding superolateral orbital rim is exposed. From the medial surface of this landmark, it is possible to start to detach the periorbita. (**D**) The initial part of periorbita detachment is usually performed with exoscopic visualization because of the narrow surgical space, which can hamper the insertion of the endoscope. After a few centimeters, it is possible to use the endoscope to continue this maneuver, exposing the entire lateral wall of the orbit and the greater sphenoidal wing.

expansion of the tumor up to the lateral wall of the CS can be exposed.[24]

At the end of tumor removal, the surgical cavity is inspected to verify the complete resection with angled (30°) scopes. We perform a multilayer closure with Biodesign (Cook Medical, Bloomington, Indiana, USA) placed intracranially intradurally, covered with abdominal fat, which is also useful to avoid the risk of enophthalmos (Figure 5). Then, the incision is sutured for anatomical layer, and the skin is closed with intradermic suture or fibrin glue.

Systematic Review of Literature

A systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines (Figure 6). The search strategy, selection criteria, and data extraction methods are reported in Appendix 1.

RESULTS

Case Series

The present series included 22 patients; 16 (72.7%) were females, and mean age was 57 ± 13 years. Of 22 patients, 12 (54.6%) were surgery naïve, and the remaining 10 (45.5%) had already undergone 9 transcranial approaches (40.9%), 4 EEAs (18.2%), 2 lateral orbitotomies (9.1%), and 5 radiotherapies (22.7%) (4 patients underwent multiple surgeries, and 5 underwent surgery and radiotherapy) (Table 2). In 12 cases (54.6%), the tumor was located in the right eye.

All patients presented with exophthalmos (18–20 mm in 8 patients [36.4%] and >20 mm in the remaining 14 patients [63.4%]), 13 (59.1%) patients had diplopia, 9 (40.9%) had visual acuity deficits, 1 (4.5%) was already blind, and 2 (9.1%) presented with trigeminal hypoesthesia (involving the V2 territory in one case and V1 in the other) (Table 2). The most common tumor extension was in the orbit, particularly in the intraconal space (12 patients [54.6%]), followed by CS (8 [36.4%]) and pterygopalatine and infratemporal fossa (7 [31.8%]), as shown in Table 2. The intradural extension of these tumors was observed in 18 patients (81.8%). En plaque meningiomas occurred in 18 patients (81.8%).

All patients underwent an eTOA, and in 3 (13.6%) it was combined with an EEA in a multistaged resection strategy with the second surgical step planned about 1 month after the eTOA. The most common histology was of meningioma, as reported in Table 2. Lateral orbit decompression was achieved in all cases, and GTR was achieved in 8 patients (36.4%) after the eTOA and in 11 (50.0%) patients after a multistaged combined approach. The most common site of tumor remnant was the CS (8 [36.4%]),

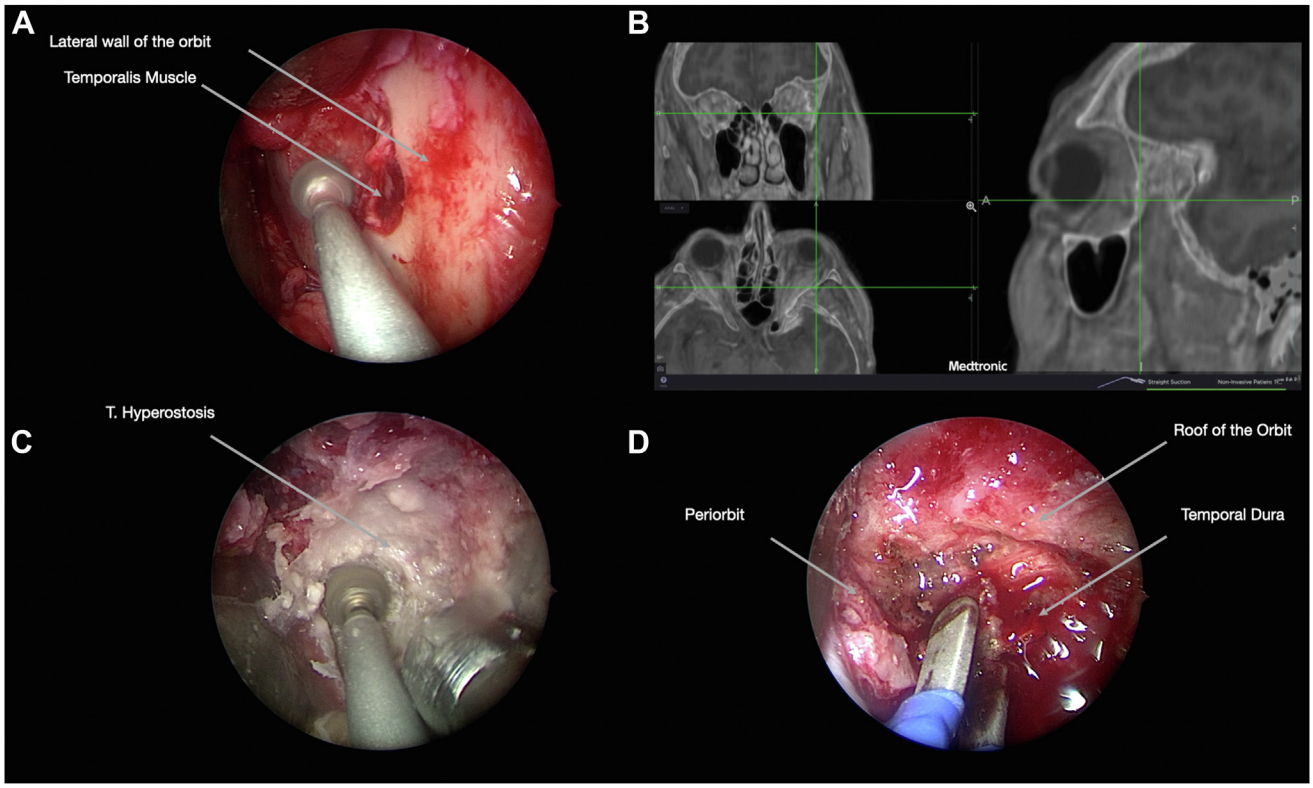

Figure 3. Greater sphenoidal wing drilling. Intraoperative endoscopic (0°) images and neuronavigation image. (**A**) After detachment of the periorbita, the lateral wall of the orbit is drilled with a diamond drill (4 mm) up to the identification of the temporalis muscle. Its fibers, the lateral canthus, and the external orbital rim should be carefully preserved for functional and cosmetic purposes. (**B** and **C**) With neuronavigation, the tumor or the tumoral hyperostosis is identified and progressively removed. (**D**) The bone is removed, according to the peculiarities of the individual. Then the temporal dura is exposed and widely coagulated.

followed by pterygopalatine and ITF (4; 18.2%) (Table 3). For en plaque tumors, GTR was achieved in 6 cases (33.3%) overall and in 5 cases (100%) for globular types. Surgical complications consisted of 1 subdural chronic hematoma (4.5%) requiring a burr hole at 3 weeks after surgery, and 1 permanent extrinsic ocular muscle deficit (4.5%), requiring ophthalmological surgical correction. Patients were discharged from the hospital after 2.4 ± 1.3 days. No surgical incision complications were observed. Periorbital edema resolved on average in 10 days (range, 5–23 days).

Postoperative adjuvant radiotherapy was advised in the 2 malignancies (grade III solitary fibrous tumors and plasmocytoma); in 2 of the 3 atypical meningiomas (the other case was a radiation-induced meningioma that we preferred to follow up avoiding further ionizing radiation exposure); and in 3 remnants of grade I meningioma with already multiple recurrences, to avoid further local relapses.

At 3 months of follow-up, the proptosis was improved in all cases. Visual acuity deficit normalized in 1 (11.1%) case, improved in 5 (55.6%), and was stable in 3 (33.3%), while diplopia regressed completely in 5 (38.5%) and partially in 5 (38.5%) and was unchanged in 3 (23.0%). No improvement in the preoperative trigeminal hypoesthesia was observed, while 3 patients (13.6%) complained of a de novo V2 trigeminal deficit.

Mean follow-up was 46.2 ± 25 months. At last control, proptosis was resolved in 5 (22.7%) patients and improved in the other 17 (77.3%) (Table 4). No cases of postoperative enophthalmos have been observed. Visual acuity deficit normalized in 2 (22.2%) cases and improved in 4 (44.4%), while diplopia regressed completely in 6 (46.2%) and partially in 4 (30.7%). No improvement was observed in 3 cases of de novo V2 trigeminal hypoesthesia. After a mean of 22 ± 12 months, 7 (31.8%) patients experienced recurrence (Table 3). Cosmetic outcome was self-scored by patients as good or excellent in 20 cases (90.1%), and 21 (95.5%) patients were fully reintegrated in their social, working, and family life at follow-up.

Recurrence was treated with a second transorbital approach in 4 patients, an EEA in 2 patients, and proton therapy in 1 patient. A further recurrence was treated with radiation therapy. Another patient refused radiotherapy and was referred to palliation due to a further multirecurrent meningioma with no possibilities of further adjuvant treatments. At follow-up 1 year after surgery, 3 (13.6%)

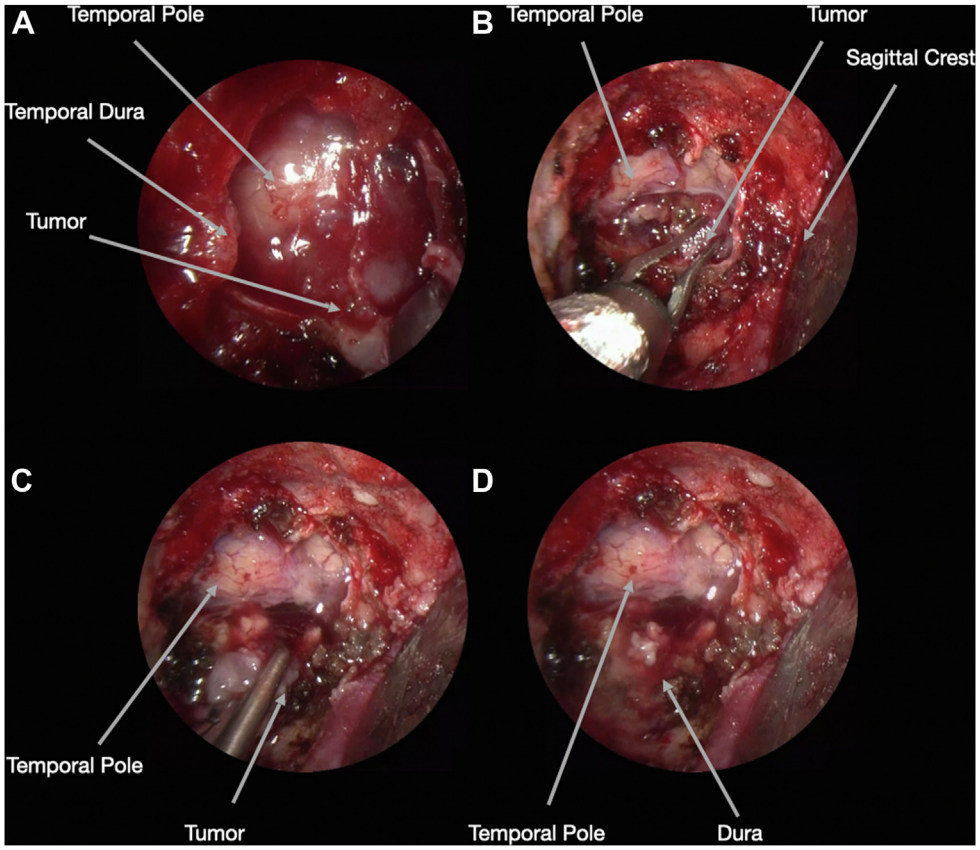

Figure 4. Tumor removal. Intraoperative endoscopic (0°) images. (**A**) The temporal dura is cut, and the fibrous part of the tumor is exposed. The tumor is removed with a 2-handed technique, while the endoscope is fixed on a holder or kept by the second surgeon. (**B**) The tumor is initially centrally debulked with curettes or for more fibrous tumors with a débrider in the extradural space and with a cavitron ultrasonic surgical aspirator in the intradural cavity. We achieve coagulation of major vessels with a bipolar forceps, which we routinely adopt for an endoscopic endonasal approach, while venous oozing can be controlled by hemostatic agents. (**C**) Afterward, the remnant of the tumor can be cleaved from the arachnoid layer, avoiding as much as possible any direct manipulation of the temporal pole. (**D**) At the end of the procedure, the surgical field is inspected to ensure complete tumor removal and the absence of active bleeding.

patients died (after a mean of 34.0 ± 24.2 months), 2 as a result of tumor progression and 1 because of coronavirus 2019–related pneumonia.

Systematic Review of Literature

Eleven studies matched the selection criteria.[25-35] Including our present report, a total of 127 spheno-orbital tumors have been operated on through an eTOA (Table 5). The majority of patients were female (87 [79.8%]), mean age was of 52.7 years (range, 18–79). Most tumors were naïve for previous treatment (79 [72.5%]).

The most common presenting symptom was proptosis (103 [81.1%]), followed by diplopia/extrinsic ocular muscle palsy (50 [39.4%]), visual impairment (47 [37.8%]), and trigeminal hypoesthesia (12 [9.5%]). These tumors frequently also involved other intracranial or extracranial regions, such as the orbit (98 [77.2%]), intraconal space (30 [23.6%]), CS (37 [29.1%]), and PPF or ITF (25 [19.7%]). Bone hypertrophy was described in 96 cases (75.4%), and the majority of tumors presented an en plaque growth pattern (49 of 71 reporting this feature [69.0%]); the remaining 22 cases (31.0%) were globular type. Intradural extension was demonstrated in 109 patients (85.8%).

Combined craniotomy/eTOA or EEA/eTOA procedures were performed in 19 (15.0%) cases with a single-stage or multistaged strategy. The most common histology was meningioma (118 [92.9%]), with 6 cases (4.7%) presenting atypical features (grade II).

GTR or near-total resection was achieved in 49 cases (38.6%). Complications included 4 cases of scar problem/infection (3.2%), 3 cases of persistent/significant palpebral edema (2.3%), 3

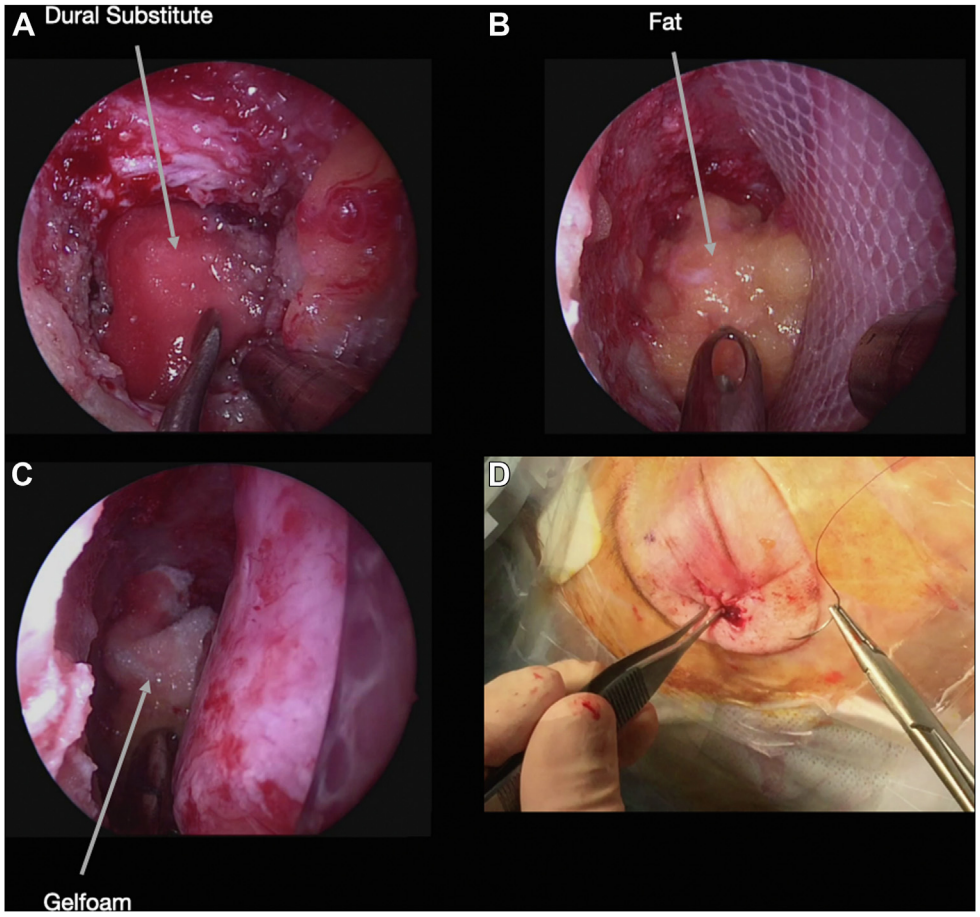

Figure 5. Closure. Intraoperative endoscopic (0°) images. (**A**) Closure is performed in a multilayer fashion. Initially, an intracranial intradural layer of dural substitute is put in place. (**B**) This layer is covered with abdominal fat, which is used also to avoid enophthalmos. (**C**) Afterward, Gelfoam (Pfizer, New York, New York, USA) is placed to cover the fat, and the orbit retraction is released. (**D**). A meticulous layer-per-layer skin suture is performed. We do not routine insert a temporary drainage tube.

cerebrospinal fluid leaks (2.3%), 1 macular hemorrhage (0.8%), and 1 chronic subdural hematoma (0.8%).

Proptosis improved or normalized in all cases. Preoperative visual deficit partially or fully regressed in 30 of 44 patients (68.2%), and diplopia/extrinsic ocular muscle palsy partially or fully regressed in 23 of 32 patients (71.9%). Postoperative de novo conditions consisted of 11 (8.6%) cases of trigeminal hypoesthesia, 6 (4.7%) cases of diplopia/extrinsic ocular muscle palsy (3 transient), and 2 (1.6%) cases of visual acuity deficit. Adjuvant radiotherapy was advised in 39 cases (30.7%). Mean follow-up was 22.4 months (range, 1–90 months). Recurrence rate was 15.3% (15 cases), and 2 (1.8%) patients died of tumor progression.

DISCUSSION

In our study, we observed that the main advantage of an eTOA for spheno-orbital tumors is represented by the favorable patient clinical outcome, characterized by an improvement at long-term follow-up of preoperative symptoms such as proptosis (in all cases), visual deficit (in 66.6.%), and diplopia (in 76.9%). Similar to the report of Corvino et al.,[36] our review of the literature confirmed that proptosis was resolved in all patients, visual deficit was resolved in 68.2%, and diplopia was resolved in 71.9%.[25-35] These results are in line with results reported in a recent review of the literature on spheno-orbital meningiomas operated on with open approaches, confirming the excellent outcome provided by this approach.[37] Moreover, the eTOA permitted a short hospitalization and complete reintegration into social and work life after a few weeks in 95.5% of cases, usually on resolution of the postoperative superior eyelid edema. The extracranial route, which requires extensive bone drilling but minimal manipulation or retraction of the brain, favors fast hospital discharge and quick recovery.[5-9] Furthermore, we have observed a GTR rate of 36.4% after the eTOA (increased to 50.0%

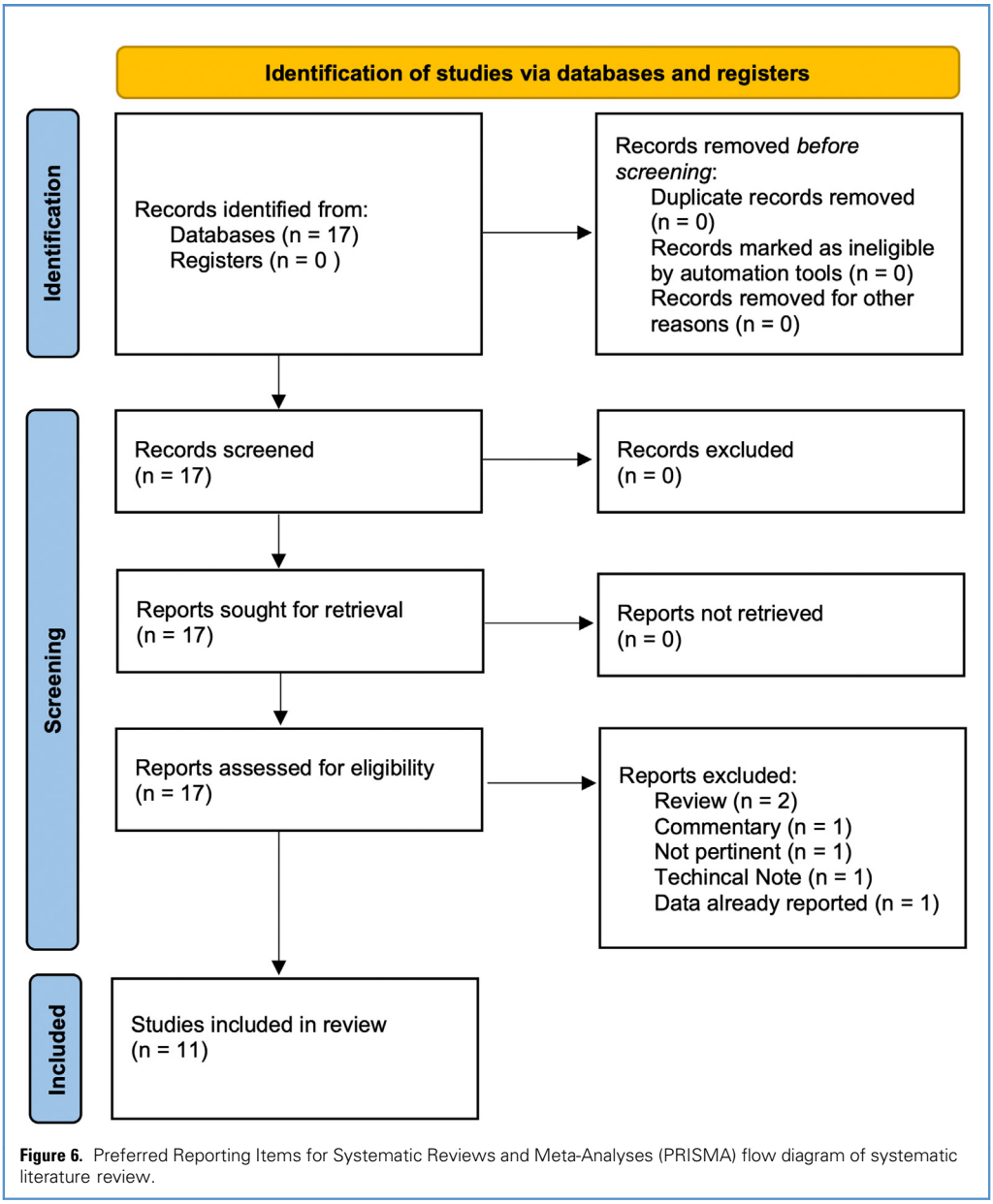

Figure 6. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of systematic literature review.

with multistaged surgery). These results are similar to results reported by Shapey et al.,[37] who observed Simpson I and II grade of resection in 24.0% in their experience with open approaches for naïve or recurrent spheno-orbital meningiomas. Moreover, we found that meningioma-induced hyperostosis of the greater sphenoidal wing can be effectively managed by this approach with a short and minimally invasive corridor.

Despite its very small external access (usually a 1- to 1.5-cm eyelid skin incision), the exposure of the entire greater sphenoidal wing up the lateral border of the superior orbital fissure provided by the eTOA is similar to the one that could be achieved through a lateral transcranial approach, such as the subtemporal or the subtemporal transzygomatic approach, but with a shorter, more direct, and straightforward angle.[38,39] Nevertheless, especially in the initial phases of the surgery (as during the dissection of the periorbita from the lateral orbit wall), the surgical corridor is very narrow, with the risk of excessive retraction of the orbit to gain space and increase endoscope and instrument maneuverability.[5-9] We agree with Kong et al.[33] that one of the most crucial maneuvers in this very early step is the drilling of the lateral wall of the orbit up to visualization of the temporalis muscle. Indeed, this maneuver expands the working room, increasing the safety of the surgical maneuvers and reducing the need for orbit compression (**Figure 1E** and **F**).

Table 2. Clinical Presentation and Tumor Features of Clinical Series

Variable	Value
Previous treatment	
Naïve	12 (54.6%)
Transcranial artery	9 (40.9%)
EEA	4 (18.2%)
Lateral orbitotomy	2 (9.1%)
Radiotherapy	5 (22.7%)
Proptosis, mm	
18–20	8 (36.4%)
>20	14 (63.6%)
Visual deficits	
No	12 (54.6%)
Visual acuity deficit	9 (40.9%)
Blindness	1 (4.5%)
Diplopia	
No	9 (40.9%)
Yes	13 (59.1%)
Trigeminal symptoms	
No	20 (90.9%)
Hypoesthesia	2 (9.1%)
Tumor location	
Orbit	22 (100%)
Intraconal space	12 (54.6%)
PPF	7 (31.8%)
ITF	7 (31.8%)
Paranasal sinuses	3 (13.6%)
CS	8 (36.4%)
Frontal bone	3 (13.6%)
Temporal bone	1 (4.5%)
Dural extension	
Extradural	4 (18.2%)
Intradural/extradural	18 (81.8%)
Histology	
Meningioma grade I	16 (72.9%)
Meningioma grade II	3 (13.6%)
Fibrous dysplasia	1 (4.5%)
Plasmocytoma	1 (4.5%)
Solitary fibrous tumor	1 (4.5%)
Hyperostosis	
Present	20 (90.9%)
Absent	2 (9.1%)
Mean	16.6 ± 8.6 mm

EEA, endoscopic endonasal approach; PPF, pterygopalatine fossa; ITF, infratemporal fossa; CS, cavernous sinus.

Moreover, it also contributes to orbit decompression and proptosis correction. We suggest being careful not to damage the temporalis muscle to avoid any postoperative contractions potentially resulting in atrophy and retraction, which could be painful or lead to masticatory disturbances.[33]

Furthermore, the eTOA can be combined with other approaches, such as an EEA or transcranial or transfacial approach, to manage the most complex tumors, involving multiple cranial base regions.[38,39] Although the possibility to expand the TONES to the temporal floor and the ITF or the paranasal sinuses has been demonstrated in anatomical and clinical studies, in our surgical experience we preferred to combine the eTOA with an EEA for these tumors to reduce the aggressiveness of the single approach and possible complications, such as enophthalmos due to orbital floor drilling or injuries to the neural structures passing through the inferior orbital fissure.[33,40-43] Conversely, for tumors involving the anterior clinoid process or with a lateral expansion into the anterior, middle, or posterior cranial fossa, the eTOA can be combined with specific transcranial approaches, such as supraorbital, pterional (or its variants), frontotemporal-orbitozygomatic, subtemporal, transpetrosal, or retrosigmoid, to complete the tumor resection.[33,40,41]

Considering the site of tumor remnants after eTOA, we can observe that the intraconal intraorbital extension of these lesions can be satisfactorily removed with this approach, unless a strong adherence between the tumor and the optic nerve or the extrinsic ocular muscle is observed (**Figure 1C** and **D**).[44] A potential caveat is represented by the CS invasion (**Figure 1C** and **D**).[5] In our experience, we limited ourselves to removing the exophytic part of the tumor, lateral to the lateral wall of CS, possibly leaving the intracavernous part of the tumor for radiation therapy (**Figure 1G** and **H**).[45,46]

In the literature, what the surgical goal for spheno-orbital tumors should be is still controversial.[11] As observed by Kong et al.,[33] the en plaque type is characterized by a reduced GTR rate (33.3%). This can be explained by its broad implant base, which can be difficult to manage entirely by the eTOA (**Figure 1A** and **B**).[33] This limitation is not exclusive to the TONES but is reported also in other surgical approaches.[33,47] Furthermore, the high rate of en plaque meningiomas in our series (81.8%) and in the literature (69.0%) can be an explanation of the low rate of GTR reported in these studies.[25-35] However, it should be considered that for these en plaque cases, the real aim of surgery probably should not be the GTR, but rather tumor debulking and orbit and neural structure decompression to improve patients' symptoms, leaving the management of the dural tumor remnants at the periphery of the surgical field to adjuvant

Table 3. Patient Outcomes and Follow-Up

Variable	Value
Tumor removal	
GTR after eTOA	8 (36.4%)
STR after eTOA	14 (63.4%)
PTR after eTOA	0 (0%)
GTR after multistaged surgeries	11 (50.0%)
Site of tumor remnant (after multistaged approach)	
Orbit	3 (13.6%)
Intraconal space	3 (13.6%)
PPF	4 (18.2%)
ITF	4 (18.2%)
Paranasal sinuses	3 (13.6%)
CS	8 (36.4%)
Frontal bone	1 (4.5%)
Temporal bone	1 (4.5%)
Complications	
Chronic subdural hematoma	1 (4.5%)
Permanent EOM deficit	1 (4.5%)
Cosmetic outcome	
1	0 (0%)
2	0 (0%)
3	2 (9.1%)
4	5 (22.7%)
5	15 (68.2%)
QOL*	
1	18 (90.0%)
2	1 (10.0%)
3	0 (0%)
4	0 (0%)
Second surgery	
EEA	3 (13.6%)
Adjuvant therapy	
Proton therapy	5 (22.7%)
EBRT	2 (9.1%)
Recurrence/progression	
Yes	7 (31.8%)
Treatment of recurrence	
EEA	2 (9.1%)
Transorbital	4 (18.2%)
Radiotherapy	2 (9.1%)
Palliation	2 (9.1%)
Mortality	
For disease progression	2 (9.1%)
For other causes	1 (4.5%)

Continues

Table 3. Continued

GTR, gross total resection; eTOA, endoscopic transorbital approach; STR, subtotal resection; PTR, partial tumor removal; PPF, pterygopalatine fossa; ITF, infratemporal fossa; CS, cavernous sinus; QOL, quality of life; EOM, extrinsic ocular muscle; EEA, endoscopic endonasal approach; EBRT, external beam radiation therapy.
*Three patients were deceased at follow-up; therefore they were not considered for QOL assessment.

therapies when appropriate.[33,47] Based on our experience, we have decided to refer to radiotherapy all malignancies and atypical meningiomas (grade II), despite the achievement of GTR (with the exception of 1 post–actinic keratosis tumor) and the postoperative remnants of grade I meningiomas that manifested progressions/recurrences in the past.

The cosmetic results of the eTOA have been scored as generally excellent by patients (90.9%) because the scar remains barely visible, and this approach avoids the temporalis muscle manipulation and the drilling of bone in esthetic areas such as the zygoma or the frontotemporal region.[5-9] Moreover, the eTOA is minimally painful and well tolerated, with the main limit of a quite constant palpebral edema that we treat aggressively with nonsteroidal anti-inflammatory drugs, corticosteroids, and ice application, achieving its resolution in a mean of 10 days.[25-35] Considering that significant/persistent eyelid edema was the second most common complication reported in the literature (2.3%), we strongly suggest a prompt treatment due to the very early postoperative time.[25-35] No studies have focused on the possible benefits of leaving a drainage tube in situ after surgery for the first 1–2 days. In our experience, we used a drainage tube only for the first two cases, but as we observed no differences in postoperative palpebral edema, we abandoned its use. Scar infections or wound problems were reported in 4 cases in the literature (3.2%), while the rate of cerebrospinal fluid leak was extremely low (0.8%).[25-35] Other rare complications were a chronic subdural hematoma in an elderly patient and one macular hemorrhage, which was presumed to be due to excessive or prolonged orbit compression.[34] Finally, particular care should be exercised when approaching the superior orbital fissure. Indeed, the heat

Table 4. Clinical Outcome at Last Follow-Up

	Normalization	Improvement	Stable	Worsening
Proptosis	5	17	0	0
Visual deficits	2	4	3	0
Blindness	0	0	1	0
Diplopia	6	4	3	0
Trigeminal symptoms	0	0	2	3

Table 5. Systematic Review of Literature

Study	Cases*	Previous Treatment	Preoperative Symptoms	Tumor Extension	Bone Hypertrophy.	Tumor Type	Intradural Extension	Histology	Type of Surgery	Complications	Tumor Resection	Clinical Outcome	Adjuvant Treatment	Recurrence	Mortality†	FU (months)
Dallan et al., 2015[25],‡	3 (2 F), mean age 53 (44–67)	2 primary, 1 previous craniotomy	3 proptosis, 1 visual deficit, 3 diplopia, 2 trigeminal hypoesthesia	3 orbit (1 intraconal), 2 pterygoids,2 sinonasal cavity, 1 ITF, 1 UPS, 1 temporal lobe	3	NA	3	3 meningioma grade I	3 combined EEA-eTOA	2 palpebral edema	1 GTR	NA	No further treatment	0	0	7 (3–12)
Almeida et al., 2018[26]	2 (1 F), mean age: 39 (53–65)	1 primary,1 previous craniotomy	2 proptosis, 2 visual deficit	2 orbit	2	2 en plaque	2	2 meningioma grade I	2 combined EEA-eTOA	No complications	0 GTR	2 proptosis improvement, 2 visual deficit improvement	2 radiosurgery	0	0	2 (1–3)
Dallan et al., 2018[27],§	11 (10 F), mean age: 46 (35–73)	9 primary, 2 previous. craniotomy	11 proptosis, 5 visual deficit, 4 diplopia, 4 pain, 3 epiphora, 1 EOM deficit, 1 ptosis	5 orbit (2 intraconal), 7 GSW, 6 LSW, 5 frontal bone, 2 zygomatic bone, 2 parietal bone, 2 ACF, 7 MCF, 1 sphenoid, 1 pterygoid	11	NA	2	11 meningioma grade I	10 eTOA, 1 combined EEA-eTOA	1 eyelid necrosis, 2 diplopia, 3 trigeminal. hypoesthesia,1 palpebral edema	2 GTR + 2 near total	11 proptosis improvement, 4 diplopia improvement, NA visual deficit	No further treatment	0	0	27 (9–47)
Kong et al., 2018[28]	18 (14 F), mean age: 52 (18–73)	10 primary, 8 previous treatment	14 proptosis, 10 visual. deficit, 7 EOM deficit	18 orbit, 8 CS	12	NA	13	11 meningioma grade I, 1 atypical meningioma (grade II), 1 salivary gland carcinoma, 1 cystic teratoma, 1 osteosarcoma, 1 plasmocytoma, 1 schwannoma, 1 fibrous dysplasia	15 eTOA, 3 combined EEA-eTOA	No complications	7 GTR	14 proptosis improvement, 6 visual deficit improvement, 3 diplopia improvement	11 radiosurgery	0	NA	5 (1–11)
De Rosa et al., 2019[29]	1 F, age: 37	1 primary	1 proptosis, 1 trigeminal hypoesthesia	1 orbit, 1 CS, 1 LSW	1	1 en plaque	1	1 meningioma	1 eTOA	No complications	0 GTR	1 proptosis improvement	No further treatment	0	0	6
In Woo et al., 2021[30]	18 (16 F), mean age: 54 ± 10)	13 primary, 4 previous craniotomy, 4 previous radiotherapy	17 proptosis, 10 visual deficit, 4 EOM deficit	18 orbit (8 intraconal), 13 CS, 8 parasellar, PPT, IFT, temporal fossa	13	NA	18	17 meningioma grade I, 1 meningioma grade II	16 eTOA, 2 combined EEA-eTOA	3 transient EOM deficit, 3 trigeminal hypoesthesia, 1 CSF leak, 1 wound infection	3 GTR	17 proptosis improvement, 10 visual deficit improvement, 3 EOM deficit improvement	11 radiosurgery, 1 radiotherapy, 1 EEA	4	0	20 ± 10
Locatelli et al., 2020[31]	18, sex and age NA	NA	18 proptosis, 7 visual acuity deficit, 10 diplopia, 4 EOM deficit, 3 visual field deficit, 4 pain, 4 epiphora	18 orbit (7 intraconal), 10 frontal bone, 5 zygomatic bone, 1 maxillary bone, 17 GSW, 16 LSW, 7 parietal bone, 5 temporal bone, 3 pterygoid muscle, 2 skin, 6 ACF, 11 MCF, 3 temporal lobe	18	NA	18	18 meningioma	13 eTOA, 5 combined craniotomy-eTOA	1 visual deficit, 2 trigeminal hypoesthesia	7 GTR	NA proptosis improvement, 4 visual acuity deficit improvement, 3 EOM deficit improvement, 1 visual field deficit improvement	1 radiotherapy	4	0	31.5 (6–84)

FU, follow-up; F, females; ITF, infratemporal fossa; UPS, upper parapharyngeal space; NA, not available; EEA, endoscopic endonasal approach; eTOA, endoscopic transorbital approach; GTR, gross total resection; EOM, extrinsic ocular muscle; GSW, greater sphenoidal wing; LSW, lesser sphenoidal wing; ACF, anterior cranial fossa; MCF, middle cranial fossa; CS, cavernous sinus; CSF, cerebrospinal fluid; PPF, pterygopalatine fossa; SFT, solitary fibrous tumor; CSDH: chronic subdural hematoma.

*Cases include number of patients (number of females) and age in years.

†Only mortality for tumor progression was considered.

‡These cases have been reported also in Dallan et al., 2018.[27] Missing data have been retrieved with the use of the other report.

§This study includes 3 cases described previously in Dallan et al., 2015.[25] In this table, these cases have been considered only once and reported in the analysis of Dallan et al., 2015.

||This study includes 12 cases also described in Kong et al., 2018.[28] In this table, these cases have been considered only once in the analysis of Kong et al., 2018.[28]

¶These data are referred to in the series of spheno-orbital meningioma reported by Kong et al., 2018[28] and by Kong et al., 2020.[33]

Continues

Table 5. Continued

Study	Cases*	Previous Treatment	Preoperative Symptoms	Tumor Extension	Bone Hypertrophy.	Tumor Type	Intradural Extension	Histology	Type of Surgery	Complications	Tumor Resection	Clinical Outcome	Adjuvant Treatment	Recurrence	Mortality†	FU (months)
Kong et al., 2020[33],‖	29 (22 F), mean age: 52 (24–73)	27 primary, 2 previous treatment	11 proptosis, 5 EOM deficit, 7 trigeminal hypoesthesia	9 orbit, 7 CS, 18 temporal floor¶, 9 IFT¶	11	26 en plaque 15 globular¶	29	29 grade I meningiomas	29 eTOA	2 CSF leak, 2 wound complications	13 GTR	NA	5 radiosurgery	NA	0	16
Colombo et al., 2022[32]	3 F, mean age: 59 (42–71)	3 primary, 1 previous craniotomy	3 proptosis, 2 visual deficit	1 orbit	3	2 en plaque, 1 globular	3	2 meningioma grade I, 1 atypical meningioma (grade II)	3 eTOA	No complications	1 GTR	3 proptosis improvement, 1 visual deficit improvement	1 radiotherapy	0	0	1 (1–2)
Foulsham et al., 2022[34]	1 F, age: 60	1 primary	1 proptosis	No extension	1	1 globular	1	1 meningioma grade I	1 eTOA	1 macular hemorrhage (visual worsening)	1 GTR	1 proptosis improvement	NA	0	0	6
Henderson et al., 2022[35]	1 F, age: 60	1 primary	1 pain	1 orbit	1	1 globular	1	1 meningioma grade	1 eTOA	No complications	1 GTR	1 pain resolution	No further treatment	0	0	1
Present study, 2023	22 (16 F), mean age: 57 (27–79)	12 primary, 10 previous treatment	22 proptosis, 10 visual deficit, 13 diplopia, 2 trigeminal hypoesthesia	22 orbit (12 intraconal), 7 PPF and IFT, 3 paranasal sinus, 8 CS, 3 frontal bone, 1 temporal bone	20	18 en plaque, 4 globular	18	16 meningioma grade I, 3 atypical meningioma grade II, 1 fibrous dysplasia, 1 plasmocytoma, 1 SFT	19 eTOA, 3 combined EEA-eTA (3 multistaged)	1 CSDH, 1 permanent EOM deficit, 3 trigeminal. hypoesthesia	8 GTR, 11 GTR after multistaged procedure	22 proptosis improvement, 6 visual deficit improvement, 10 diplopia improvement	7 radiotherapy	7	2	46 (6–90)

FU, follow-up; F, females; ITF, infratemporal fossa; UPS, upper parapharyngeal space; NA, not available; EEA, endoscopic endonasal approach; eTOA, endoscopic transorbital approach; GTR, gross total resection; EOM, extrinsic ocular muscle; GSW, greater sphenoidal wing; LSW, lesser sphenoidal wing; ACF, anterior cranial fossa; MCF, middle cranial fossa; CS, cavernous sinus; CSF, cerebrospinal fluid; PPF, pterygopalatine fossa; SFT, solitary fibrous tumor; CSDH: chronic subdural hematoma.

*Cases include number of patients (number of females) and age in years.

†Only mortality for tumor progression was considered.

‡These cases have been reported also in Dallan et al., 2018.[27] Missing data have been retrieved with the use of the other report.

§This study includes 3 cases described previously in Dallan et al., 2015.[25] In this table, these cases have been considered only once and reported in the analysis of Dallan et al., 2015.

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¶These data are referred to in the series of spheno-orbital meningioma reported by Kong et al., 2018[28] and by Kong et al., 2020.[33]

from the drilling of the sagittal crest or any traction could jeopardize the neural structures of this region.[23,46] Similar attention should be paid also when resecting the tumor at the level of the lateral wall of the CS to avoid postoperative neuropathies, such as trigeminal hypoesthesia (8.6%) and diplopia/extrinsic ocular muscle palsy (4.7%).[25-35] Although we considered that intraoperative monitoring could be useful, we wondered about its reliability regarding the presence of possible artifacts due to the mechanical stretch of the extrinsic muscles and the skin deformation due to orbit compression.

Finally, we have observed that the eTOA can be used for second surgeries to address local relapses of tumors. In our experience, we have repeated this approach for 4 locoregional recurrent cases, with no additional morbidity (**Figure 1I** and **J**). However, it should be recalled that the eTOA, particularly for already operated cases, is a technically demanding procedure, requiring a long training curve in endoscopic surgery, and should be performed at tertiary dedicated centers.[48]

Limits of this study include the small sample of collected cases, the heterogeneity of their histotypes, even though the vast majority were meningiomas, and the lack of a comparison group. Our study has a longer follow-up (mean 46.2 months) than the mean of the studies in the literature (22.4 months), which can explain the higher rate of local recurrence that we observed (31.8% vs. 15.3%). However, the follow-up is still shorter than that available for other, better consolidated approaches. Therefore, this study still represents a preliminary experience, despite the presence of >100 cases in literature with an outcome similar to ours increasing the strength of these results.

CONCLUSIONS

Despite their recent introduction, TONES are a promising group of approaches for many cranial or cranio-orbital tumors. In particular, a significant number of cases of spheno-orbital lesions operated through an eTOA have been reported, with results similar to the results observed in our series. We found that the main advantages of the eTOA is the favorable patient outcome, especially for proptosis, diplopia, and visual acuity deficits, with optimal cosmetic results, as well as the possibility of effectively drilling out the tumor-induced hyperostosis, minimal morbidity, and quick recovery. For more complex lesions involving multiple skull base or extracranial compartments, the eTOA can be combined with other surgical routes or adjuvant therapies to maximize the tumor resection or control without adding significant morbidity. En plaque tumors remain the most challenging forms, with a reduced rate of GTR. The eTOA is a technically demanding approach, and it should be performed at tertiary dedicated centers with experience in endoscopic surgery.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Matteo Zoli: Investigation, Writing — original draft. **Giacomo Sollini:** Writing — original draft. **Arianna Rustici:** Writing — original draft. **Federica Guaraldi:** Writing — review & editing. **Sofia Asioli:** Supervision. **Maria Vittoria Altavilla:** Investigation. **Agnese Orsatti:** Investigation. **Marco Faustini-Fustini:** Writing — review & editing. **Ernesto Pasquini:** Supervision. **Diego Mazzatenta:** Supervision.

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APPENDIX 1

METHODS OF REVIEW OF LITERATURE

Search Strategy

MEDLINE database was queried using individual keywords, including MeSH terms. The specific search strategies were entered as follows: ((trans-orbital) OR (transorbital) OR ("trans orbital")) OR ((transpalpebral) OR (trans-palpebral) OR ("trans palpebral)) OR ((transeyelid) OR (trans-eyelid) OR ("trans eyelid")) AND ((sphenoorbital) OR (spheno-orbital) OR ("spheno orbital")) AND ((tumor) OR (tumour)) OR (lesion) OR (meningioma) OR (neoplasm) AND ((endoscopy) OR (endoscopic) OR (endoscope)). The results were limited to the English language and human subjects. After removal of duplicates, title and abstract were first screened; for articles deemed to be of interest, full texts were obtained and reviewed for appropriateness and extraction of data. References from some other articles were examined to identify any relevant studies.

Selection Criteria

Only studies with data regarding patients who underwent any eTOA for spheno-orbital neoplastic lesions were included. Articles were excluded if they involved nonendoscopic approaches, non–spheno-orbital tumors, or other nontumoral lesions. Studies that involved a variety of surgical procedures or patient populations were included only if sufficient individual data on endoscopic removal of spheno-orbital tumors could be obtained to meet the inclusion criteria. Nonhuman, cadaveric, anatomical, technical, radiological, and review studies were excluded, as were articles with insufficient data.

Data Extraction

Data from the included studies were extracted, organized, and analyzed in Microsoft Excel 2019 (Microsoft Corp., Redmond, Washington, USA). Variables collected included first author, year of publication, number of cases, previous treatments, preoperative symptoms, tumor location and extension, presence of bone hypertrophy, en plaque or globular pattern of tumor growth, dural invasion, histology, surgical technique, complications, tumor resection, symptom outcome, adjuvant treatments, mean follow-up, mortality, and recurrence rate.