Journal of Clinical Neuroscience 129 (2024) 110837

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.journals.elsevier.com/journal-of-clinical-neuroscience

Original Research

Impact of extent of resection and adjuvant radiation therapy in the progression free survival in patients with spheno-orbital meningioma

Samuel Moscovici [a,1,*], Andrew H. Kaye [a], Carlos Candanedo [a], José E. Cohen [a], Yigal Shoshan [a,1], Sergey Spektor [b,1]

[a] Department of Neurosurgery, Hadassah Hebrew University Medical Center, Jerusalem, Israel
[b] Assuta Hospital, Tel Aviv, Israel

ARTICLE INFO

Keywords:
Spheno-orbital meningioma
Hyperostosis
Proptosis
Skull base
Radiosurgery
Optic nerve

ABSTRACT

Background: Spheno-orbital meningiomas (SOM) are known to invaded critical skull base areas. The authors report a series of WHO I SOM, propose a subclassification of this tumor according to its extension to critical positions and analyze the impact of extent of resection and the role of stereotactic radiotherapy in tumor recurrence.

Methods: A prospective maintained university medical center registry was utilized to undertake a retrospective review of patients operated with WHO I SOM. Details related to critical skull base region's extension (superior orbital fissure, cavernous sinus, orbital apex), extent of resection and adjuvant radiosurgery were collected. Statistical calculations were preformed using IBM SPSS Statistics version 25. A p value < 0.05 was considered significant. Survival analysis was performed using Kaplan-Meier survival analysis and the log rank test.

Results: A total of 77 patients operated from 2002 to 2021 were included. There were 65 women (84.4 %) and 12 men (15.6 %). Mean age at surgery was 54.8 years (median 53 years, range 23 – 88). Tumors were defined as local in 28 (35.4 %) and with extension into the skull base critical structures in 51 (64.6 %). GTR was achieved in 35 (44.3 %), STR in 40 (50.6 %), and PR in four (5.1 %). Surgical morbidity was 10 %. There was no surgical mortality. 28 patients with STR or PR were treated with adjuvant radiotherapy. The total length of follow up was a mean of 172.3 months. There were 14 recurrences/progressive growth (17.7 %), 63 patients (79.7 %) had no recurrence/progressive growth, and two patients (2.5 %) were lost to follow-up. PFS was significant statistically different in patients with invasive tumors in whom the extent of resection was subtotal, with a longer PFS in patients that were treated with adjuvant radiotherapy. (P value < 0.001).

Conclusions: SOM could be divided in two groups according to its skull base extension facilitating decision management and outcome prediction. Patients with local WHO I SOM had higher rate of GTR and better PFS than tumors extending to involve critical regions. When STR or PR is achieved postoperative adjuvant radiotherapy is advised if there is evidence of previous tumor growth.

1. Introduction

Spheno-orbital meningiomas (SOM) arise from the dura covering the sphenoid wing with extension into the orbit via bony invasion of the lateral wall and/or roof of the orbit. The meningioma tissue, either "en plaque" or as a "globular" mass involves the dura mater of the adjacent anterior aspect of the middle cranial fossa and periorbita.[1] SOM are noted for their ability to produce hyperostosis and capacity to invade critical areas in the skull base, notably the superior orbital fissure (SOF), orbital apex (OA), and cavernous sinus (CS). Patients may present being

Abbreviations: SOM, Spheno-orbital meningiomas; WHO, World Health Organization; GTR, Gross Total Resection; STR, Subtotal Resection; PR, Partial Resection; PFS, Progression Free Survival; SOF, Superior Orbital Fissure; OA, Orbital Apex; CS, Cavernous Sinus; CT, Computed Tomography; MRI, Magnetic Resonance Imaging; EI, Exophthalmos Index; SG, Simpson grade; OC, Optic Canal; ACP, Anterior Clinoid Process; FSR, Fractionated Stereotactic Radiotherapy; SRS, Stereotactic Radiosurgery; IMRT, Intensity Modulated Radiotherapy; CSF, Cerebrospinal Fluid; IDL, Isodose Line.

* Corresponding author.
E-mail addresses: samuelm@hadassah.org.il (S. Moscovici), andrewk@hadassah.org.il (A.H. Kaye), yigal@hadassah.org.il (Y. Shoshan), sergeyspektor@gmail.com, spektorclinic@gmail.com (S. Spektor).

[1] Equal author contribution.

https://doi.org/10.1016/j.jocn.2024.110837
Received 8 June 2024; Accepted 7 September 2024
Available online 16 September 2024

almost asymptomatic or with symptoms, including proptosis, visual disturbances, and retroorbital pain [2–5]. Tumor size and invasion of critical structures vary from small lateral hyperostotic tumors to giant invasive tumors. Management options include debate on timing of surgery, extent of the surgery and the role and timing of radiotherapy. The extent of surgical resection related to tumor invasion and outcome has been discussed in numerous publications [2,5–18].

Radiation therapy has also evolved and has been used with promising results as adjuvant therapy or upon recurrence in skull base meningiomas, including SOMs. In patients with residual tumor of World Health Organization (WHO) grade II or III pathology, some form of adjuvant stereotactic radiotherapy is increasingly recommended; however, a consensus regarding the optimal timing for adjuvant radiation treatment is lacking in those with WHO I tumors, which represent the great majority of SOM patients, being more than 80 % in most series [12,19,20]. Debate focuses on the management of small residuals in the SOF, OA, or/and CS [8,10,21–25]. There has been no clear evidence as to whether radiation should be used following resection as an adjuvant treatment or only at the time of radiological or clinical progression.

Since 2007, we have recommended adjuvant stereotactic radiotherapy to patients who have undergone subtotal or partial resection of WHO I SOMs that had invaded critical anatomical areas such as SOF, OA, and CS, preventing their complete safe removal, and if there is clinical or radiological evidence of pre-operative tumor growth. We present our experience treating patients with WHO I SOMs, with a focus on the impact of skull base invasion, extent of resection and the role of stereotactic radiotherapy in their progression free survival.

2. Methods and materials

2.1. Definition

In this series of SOM, we included those tumors with associated hyperostosis of the greater and lesser sphenoidal wings, which may also have invaded the orbital roof, lateral orbital wall, and anterior part of the middle cranial fossa floor, as well as intraorbital, intracranial and infratemporal fossa extension.

2.2. Patients

From the prospective Skull Base Registry of the Hadassah Hebrew University Medical Center, we selected patients who satisfied the definition criteria of SOM and were operated in between 2002 – 2021. Only patients with WHO I SOMs were included. We performed a retrospective review of hospital records and the surgeon's notes. Patients who did not strictly satisfy the inclusion criteria, such as those with non-hyperostotic sphenoid wing meningiomas, clinoid meningiomas, or primary optic nerve sheath meningiomas, and those with WHO II or III pathology, were excluded from this study.

Operative criteria included those patients with visual deterioration or visual impairment as assessed by a neuro-ophthalmologist, a progressive proptosis, or radiological evidence of tumor progression.

Data summarizing patients' medical histories, pre- and postoperative clinical and neurological status, ophthalmological evaluation (visual acuity, visual field changes, and exophthalmos), imaging evaluation, surgical technique, extent of resection, orbital reconstruction, pathology, surgical complications, morbidity and mortality, adjuvant radiotherapy, and long-term clinical and radiological follow-up were recorded. Our Institutional Review Board waived the requirement for informed consent for this retrospective review.

The extent of bone hyperostosis or invasion was assessed with computed tomography (CT), and extent of extracranial (infratemporal fossa), intracranial, and intraorbital invasion by the tumor was evaluated with magnetic resonance imaging (MRI) in all patients. The extent of periorbital invasion, dura matter infiltration, optic canal (OC), SOF, OA, and CS tumor infiltration by the tumor were recorded. MRI was also used to measure the radiological exophthalmos index (EI) [8] (Fig. 1).

Initially we divided tumors in two groups according to their radiological features, and then refined the group assignment based on findings at surgery. Tumors that had not invaded the SOF, OA, or CS were defined as local. If the tumor invaded either the SOF, or the OA or the CS they were defined as "extended" (Fig. 2). Operations were defined as gross total resection (GTR) when the surgeon was able to resect all the tumor including bone hyperostosis macroscopically and on postoperative MRI, there was no radiological features of residual in the SOF, OA, or CS–the equivalent of a Simpson grade (SG) I–II [26]; subtotal resection (STR) when a minimal residual was left, such as a tail of tumor inside the SOF, OA, or CS or beneath the optic nerve in its canalicular segment (SG III); and partial resection (PR) when an obvious macroscopic residual was left in the skull base, SOF, OA, CS or any intracranial soft tissue (SG IV).

2.3. Surgical technique

Operations were performed under general anesthesia and endotracheal intubation using an operating microscope, neuronavigation based on fused preoperative CT and T1-weighted gadolinium-enhanced MRI, high-speed drills, and microsurgical techniques.

A frontotemporal bone flap was elevated [27]. The hyperostotic bone was removed with the high-speed drill and included extradural drilling of the major and minor sphenoid wings, orbital roof, and middle cranial fossa floor. The extent of the drilling to remove the hyperostotic part of the tumor was determined by tumor extension and bone involvement. This usually involved resection of varying amounts of the major and minor sphenoid wings along with the roof and lateral orbital wall, followed, when necessary, by OC unroofing and when the anterior clinoid process (ACP) was invaded extradural anterior clinoidectomy. Any extracranial component of the tumor in the infratemporal fossa was removed at this stage, during bone drilling.

Incision of the dura mater was started over the frontal lobe basally, continued across the Sylvian fissure to the temporal lobe, and inverted

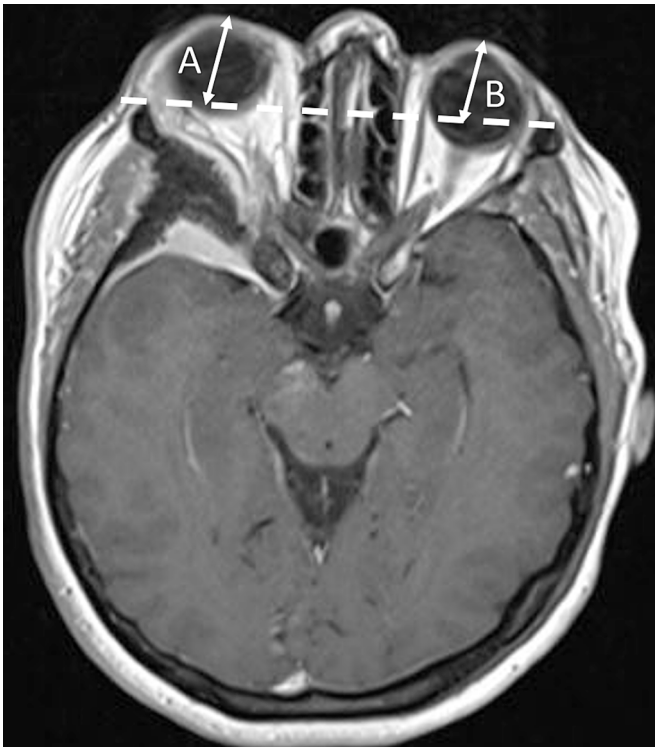

Fig.1. MRI was used to measure the radiological exophthalmos index (EI). EI=A/B [8].

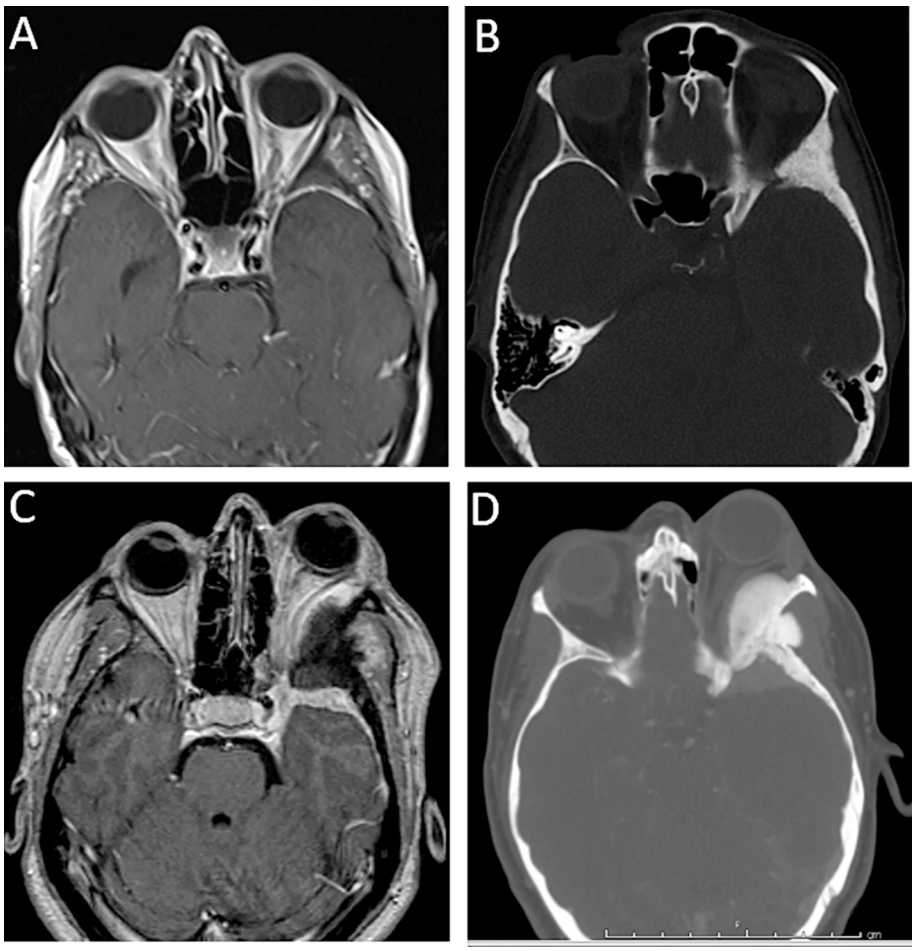

Fig.2. Preoperative CT and MRI images showing our definition of WHO1 SOM as local when there was no invasion of the SOF, OA and CS (A-B) and as "extended" when tumor was localized into one of these critical structures (C-D). (C) shows CS involvement.

basally, exposing the intradural meningioma. The tumor was removed together with varying amounts of the obviously infiltrated dura, depending on the extent of the "en plaque" invasion. If the tumor extended into the CS, the external layer of the lateral wall was peeled away or diathermied, but tumor inside the CS was not resected. In cases of OC involvement, the falciform ligament was transected and the tumor was removed from inside the optic canal to the extent possible while preserving the optic nerve.

Surgery then proceeded with removal of intraorbital tumor. Usually, the tumor invaded the periorbita as well. Dissection of this component was completed as a late or last step of tumor removal to avoid extrusion of the periorbital fat that is usually contained by the periorbita, since this interferes with the dissection. The periorbita was opened even when it was not invaded by the tumor to decrease intraconal pressure and improve proptosis.

If the tumor had invaded the area of the OA, a small remnant was usually left. If the tumor had expanded medially and deeper than the optic nerve, OC, maxillary nerve, foramen rotundum, or structures of the SOF, OA, or CS, this tumor was left as residual. Our approach in these patients was not to cross the neurovascular structures.

2.4. Reconstruction

Dural infiltration is a consistent feature of the SOMs, and there was a significant dural defect after tumor removal and as such it was not possible to achieve a primary watertight dural closure. A dural substitute (Duragen, Integra Life Sciences, Plainsboro, NJ, USA) was placed to cover the dural defect with addition of a small volume of the cryoprecipitate and thrombin mixture.

In cases of relatively small bone defects, we replaced the fronto-temporal bone flap and packed the basal gaps with compressed Gelfoam (Pfizer Inc.). If the lack of bone in the infratemporal fossa was significant, we used titanium mesh to prevent future hollowing out and cosmetic deformity. In some cases of large orbital wall defects, we reconstructed the orbit with titanium mesh and in one patient we used a custom-made Su-pore implant (Poriferous, LLC).

2.5. Postoperative Course

A brain CT scan was performed the day after surgery to rule out intracranial hematoma or pneumocephalus and to determine the extent of hyperostotic bone resection. MRI scans were obtained 3-to-6 months and 1 year after surgery, and then annually. Neurological and neuro-ophthalmological evaluation were performed at the same intervals.

The extent of resection was determined based on intraoperative assessment, and the postoperative gadolinium enhanced MRI obtained approximately 6 months after surgery. Subsequent MRI studies were used to evaluate tumor recurrence or progressive growth of residual tumor. Recurrence is defined as tumor recurring after seemingly total resection and progressive growth as when there is further growth after STR or PR.

Postoperative proptosis was evaluated using MRI obtained 1 year after surgery, since the corrective effect of surgery cannot be effectively evaluated on earlier studies. This also avoids the error of labeling residual proptosis as a new recurrence. The exophthalmos index EI (Fig. 1) was defined as improved with a decrease to < 0.05 of the preoperative

level, a deterioration when there was an increase to ≥ 0.05 from the preoperative level, or as unchanged when the change was not more or less than 0.05 compared with the preop index. [8].

2.6. Stereotactic radiotherapy

Patients were treated with either Fractionated Stereotactic Radiotherapy (FSR) or Stereotactic Radiosurgery (SRS) based on a multidisciplinary discussion as recommended by consensus guidelines. [28] Until 2016, a rigid stereotactic frame head fixation was used for single fraction SRS treatment and a rigid thermoplastic face-specific mask was used for FSR treatments. As of 2016, a rigid thermoplastic face-specific mask was used for SRS and FSR patients. High-definition CT scans were obtained followed by Axial 3D T1-gadolinium MRI, 0.5 mm slice thickness sequences. Image data sets were fused using treatment planning and tumor volume and regions at risk were defined. Treatment planning was performed using dynamic conformal arc therapy or Intensity Modulated Radiotherapy (IMRT) and approved by the treating physician.

Treatment delivery was performed on a LINAC-based platform available at the time (2005–2015 – Varian DBX with Brainlab M3; 2016–2020 – Truebeam Novalis STx with ExacTrac X-Ray). Radiotherapy treatment parameters (number of fractions, radiation dosage, treated tumor volume, etc.) were collected from the patient's medical files and documented.

2.7. Statistical analysis

Statistical calculations were preformed using IBM SPSS Statistics version 25. A p value < 0.05 was considered significant. Associations between categorical variables were assessed with the chi-square test. Progression-free survival (PFS) was calculated from the date of surgery to the date of last follow-up or date of recurrence or progressive growth. Analysis was performed using Kaplan-Meier analysis and the log rank test.

3. Results

3.1. Patients

A total of 79 operations were performed in 77 patients during the study period, including 16 patients (20.8 %) who had been operated elsewhere before presenting to our hospital with growing residuals or recurrent tumors. There were 65 women (84.4 %) and 12 men (15.6 %). Mean age at surgery was 54.8 years (median 53 years, range 23 – 88). Tumors were defined as local in 28 (35.4 %) and "extended" in 51 (64.6 %). Clinical presentation, which is summarized in Table 1, was similar for the two groups except for proptosis, which was significantly more common in patients with "extended" SOMs. Tumor features, including extensions, are also shown in Table 1.

3.2. Extent of resection

Surgical details and extent of resection are summarized in Table 1. GTR was achieved in 35 (44.3 %) surgeries, STR in 40 (50.6 %), and PR in four (5.1 %). GTR was achieved in 27 patients with local tumors (96.4 %) and eight with "extended" tumors (15.7 %). In one patient with a local tumor, we limited the surgery to STR to prevent CSF leak, leaving a residual in the ethmoid sinus. Details regarding the location of residuals are shown in Table 2. Surgical reconstruction details are shown in Table 1.

3.3. Morbidity and mortality

There was no surgical mortality. Surgical complications are summarized in Table 1. Two patient (2.5 %), both with pre-operative

Table 1
Clinical presentation and surgical details of 79 operation of SOMs from 2002 to 2021.

Characteristic	Total Op (%) N=79	Local SOM (%) N=28	Invasive SOM (%) N=51	P
Clinical Presentation				
Proptosis	72 (91.1 %)	23 (82.1)	49 (96.1 %)	**0.037**
Visual impairment	32 (40.5 %)	8 (25 %)	24 (47.1 %)	0.109
Temporal Swelling	27 (34.2 %)	7 (25.0 %)	20 (39.2 %)	0.2
Headache	24 (30.4 %)	9 (32.1 %)	15 (29.4 %)	0.8
Retro-ocular pain	24 (30.4 %)	7 (25.0 %)	17 (33.3 %)	0.4
Incidental Finding	7 (8.9 %)	4 (14.3 %)	3 (5.8 %)	0.2
Diplopia	4 (5.1 %)	1 (3.5 %)	3 (5.95 %)	0.66
Lacrimation	4 (5.1 %)	2 (7.1 %)	2 (3.9 %)	0.52
Confusion	1 (1.3 %)	0	1 (1.9 %)	
Aphasia	1 (1.3 %)	0	1 (1.9 %)	
Instability	1 (1.3 %)	0	1 (1.9 %)	
Trigeminal pain	1 (1.3 %)	0	1 (1.9 %)	
SOM Features				
Infiltrated Infratemporal fossa	59 (74.7 %)	15 (53.6 %)	44 (86.3 %)	**0.001**
Optic canal hyperostosis	53 (67.1 %)	13 (46.4 %)	40 (78.4 %)	**0.004**
Infiltrated ACP	51 (64.6 %)	9 (32.1 %)	42 (82.4 %)	**<0.001**
Infiltrated OA/SOF	55 (69.6 %)	13 (46.4 %)	42 (82.4 %)	**0.001**
CS infiltration	38 (48.1 %)	2 (7.1 %)	36 (70.6 %)	**<0.001**
Temporal muscle infiltration	20 (25.3 %)	3 (10.7 %)	17 (33.3 %)	**0.027**
Sphenoid sinus infiltration	18 (22.8 %)	0	18 (35.3 %)	**<0.001**
Ethmoid sinus infiltration	15 (19.0 %)	1 (3.5 %)	15 (29.4 %)	**0.001**
Tumor inside optic canal	14 (17.7 %)	0	14 (27.5 %)	**0.002**
Vascular (ICA, MCA) encasement	5 (6.3 %)	0	5 (9.8 %)	0.087
Surgical Details				
Optic canal unroofing	52 (65.8 %)	13 (25 %)	39 (75 %)	**0.007**
Optic sheath opening	52 (65.8 %)	12 (23.1 %)	40 (76.9 %)	**0.001**
Anterior clinoidectomy	40 (50.6 %)	9 (22.5 %)	31 (77.5 %)	**0.015**
Extent of Resection				
Gross total resection (GTR)	35 (44.3 %)	27 (96.4 %)	8 (15.7 %)	
Subtotal resection (STR)	40 (50.6 %)	1 (3.6 %)	39 (76.5 %)	
Partial resection (PR)	4 (5.1 %)	0	4 (7.8 %)	
Location of Residual				
Cavernous sinus	36 (45.5 %)	0	36 (70.6 %)	
SOF/OA	42 (53.2 %)	0	42 (82.4 %)	
Ethmoid and/or sphenoid sinus	18 (22.8 %)	1 (3.6 %)	17 (33.3 %)	
Type of Reconstruction				
Type 1	35 (44.3 %)	15 (53.6 %)	20 (39.2 %)	

(*continued on next page*)

Table 1 (*continued*)

Characteristic	Total Op (%) N=79	Local SOM (%) N=28	Invasive SOM (%) N=51	P
Type 2	35 (44.3 %)	12 (42.9 %)	23 (45.1 %)	
Type 3	9 (11.4 %)	1 (3.6 %)	8 (15.7 %)	
Surgical Complications				
Pseudomeningocele	5 (6.3 %)	2 (7.1 %)	3 (5.9 %)	
Wound infection	3 (3.8 %)	2 (7.1 %)	1 (2.0 %)	
Ophthalmoplegia (partial)	3 (3.8 %)	0	3 (5.9 %)	
CSF leak	2 (2.5 %)	0	2 (3.9 %)	
Seizures	1 (1.3 %)	0	1 (2.0 %)	
Unilateral blindness	2 (2.5 %)	0	2 (3.9 %)	
Bilateral PE with intracranial hemorrhage after clexane	1 (1.3 %)	0	1 (2.0 %)	

Op = operation, SOM=Spheno-orbital meningioma, ACP=Anterior clinoid process, OA=Orbital Apex, SOF=Superior orbital fissure, CS=Cavernous sinus, ICA=Internal Carotid Artery, MCA=Middle cerebral artery, GTR=Gross total removal, STR=Subtotal removal, PR=Partial removal, CSF=Cerebro spinal fluid.

Table 2
FSR/SRS adjuvant therapy details of 28 patients operated with SOMs from 2002 to 2021. Main Treatment-related parameters.

Parameter	No. of Patients (%) N=28	Mean marginal dose for 80–90 % isodose line. Gy (range)	Maximal dose Gy (range)
FSR, full fractionation 27–28 fractions	22 (78.6 %)	48.6	53.8 (50.4–54)
SRS	4 (14.3 %)	12.8 (12–13)	15.8 (13–16.2)
FSR, hypofractionation 5–16 fractions	2 (7.1 %)	35.5 (30–40)	40.9 (37.5–44.4)
Mean Time from operation to adjuvant radiotherapy. Months (range) – 9.2 (1–28)	28 (100 %)	––	––

Gy = gray, FSR=Fractionated stereotactic radiosurgery, SRS=Single fraction stereotactic radiosurgery.

impaired vision, became blind in the operated eye. New permanent partial ophthalmoplegia developed after three operations (3.8 %). New onset seizures in one patient (1 %) were successfully controlled with medication. Cerebrospinal fluid (CSF) wound leak occurred in one patient (1 %). CSF rhinorrhea via the ethmoid sinus occurred in one patient (1 %) and this resolved with continuous lumbar drainage. A pseudomeningocele developed after five operations. All were managed successfully with temporary continuous CSF drainage. Bilateral pulmonary embolism (PE) occurred in one patient (1 %) two days after surgery and was treated with clexane and an inferior vena cava filter. Superficial wound infections in three patients resolved with oral antibiotics.

There were 7 patients with post radiation tiredness, and 5 with a permanent dry eye. 2 patients had visual deterioration following radiation, one of them returned baseline status during the follow up 6 months and one had a permanent visual impairment.

3.4. Visual outcomes

A total of 32 (40.5 %) patients had preoperative visual acuity deficits. Among them, 19 (59.3 %) improved, 10 (31.3 %) remain unchanged, and three (9.3 %) had visual deterioration following surgery, including two who became blind in the ipsilateral eye.

Proptosis was seen in 72 (91.1 %) patients before surgery. It improved in 56 (77.8 %), was stable in 14 (19.4 %), and was worse in one. One patient developed enophthalmos.

3.5. Radiation

In patients with STR or PR we recommended adjuvant radiotherapy if there had been clinical or radiological evidence of preoperative growth of the tumor.

Of the 28 patients treated with adjuvant radiotherapy 24 (78.6 %) were treated with full fractionation FSR, receiving the protocol of 27 daily fractions of 1.8 Gray (Gy) to the 90 % isodose line (IDL), (accumulated 54 Gy to isocenter) in 5 fractions per week. Four patients were treated with single fraction SRS with 13 Gy to 80 % IDL while 2 (7.1 %) patients were treated with 5–16 fractions of 30 to 40 Gy to the 90 % IDL. Single dose SRS was performed for patients with relatively small target-volume and when the tumor is sufficiently separated from the optic pathways. [12] The mean time from surgery to stereotactic radiotherapy was 9.2 months (range 1–28 months). Table 2. The delay of radiation in some patients related to the patient preference regarding timing of the radiation.

3.6. Tumor recurrence or progressive growth

Tumor progression of local and "extended" SOMs according to extent of resection and administration (or not) of stereotactic radiotherapy is summarized in Fig. 3. The total length of follow up for all the group was a mean of 172.3 months. 14 patients showed tumor progression (17.7 %), 63 patients (79.7 %) had no recurrence or progressive growth, and two patients (2.5 %) were lost to follow-up.

Overall, 5-year and 10-year progression-free survival rates (PFS) were 80.4 % and 75.8 %.

In patients in whom GTR was achieved, 5y PFS was 93.1 % and 10y PFS was 86.4 % (mean 187.72 months). In patients with STR and PR resection the 5y PFS was 71.8 % and 10y PFS 68.4 % (mean 158.4 months). It was not statistically significant (p 0.1) (Fig. 4).

PFS was statistically significant when comparing between the local and "extended" type of SOM (P value = 0.032). In the local type of tumor there was one recurrence (mean time 197.3) while in the invasive group there were 13 (mean 157.1 months) patients with SOM progression. In those patients with local type SOM 5 and 10 y PFS was the identical 95.5 %, and in the "extended" group 5 year was 72.9 % and 10 year was 66.8 %. (Fig. 5).

Adjuvant radiation treatment made a significant difference to the PFS in patients in whom the extent of resection was subtotal, with a longer PFS in patients that were treated with adjuvant radiotherapy in comparison with patients who did not receive radiation. (P value $<$ 0.001). In those patients following radiation the PFS was 205.8 months compared with those not treated with adjuvant radiation 92.7 months. In patients having a subtotal resection without radiation the PFS at 5y was 42.4 % and at 10y 31.8 % compared to 100 % 5- and 10-year PFS with radiation treatment. However, in one patient who had subtotal resection and adjuvant radiation there was a recurrence 121 month after the treatment (Fig. 6).

Patients with GTR in the local group had no recurrence, but recurrences occurred in 3 of the 8 patients in the" extended" group who had GTR (P value 0.001) (Fig. 3) These patients had not received adjuvant radiation treatment as it was our policy not to give radiation if there was no residual tumor on the post-operative imaging.

There were no recurrences in those patients with local disease in whom GTR was achieved. The PFS was worst in the patients following STR/PR who did not have adjuvant radiation treatment.

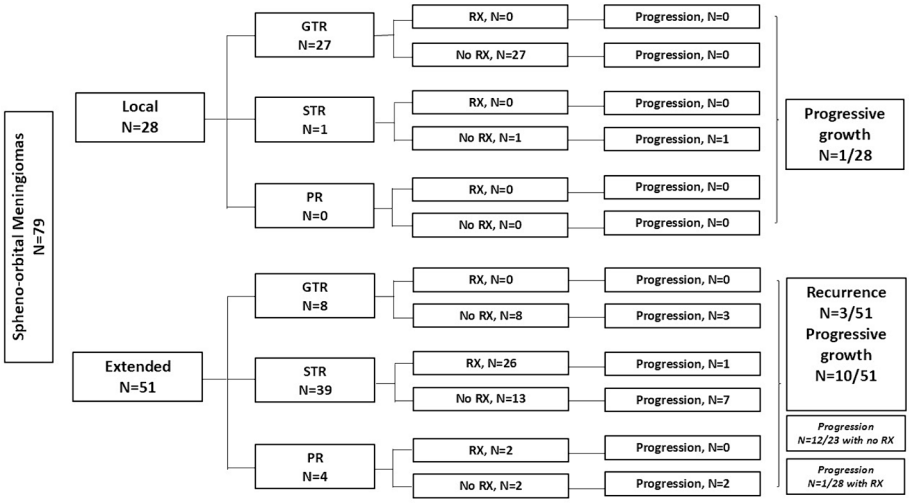

Fig.3. Flowchart of 79 WHO1 operated for SOM, its subclassification in local and "extended" type of tumor, extent of resection, adjuvant radiation treatment and tumor progression. (defined in the text as "tumor recurrence" when there has previously been a complete resection of the tumor, and "progressive growth" when the residual tumor has progressive growth).

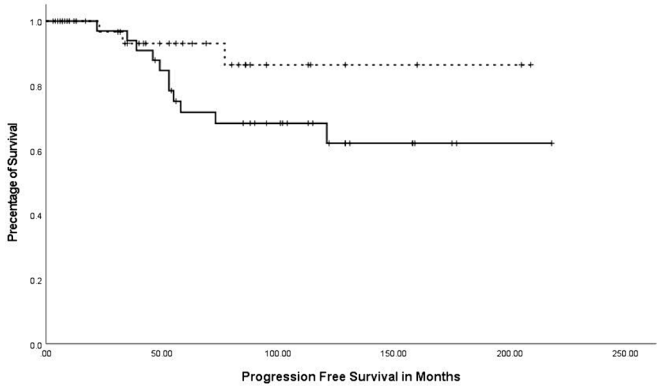

Fig.4. PFS when EOR was compared. GTR (dotted line) vs STR/PR (solid line).

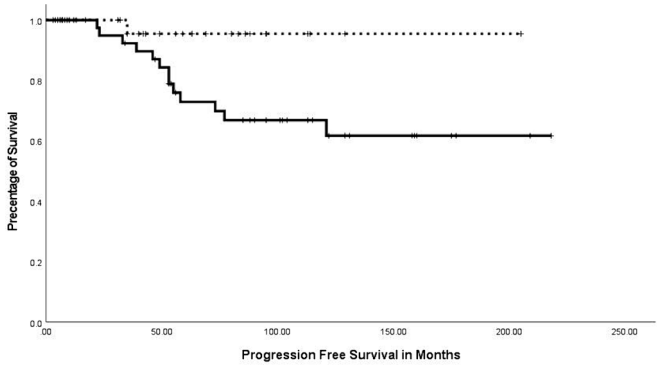

Fig.5. PFS comparing Local (dotted line) vs "extended" tumors. (solid line).

4. Discussion

We present a cohort of patients with WHO I SOMs who were divided in two main group; local or "extended" SOM, according to the structures invaded in the skull base. Not surprisingly, extent of resection and progression free survival were significantly better in patients with local SOMs compared to those with tumors invading the orbital apex, superior orbital fissure or cavernous sinus tumors (P value 0.032). Among patients who had a subtotal resection, PFS was significantly better in those who had adjuvant stereotactic radiotherapy (P value < 0.001).

There are many publications dedicated to SOMs that focus on clinical manifestations, tumor extension, surgical details, extent of resection, surgical reconstruction, complications, proptosis, and visual outcomes. [2–6,8,10–13,16,17,29] Our results in do not differ significantly from other reports. Proptosis was the most frequent clinical presentation. Residual tumor remained when the SOF, OA and CS were invaded, and surgical treatment led to improvement of proptosis and visual impairment in most patients. However, there has been no consensus regarding strategies for classifying SOMs to enable clear recommendations regarding optimal management strategies, especially with respect to adjuvant radiotherapy after STR in patients with WHO I tumors.

In terms of surgical approach, we used exclusively the pterional based craniotomy with local modifications depending on the extension of the tumor. This type of approach has been the standard surgical technique utilized for SOM resection in 92 % of the series. [16] More recently other approaches including the orbitozygomatic approach, endoscopic endonasal and transorbital techniques have been advocated. [30–32] The utilization of these approaches may be worth considering, depending on the extension of the tumor and local experience with the techniques.

The majority of other series included SOMs that we defined as local or "extended" in a single group and analyzed their data collectively and most studies have also included WHO II patients in the series. We excluded patients with WHO II and III tumors from our study because we believe adjuvant radiation is always indicated in these patients. In addition to the WHO grade of meningioma, the proliferation index and progesterone receptor expression are known to possibly influence tumor recurrence and management. In our series we assessed only the WHO grade but other features could be considered in future studies. [33] Some authors have defined subtypes of SOMs. In a series of 30 patients, Scarone et al [8] defined Type A SOM to be characterized by enhanced intraosseous extension, often with intradural and periorbital components, but no ACP or CS invasion. In contrast, their Type B SOM always showed an intradural mass, a periorbital component displacing intraorbital muscles, and invasion of the ACP and/or CS. [8]. They found that 11 % of patients with Type B tumors had recurrences compared with a slightly lower rate of 9 % in patients with Type A SOMs. [8] As in our series several publications indicate that CS, intraconal, and SOF invasion are associated with worse PFS because of more limited extent of resection and they also had higher incidence of postoperative neurological deficits. [11,12,34,35].

The surgical morbidity in our series was 10 %. Post operative

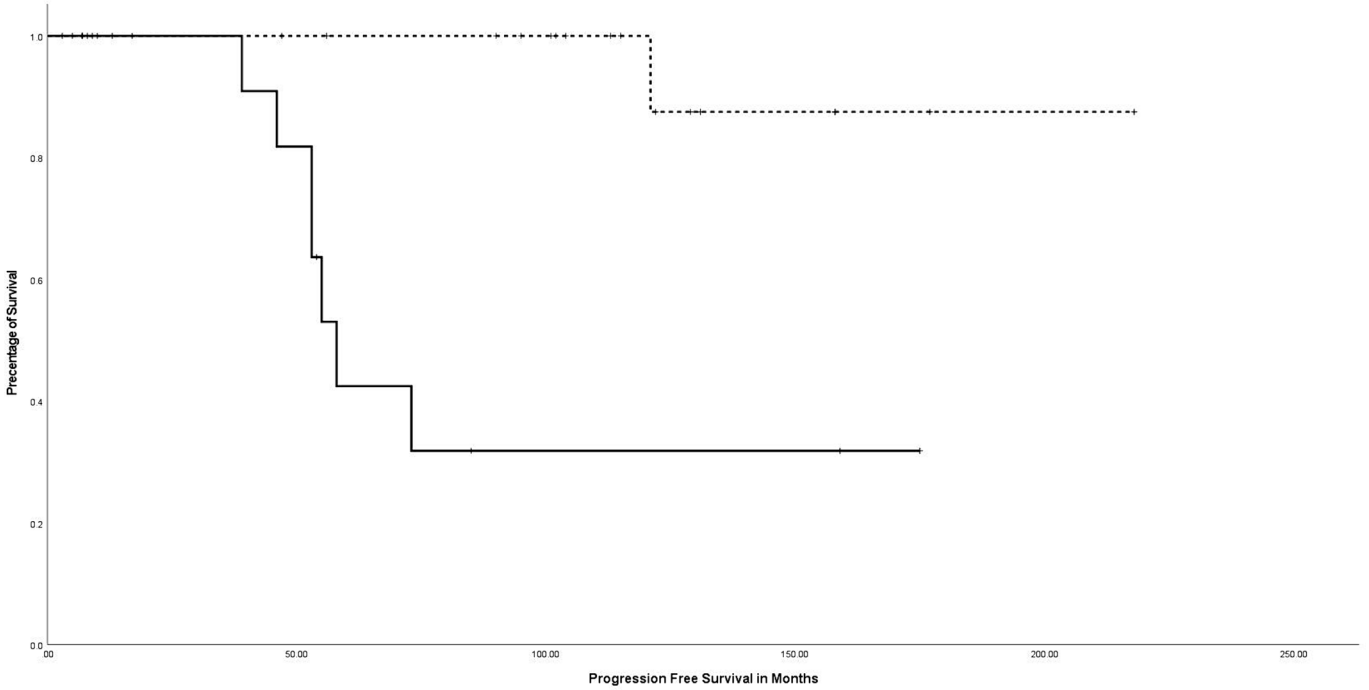

Fig.6. PFS comparing STR+Rx (dotted line) vs STR nonRx (solid line).

morbidity has previously been reported ranging from 3.3 % to 63.1 %. [8,20] A 2021 metanalysis reported that the most common surgical complications were hypoesthesia (19 %), ptosis (17 %), diplopia (17 %) and ophthalmoplegia (16 %). However, in one series post-operative ophthalmoplegia was noted to improve in nearly all patients (96 %). [16].

Previous series reported GTR in approximately a third [5,11,12] to a half of patients [2,7,13]. In our series, GTR was achieved in 44.3 % of surgeries. However, it is difficult to analyze SOM patients as one homogeneous group, since extent of resection is critically dependent on the extension into critical locations. We achieved GTR in 27/28 (96.4 %) patients with local tumors but in only 8/51 (15.7 %) of those with "extended" tumors. The true extent of SOM extension to the skull base can be difficult to assess in preoperative imaging. [2] In our series, tumor extensions were underestimated in one patient who was misclassified as local based on preoperative imaging. For this reason, classification was reassessed after intraoperative assessment of tumor extensions. This difference could explain some of the differences between rates of GTR in various reports. [11].

The relationship between extent of resection and recurrence remains unclear in the literature, with reported rates of recurrence ranging from 0 – 71 %. Some authors have argued that these factors are not related [11] and others have reported an inverse relationship. [2,5,23,36–38] In one series, 61 % of patients with residual tumor remained radiologically stable at a mean follow-up of 7 years (range 1–21 years) [39], but in another series where only about half of the patients had GTR, there was recurrence in about one third. [7] Alzhrani G et al [40] assert that total removal of all the tumor, including soft tissue and hyperostotic bone, provides the longest recurrence-free survival and symptomatic relief for patients. However, this report noted a case of a recurrent hyperostosis after GTR of a SOM that had included complete removal of the involved bone.

Two series with relatively high gross total resection rates reported recurrences in 6 % and 7 % of patients at mean follow-up of 4.5 and 3 years respectively, and one report in which 70 % of patients had GTR found had recurrences in 8 % at 5-year follow-up [2,38,41]. Nagahama et al, reported an increase in tumor recurrence beginning at 6 years after surgery [12]. We have a 18.8 % of recurrences or progressive growth at a mean follow-up time of 172.3 months, which was significantly higher in patient with STR/PR than GTR (p 0.1), with 13 patients having tumor progression in the 'extended" group and only one in the local group.

Over the past two decades, stereotactic radiotherapy has emerged as an effective and safe adjuvant therapy for inoperable meningiomas, including cavernous sinus meningiomas and high-grade residual meningiomas. [42–44] Fractionated stereotactic radiotherapy has been established as an effective treatment modality for SOMs. [21,28,37].

There is no clear consensus on the timing of adjuvant radiation after resection. Terpolli et al. suggest that giving radiation within 6 months after maximal SOM resection, improves vision and tumor control. [45] In our series, we recommended radiation treatment in all patients with STR (43 patients) who had previous clinical or radiological evidence of tumor growth, but 15 patients declined treatment. The mean time to adjuvant treatment was 9.2 months as some patients delayed treatment due to personal reasons.

As indicated our policy was to offer post operative radiation to all the patients with residual tumor when there was pre or post operative radiological or clinical tumor progression. However, the alternative option of reoperation at tumor progression and or recurrence has also been advocated by some authors. Mariniello et al [46] has described reoperation achieving an overall control in 88 % with one or more operations in a time period from 5 to 28 years, mean 136 months. We acknowledge that there is variation in management with some centers either advising re-operation at time of progression and or radiation only if there is evidence of post-operative tumor progression. [46].

Our analysis showed that those patients who underwent STR and received adjuvant stereotactic radiotherapy had significantly better tumor control than those who underwent STR without irradiation ($p = 0.001$; 5-and 10-years progression free survival rates of 100 % vs. 42 % and 100 % vs 32 % respectively. (Graph 3).

We recommend SRS treatment for patients with relatively small target-volume and when the residual tumor is sufficiently separated from the optic pathways [12], but only four out of our 28 irradiated patients were eligible for this treatment. Consequently, due to anatomical and pathological characteristics of SOMs, most of our patients received FSR (24/28).[47,48] With the exception of one patient with permanent visual deterioration, the absence of new visual deficits and

other cranial nerves neuropathies following radiation support the relative safety and the effectiveness of our radiation schema and technique.

5. Conclusions

1. 1.Dividing SOMs in two clear groups, local and "extended" types, according to whether there is invasion to the SOF, OA, and/or CS, is a practical and central factor in management decisions and patient's outcomes. In patients with local tumors, a higher rate of GTR can be achieved, avoiding the need for further treatment, although long-term radiological and clinical follow-up is mandatory.
2. If sub-total resection was performed, we advise postoperative adjuvant stereotactic radiotherapy in patients in whom there was pre-operative clinical or radiological evidence of tumor growth. For residual tumors with a diffuse pattern and/or located with proximity to the optic apparatus, full FSR should be considered. However, for residual meningiomas that are clearly defined and distant from the optic apparatus, single fraction radiosurgery may be suitable option.

We acknowledge that a limitation of this study includes the relatively small sample size and single center dataset, although this is offset by the ability to compare this uniform management plan with other series.

Code availability: not applicable.

Authors' contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Samuel Moscovici, Carlos Candanedo and Sergey Spektor. Radiotherapy management, data collection and co-author of radiotherapy section were performed by Samuel Moscovici and Yigal Shoshan.

The first draft of the manuscript was written by Samuel Moscovici, Jose Cohen and Andrew Kaye. All the authors commented on previous version of the manuscript.

- Ethics approval: yes, # 0132–22-HMO.
- Consent to participate: not applicable.
- Consent for publication: all author consent for publication
- Funding: nil.

CRediT authorship contribution statement

Samuel Moscovici: Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Andrew H. Kaye: . Carlos Candanedo:** Investigation, Formal analysis, Data curation. **José E. Cohen: . Yigal Shoshan:** Writing – review & editing, Visualization, Validation, Supervision, Data curation, Conceptualization. **Sergey Spektor:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jocn.2024.110837.

References

[1] Mariniello G, Corvino S, Corazzelli G, de Divitiis O, Fusco G, Iuliano A, et al. Spheno-orbital meningiomas: the rationale behind the decision-making process of treatment strategy. Cancers (Basel) 2024;16.
[2] Shrivastava RK, Sen C, Costantino PD, Della RR. Sphenoorbital meningiomas: surgical limitations and lessons learned in their long-term management. J Neurosurg 2005;103:491–7.
[3] De Jesus O, Toledo MM. Surgical management of meningioma en plaque of the sphenoid ridge. Surg Neurol 2001;55:265–9.
[4] Saeed P, van Furth WR, Tanck M, Kooremans F, Freling N, Streekstra GI, et al. Natural history of spheno-orbital meningiomas. Acta Neurochir (Wien) 2011;153:395–402.
[5] Ringel F, Cedzich C, Schramm J. Microsurgical technique and results of a series of 63 spheno-orbital meningiomas. Neurosurgery 2007;60. 214 –21; discussion 21–2.
[6] Boari N, Gagliardi F, Spina A, Bailo M, Franzin A, Mortini P. Management of spheno-orbital en plaque meningiomas: clinical outcome in a consecutive series of 40 patients. Br J Neurosurg 2013;27:84–90.
[7] Talacchi A, De Carlo A, D'Agostino A, Nocini P. Surgical management of ocular symptoms in spheno-orbital meningiomas. Is orbital reconstruction really necessary? Neurosurg Rev 2014;37. 301 –9; discussion 9–10.
[8] Scarone P, Leclerq D, Heran F, Robert G. Long-term results with exophthalmos in a surgical series of 30 sphenoorbital meningiomas. Clinical article J Neurosurg 2009;111:1069–77.
[9] Gonen L, Nov E, Shimony N, Shofty B, Margalit N. Sphenoorbital meningioma: surgical series and design of an intraoperative management algorithm. Neurosurg Rev 2018;41:291–301.
[10] Terrier LM, Bernard F, Fournier HD, Morandi X, Velut S, Henaux PL, et al. Spheno-orbital meningiomas surgery: multicenter management study for complex extensive tumors. World Neurosurg 2018;112:e145–56.
[11] Leroy HA, Leroy-Ciocanea CI, Baroncini M, Bourgeois P, Pellerin P, Labreuche J, et al. Internal and external spheno-orbital meningioma varieties: different outcomes and prognoses. Acta Neurochir (Wien) 2016;158:1587–96.
[12] Yannick N, Patrick F, Samuel M, Erwan F, Pierre-Jean P, Michel J, et al. Predictive factors for visual outcome after resection of spheno-orbital meningiomas: a long-term review. Acta Ophthalmol 2012;90:e663–5.
[13] Nagahama A, Goto T, Nagm A, Tanoue Y, Watanabe Y, Arima H, et al. Spheno-orbital meningioma: surgical outcomes and management of recurrence. World Neurosurg 2019;126:e679–87.
[14] Forster MT, Daneshvar K, Senft C, Seifert V, Marquardt G. Sphenoorbital meningiomas: surgical management and outcome. Neurol Res 2014;36:695–700.
[15] Shapey J, Jung J, Barkas K, Gullan R, Barazi S, Bentley R, et al. A single centre's experience of managing spheno-orbital meningiomas: lessons for recurrent tumour surgery. Acta Neurochir (Wien) 2019;161:1657–67.
[16] Fisher FL, Zamanipoor Najafabadi AH, Schoones JW, Genders SW, van Furth WR. Surgery as a safe and effective treatment option for spheno-orbital meningioma: a systematic review and meta-analysis of surgical techniques and outcomes. Acta Ophthalmol 2021;99:26–36.
[17] Agosti E, Zeppieri M, De Maria L, Mangili M, Rapisarda A, Ius T, et al. Surgical treatment of spheno-orbital meningiomas: a systematic review and meta-analysis of surgical techniques and outcomes. J Clin Med 2023:12.
[18] Mariniello G, Bonavolonta G, Tranfa F, Iuliano A, Corvino S, Teodonno G, et al. Management of the skull base invasion in spheno-orbital meningiomas. Br J Neurosurg 2023;1–8.
[19] Mariniello G, Bonavolonta G, Tranfa F, Maiuri F. Management of the optic canal invasion and visual outcome in spheno-orbital meningiomas. Clin Neurol Neurosurg 2013;115:1615–20.
[20] Honig S, Trantakis C, Frerich B, Sterker I, Schober R, Meixensberger J. Spheno-orbital meningiomas: outcome after microsurgical treatment: a clinical review of 30 cases. Neurol Res 2010;32:314–25.
[21] Amirjamshidi A, Abbasioun K, Amiri RS, Ardalan A, Hashemi SM. Lateral orbitotomy approach for removing hyperostosing en plaque sphenoid wing meningiomas. Description of surgical strategy and analysis of findings in a series of 88 patients with long-term follow up. Surg Neurol Int 2015;6:79.
[22] Bowers CA, Sorour M, Patel BC, Couldwell WT. Outcomes after surgical treatment of meningioma-associated proptosis. J Neurosurg 2016;125:544–50.
[23] Maroon JC, Kennerdell JS, Vidovich DV, Abla A, Sternau L. Recurrent spheno-orbital meningioma. J Neurosurg 1994;80:202–8.
[24] Gaillard S, Pellerin P, Dhellemmes P, Pertuzon B, Lejeune JP, Christiaens JL. Strategy of craniofacial reconstruction after resection of spheno-orbital "en plaque" meningiomas. Plast Reconstr Surg 1997;100:1113–20.
[25] Peele KA, Kennerdell JS, Maroon JC, Kalnicki S, Kazim M, Gardner T, et al. The role of postoperative irradiation in the management of sphenoid wing meningiomas. A preliminary report. Ophthalmology 1996;103. 1761 –6; discussion 6–7.
[26] Oya S, Sade B, Lee JH. Sphenoorbital meningioma: surgical technique and outcome. J Neurosurg 2011;114:1241–9.
[27] Moscovici S, Mizrahi CJ, Margolin E, Spektor S. Modified pterional craniotomy without "MacCarty keyhole". J Clin Neurosci 2016;24:135–7.
[28] Shoshan Y, Wygoda M, Umansky F. Stereotactic radiosurgery and fractionated stereotactic radiotherapy: background, definitions, applications. Isr Med Assoc J 2005;7:597–9.
[29] Schneider M, Potthoff AL, Borger V, Hadjiathanasiou A, Schafer N, Guresir A, et al. Outcome of tumor-associated proptosis in patients with spheno-orbital meningioma: single-center experience and systematic review of the literature. Front Oncol 2020;10:574074.
[30] Kim W, Ghodrati F, Mozaffari K, Samarage HM, Zhang AB, Pradhan A, et al. Endoscopic endonasal approach for resection of a recurrent spheno-orbital meningioma resulting in complete resolution of visual symptoms: a case report and review of literature. J Neurooncol 2022;160:545–53.

[31] Kong DS, Kim YH, Hong CK. Optimal indications and limitations of endoscopic transorbital superior eyelid surgery for spheno-orbital meningiomas. J Neurosurg 2021;134:1472–9.
[32] Corvino S, Sacco M, Somma T, Berardinelli J, Ugga L, Colamaria A, et al. Functional and clinical outcomes after superior eyelid transorbital endoscopic approach for spheno-orbital meningiomas: illustrative case and literature review. Neurosurg Rev 2022;46:17.
[33] Maiuri F, Mariniello G, Guadagno E, Barbato M, Corvino S, Caro DBD, et al. WHO grade, proliferation index, and progesterone receptor expression are different according to the location of meningioma. Acta Neurochir (Wien) 2019;161: 2553–61.
[34] Freeman JL, Davern MS, Oushy S, Sillau S, Ormond DR, Youssef AS, et al. Spheno-Orbital Meningiomas: a 16-Year Surgical Experience. World Neurosurg 2017;99: 369–80.
[35] Masalha W, Heiland DH, Steiert C, Kruger MT, Schnell D, Scheiwe C, et al. Progression-free survival, prognostic factors, and surgical outcome of spheno-orbital meningiomas. Front Oncol 2021;11:672228.
[36] Mirone G, Chibbaro S, Schiabello L, Tola S, George B. En plaque sphenoid wing meningiomas: recurrence factors and surgical strategy in a series of 71 patients. Neurosurgery 2009;65. 100 –8; discussion 8–9.
[37] Sandalcioglu IE, Gasser T, Mohr C, Stolke D, Wiedemayer H. Spheno-orbital meningiomas: interdisciplinary surgical approach, resectability and long-term results. J Craniomaxillofac Surg 2005;33:260–6.
[38] Sughrue ME, Rutkowski MJ, Chen CJ, Shangari G, Kane AJ, Parsa AT, et al. Modern surgical outcomes following surgery for sphenoid wing meningiomas. J Neurosurg 2013;119:86–93.
[39] Pompili A, Derome PJ, Visot A, Guiot G. Hyperostosing meningiomas of the sphenoid ridge–clinical features, surgical therapy, and long-term observations: review of 49 cases. Surg Neurol 1982;17:411–6.
[40] Alzhrani G, Couldwell W. Bony hyperostosis recurrence after complete resection of sphenoorbital meningioma. Cureus 2017;9:e1540.
[41] Bikmaz K, Mrak R, Al-Mefty O. Management of bone-invasive, hyperostotic sphenoid wing meningiomas. J Neurosurg 2007;107:905–12.
[42] Goldbrunner R, Minniti G, Preusser M, Jenkinson MD, Sallabanda K, Houdart E, et al. EANO guidelines for the diagnosis and treatment of meningiomas. Lancet Oncol 2016;17:e383–91.
[43] Jenkinson MD, Weber DC, Haylock BJ, Mallucci CL, Zakaria R, Javadpour M. Radiotherapy versus observation following surgical resection of atypical meningioma (the ROAM trial). Neuro Oncol 2014;16:1560–1.
[44] Kaur G, Sayegh ET, Larson A, Bloch O, Madden M, Sun MZ, et al. Adjuvant radiotherapy for atypical and malignant meningiomas: a systematic review. Neuro Oncol 2014;16:628–36.
[45] Terpolilli NA, Ueberschaer M, Niyazi M, Hintschich C, Egensperger R, Muacevic A, et al. Long-term outcome in orbital meningiomas: progression-free survival after targeted resection combined with early or postponed postoperative radiotherapy. J Neurosurg 2019;1–11.
[46] Mariniello G, de Divitiis O, Corvino S, Strianese D, Iuliano A, Bonavolonta G, et al. Recurrences of spheno-orbital meningiomas: risk factors and management. World Neurosurg 2022;161:e514–22.
[47] Astradsson A, Wiencke AK, Munck af Rosenschold P, Engelholm SA, Ohlhues L, Roed H, Juhler M. Visual outcome after fractionated stereotactic radiation therapy of benign anterior skull base tumors. J Neurooncol 2014;118:101-8.
[48] Combs SE, Adeberg S, Dittmar JO, Welzel T, Rieken S, Habermehl D, et al. Skull base meningiomas: Long-term results and patient self-reported outcome in 507 patients treated with fractionated stereotactic radiotherapy (FSRT) or intensity modulated radiotherapy (IMRT). Radiother Oncol 2013;106:186–91.