

Review

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The role of endoscopy and radiosurgery in the management of cavernous sinus meningiomas

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Abstract

Cavernous sinus (CS) meningiomas represent a formidable neurosurgical pathology. The desired treatment depends on tumor size and extensions apart from the presenting clinical symptoms of the patient. The last few decades have shown a paradigm shift in the management towards a multimodal treatment. For patients with tumors presenting with a medial extension or when the meningioma occupies the antero-inferior portion of the CS, an endoscopic biopsy can be safely performed through the endonasal route. The boundaries of endoscopic endonasal approaches have been pushed during the last decade, and a direct access to the CS may now be performed. At the same time, an extensive bony decompression to decompress the optic canal and the pituitary gland may be performed. Autologous fat may be interposed between the residual tumor and radiosensitive structures to safely perform adjuvant radiation therapy. The aim of this manuscript is to describe the role of endoscopic surgery in the management of cavernous sinus meningiomas along with the complementary role of radiotherapy. We describe the endoscopic anatomy and the surgical technique to safely perform the procedure and we review the surgical series reported in the literature dealing with the endoscopic approach for CS meningiomas with or without complementary radiation therapy. Endoscopic endonasal approaches have shown promising results in terms of improvement or stabilization of cranial neuropathy and hypopituitarism. Furthermore, the endoscopic approach may enhance the efficacy and safety of stereotactic radiosurgery through the performance of an hypophysopexy and/or chiasmopexy.



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Keywords: Cavernous sinus, meningioma, skull base, surgery, endoscopy, radiosurgery, radiotherapy

INTRODUCTION

Meningiomas account for one third of primary intracranial tumors with an incidence of 3-8 per 100,000 persons^[1]. They represent more than 40% of lesions involving the cavernous sinus (CS)^[2]. CS meningiomas originate or invade the parasellar space: they may start primarily within the CS or it may be involved secondarily in clinoidal or other sphenoid wing meningiomas, in addition to those arising from the tuberculum sellae or speno-petro-clival region. CS meningiomas are deeply located near critical neurovascular structures such as the optic pathways, the hypothalamo-hypophyseal axis, the internal carotid artery and its branches, and the oculomotor and trigeminal nerves. They may further extend into the supra and latero-sellar spaces, orbital apex and optic canal, sphenoid ridge, middle temporal fossa, and petroclival angle. The CS region, due to its complex anatomy and its particular position in the antero-lateral skull base, has always been a challenging area of treatment for neurosurgeons.

As with the great majority of intracranial meningiomas, CS meningiomas are WHO grade I tumors with a very slow growing rate. Their surgical treatment may result in significant neurological morbidity and even death. For this reason, the management of these patients should be multidisciplinary discussed according to the size, extension, clinical presentation, and evolutive pattern to grant the patients the longest survival possible with the lowest cranial nerve morbidity.

Small and asymptomatic meningiomas are often managed conservatively^[3]. In general, 15% of patients have neurological deficits at presentation^[4,5]. Ophthalmoplegia, secondary to tumor growth or as a complication of treatment, can represent a serious issue that strongly impairs the quality of life of these patients, affecting their self-image and their private and professional life. Thus, a balance between the different therapeutic options should be found for symptomatic CS meningiomas. A complete preoperative endocrinological assessment and an ophthalmological evaluation should be performed for every patient with visual complaints and/or radiological compression of the optic apparatus.

Symptomatic meningiomas enclosed in the cavernous sinus are offered up front radiosurgery or stereotactic fractionated modality. Tumors presenting a lateral extension should be addressed through a transcranial approach for the resection of the extracavernous portion. In surgical series, recurrences and progression free-survival rates range from 6% to 25% and from 4.5% to 65%, respectively, while the mortality rate varies between 2% and 7% and the morbidity from 10% to 65%^[6-8]. Thus, the results in terms of complete tumor removal, preservation of neurological functions, and quality of life do not always correspond to the expectations. Saberi *et al.*^[9] showed that the most important variable influencing the surgical outcome was the grade of encasement of nerves and vessels. The histological type, extent of dural attachment, and relationship and encasement with neurovascular structures should thus be carefully considered for the optimal management of CS meningiomas.

With CS meningiomas presenting a medial extension into the sphenoid sinus or extending into the antero-inferior portion of the CS, an endonasal approach can be performed as the tumor itself may create a safe space between the anterior dura and the internal carotid artery (ICA). Over the last few decades, endoscopic endonasal approaches have remarkably developed with the development of extended approaches^[10-14]. Through the transnasal route, it is possible to safely remove the tumor with a partial debulking, to decompress the optic canal or to perform a tissue biopsy when the diagnosis is not clear, particularly when another histological nature is suspected (lymphoma, granuloma, ectopic pituitary adenoma, neurofibroma, cavernous hemangioma, *etc.*)^[15-19]. The goals of endoscopic endonasal procedures

Table 1. The advantages and disadvantages of the different surgical approaches for cavernous sinus meningiomas are here summarized

	Transcranial surgery	Endoscopic surgery	Radiosurgery
PROS	To address the extracavernous portion of the tumor in the temporal fossa	Direct access for optic nerve and pituitary gland decompression	Non-invasive procedure
	To address the supraclinoid portion of the tumor lateral to the ICA or with an encasement	To avoid brain retraction and manipulation	Low risk of complications
	To decompress the lateral portion of the optic canal	To interpose autograft fat to protect radiosensitive structures (optic nerve and pituitary gland)	Good control rate (equivalent to Simpson grade I)
CONS	High risk of cranial nerve palsy if the lateral wall of the CS is entered	Limited resection of the lateral portion of the tumor	Tumor too close to pituitary gland and optic nerve are a relative contraindication
	Risk of vascular injury	Risk of vascular injury and of cranial nerve palsy	No pathological analysis
	Risk of damage of brain parenchyma/epilepsy	Risk of hypopituitarism	Limited to small volumes
		Risk of CSF leakage	No decompression, thus less chance to improve pre-existing symptoms

CS: cavernous sinus; CSF: cerebrospinal fluid; ICA: internal carotid artery

are: (1) to perform an adequate bony decompression of the cavernous sinus, sella turcica and optic canal in cases with optic nerve compression; (2) to obtain tissue for a pathological analysis and a genomic profiling; (3) to reduce the volume of tumor to be treated by radiosurgery; and (4) to perform an hypophysopexy or chiasmopexy and allow a safer irradiation at a later date.

In most cases, the combination of a less aggressive surgical approach with a complementary radiation treatment seems to be the best management^[20,21]. Indeed, aggressive surgical resections are associated with a higher risk of complications and do not improve the natural history of the disease or the global outcome except in carefully selected cases^[22,23] [Table 1]. Furthermore, many of these tumors tend to recur over the long term. The combined treatment should be realized in tertiary care centers with a large experience in this area and a sufficient caseload [Figure 1].

Herein, we detail the relevant endoscopic endonasal anatomy of the cavernous sinus region and review the results of the surgical series reported in the literature dealing with the endoscopic endonasal management of CS meningiomas.

ENDOSCOPIC ANATOMY

The cavernous sinus is a paired venous sinus surrounded by dural layers and located in the middle cranial fossa. It is limited medially by the sphenoid bone and the sellar region, and laterally by the mesial face of the temporal lobe. The posterior margin is limited by the posterior cranial fossa, while anteriorly the cavernous sinus reaches the superior orbital fissure and the inferior surface of the anterior clinoid process. Cavernous sinus floor extends from the anterior to the posterior clinoid process and faces the basal cisterns. The lateral dural wall of the cavernous sinus is composed of the outer dural layer and the inner membranous layer. The inner layer contains the most critical nervous structures. The existence of a medial dural wall separating the pituitary from the CS remains a matter of debate^[24]. The CS contains multiple neurovascular structures: the sympathetic plexus around the internal carotid artery, the oculomotor nerves (III, IV, and VI) and the first and second roots of the trigeminal nerve (V1 and V2). In a cranio-caudal direction the III, IV, V1, and V2 course within the lateral wall of the sinus, while the VI cranial nerve is positioned within the CS, just lateral to the ICA [Figures 2 and 3].

To reach the CS through an endoscopic endonasal corridor, the extent of the approach varies from a standard transsphenoidal approach to more extended accesses, which include transpterygoid approaches

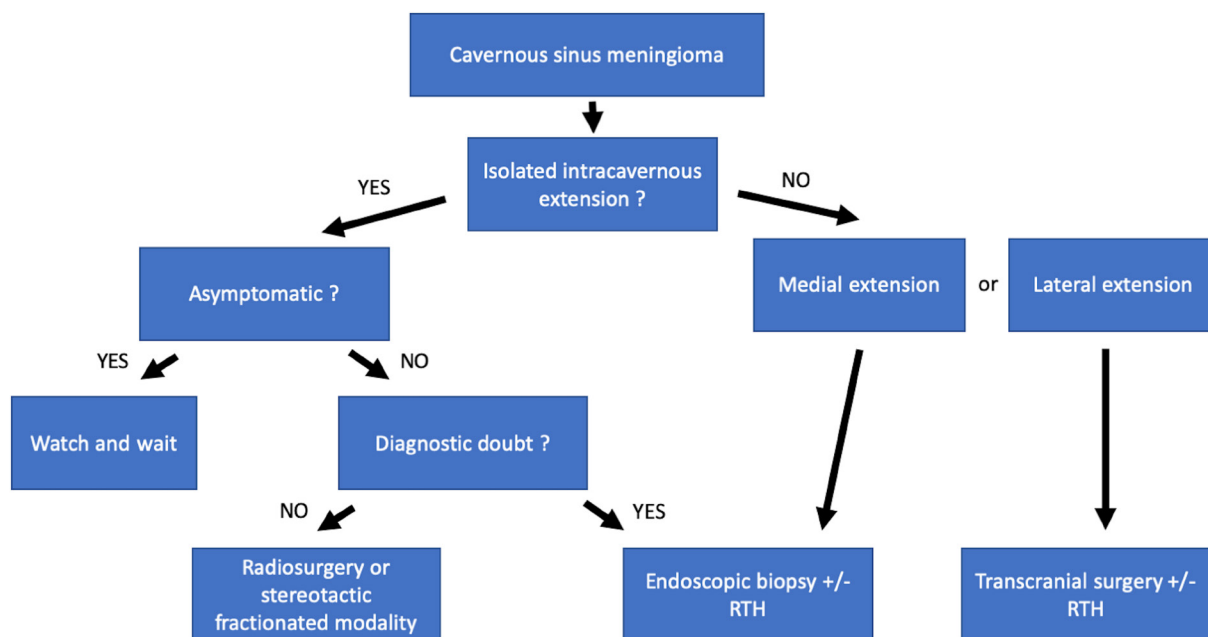


Figure 1. Algorithm showing the management of patients with cavernous sinus meningiomas according to the extension of the tumor and the clinical presentation or the doubt on the histological diagnosis. RTH: radiation therapy

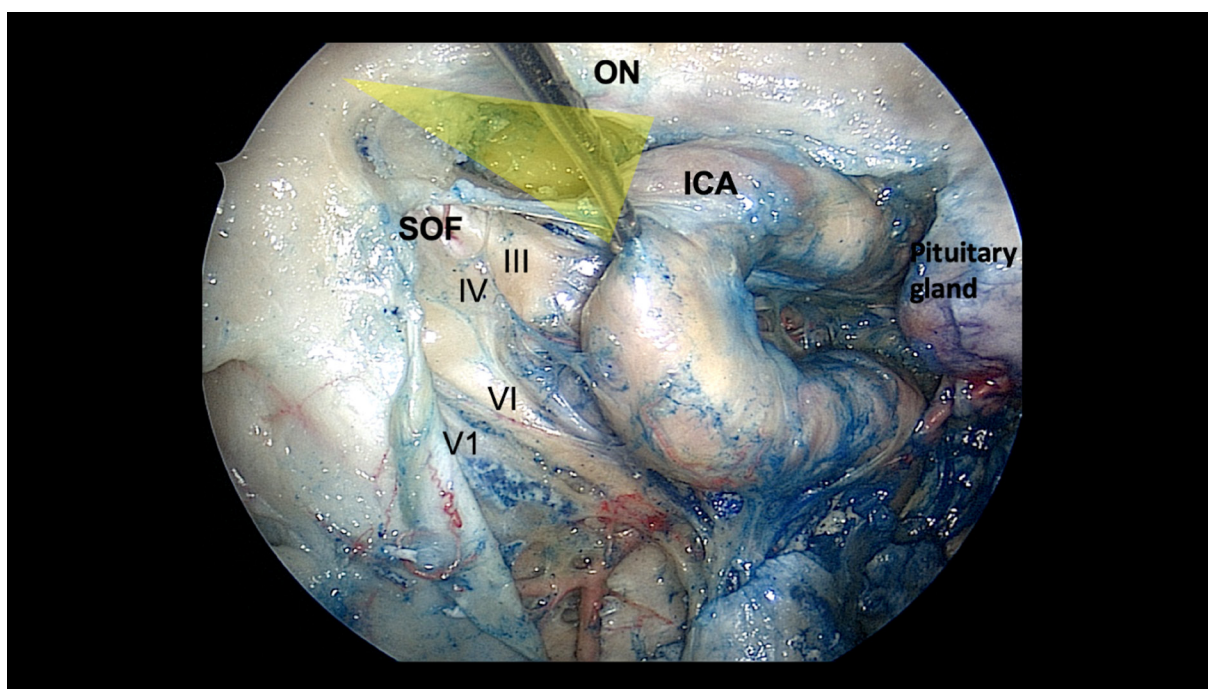


Figure 2. Endoscopic endonasal view of the right CS in a cadaveric specimen. The bone covering the CS was completely drilled to expose the ICA, the oculomotor nerves (III, IV, and VI) going to the SOF, and the first branch of the trigeminal nerve (V1). Superiorly, the ON is still covered by a thin layer of bone. The lateral optico-carotid recess is colored in yellow. Medially, the pituitary gland is also exposed. CS: cavernous sinus; ICA: internal carotid artery; ON: optic nerve; SOF: superior orbital fissure

with anterior and posterior ethmoidectomies and vidian canal dissection. The anatomy of the sphenoid sinus in terms of pneumatization and presence of septa should be carefully considered on preoperative imaging. The sphenopalatine artery courses at the inferior portion of the sphenoid ostium and should

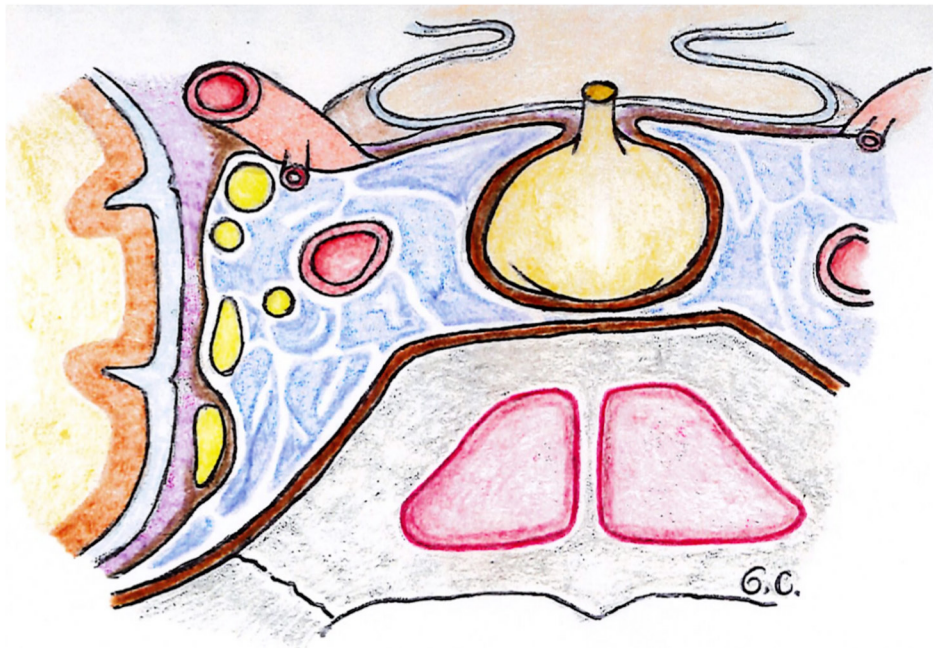


Figure 3. Schematic representation of the right cavernous sinus. The III, IV, VI, and V2 course within the lateral wall of the sinus in a craniocaudal order, while the VI cranial nerve is the only one inside the cavernous sinus, just lateral to the internal carotid artery

be preserved. Once the sphenoid sinus is entered, the sellar floor is identified in the midline with the tuberculum sellae and the landmarks of the optic canals superiorly and laterally, as well as the carotid prominences laterally. The medial and lateral optico-carotid recesses are also recognized [Figure 4]^[25]. Within the sphenoid sinus, the anterior CS corresponds to the anterior carotid prominence, easily identified on the lateral sphenoid sinus wall.

In cases where a transpterygoid approach is performed, the bony anatomy of the maxillary and ethmoid sinuses should be analyzed. The pterygopalatine fossa is a pyramidal space located between the pterygoid bone posteriorly, the palatine bone anteromedially, and the maxillary bone anterolaterally^[10,11]. Once the maxillary sinus is entered, the infraorbital nerve is a consistent landmark and the pterygopalatine fossa is medial to it. It has a rich vasculonervous content, namely the third segment of the maxillary artery and its branches (anterior compartment of the fossa) [Figure 5], the pterygopalatine ganglion, the greater and lesser palatine nerves, the maxillary and infraorbital nerves, and the vidian nerve (posterior compartment)^[10-14]. The anterior opening of the vidian canal is located medially while the foramen rotundum is located laterally^[10]. Foramen lacerum and petrous ICA may be exposed following the vidian nerve postero-medially, while the lateral portion of the clival recess is the landmark for the medial wall of the paraclival ICA. The foramen rotundum can also be used as an anatomical landmark for the antero-inferior wall of the CS during extended approaches.

IMAGING

Both CT-Scan and MRI are essential to assess the bony and neurovascular relationships of the meningioma. MRI shows the exact location and the extension of the meningioma. It helps in defining the limits of the tumor in relationship with the neurovascular structures inside and outside the CS. T2-weighted coronal sequences allow a good analysis of the meningioma's relationships with the CS dural layers [Figure 6]. The distance from the optic pathways, the cranial nerves anatomy, and the pituitary region can also be carefully appraised particularly using CISS-3D or FIESTA sequences as well as cranial nerve tractography.

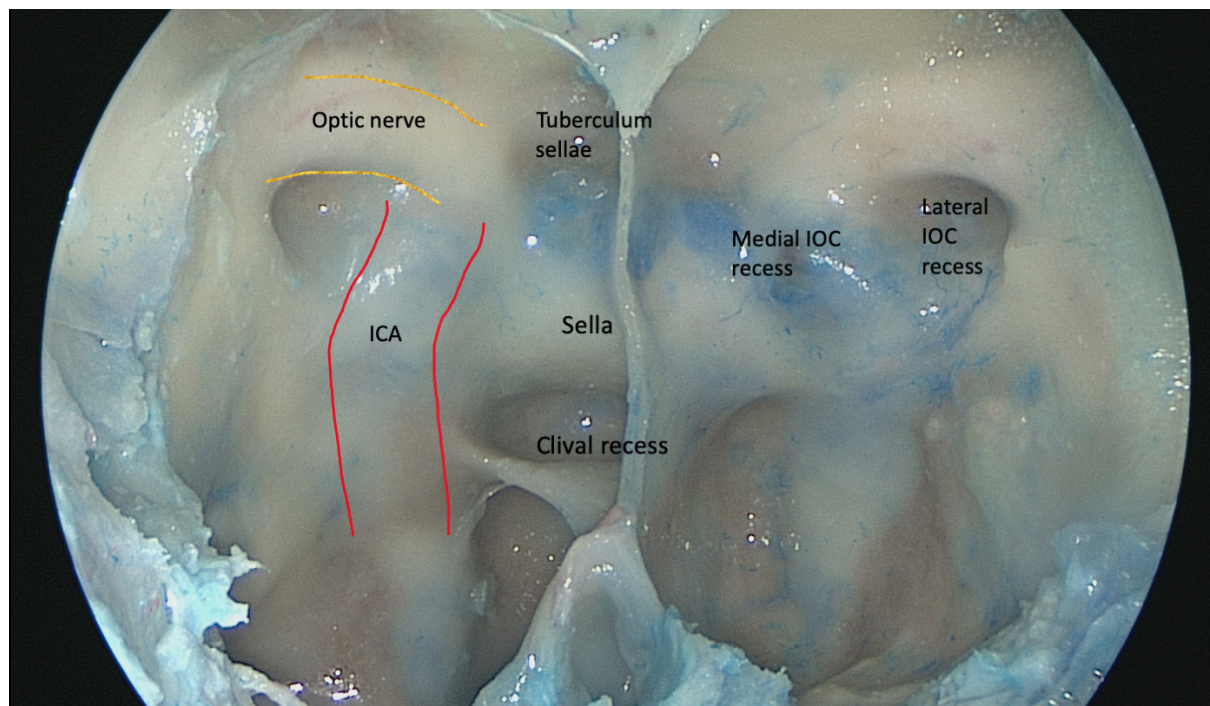


Figure 4. Endoscopic endonasal view of the posterior wall of the sphenoid sinus in a cadaveric specimen. A midline septum was partially drilled. In the midline, in a craniocaudal direction, the tuberculum sellae, the sella, and the clival recess are evident. Laterally, the carotid prominence (red lines) and, superiorly, the optic nerve (golden lines) are delimited. The medial and lateral IOC recesses are also marked. ICA: internal carotid artery; IOC: interoptico-carotid

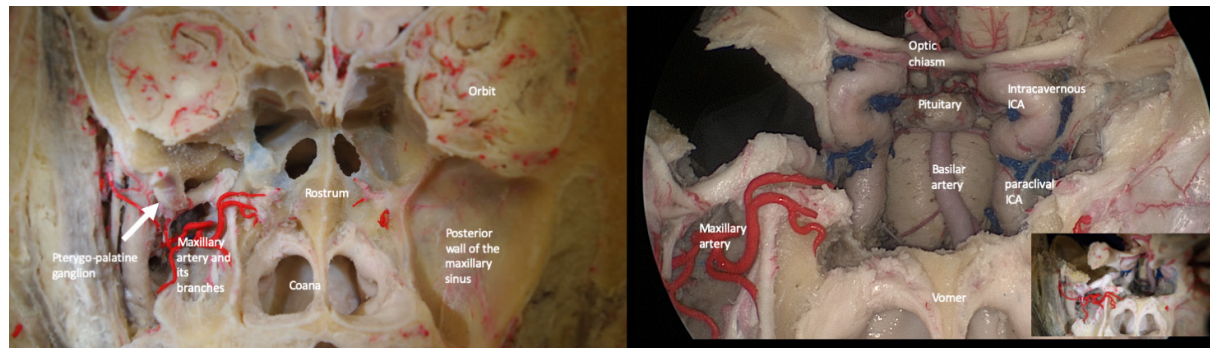


Figure 5. Coronal view of the pterygo-palatine fossa in a cadaveric specimen. Once that the posterior wall of the maxillary sinus is opened, the maxillary artery and the pterygopalatine ganglion are exposed (left). A large sphenoidotomy is performed to illustrate the close relationships between the different structures. Once that the vidian nerve is identified, it can be followed posteriorly until the foramen lacerum and the petrous ICA (right). ICA: internal carotid artery

High-resolution contrast-enhanced axial MRI is necessary in the preoperative planning and fat suppression images may be used for tumors adjacent to the orbit or when a chiasmectomy has been previously performed. The angio-MRI is useful to delineate the caliber and the displacement of the ICA and its branches, while the MR-venography illustrates the venous drainage of the skull base^[26]. A detailed study of the ICA course and of the collateral systems is fundamental before starting the resection of a CS meningioma.

Thin-slices bone CT scan is valuable to study the presence and direction of septa and the degree of pneumatization of the sphenoid sinus, the anatomy of the anterior and posterior clinoid processes, the sella turcica and the orbital apex, the sphenoid wing and its foramina, and the petrous apex. The invasion of

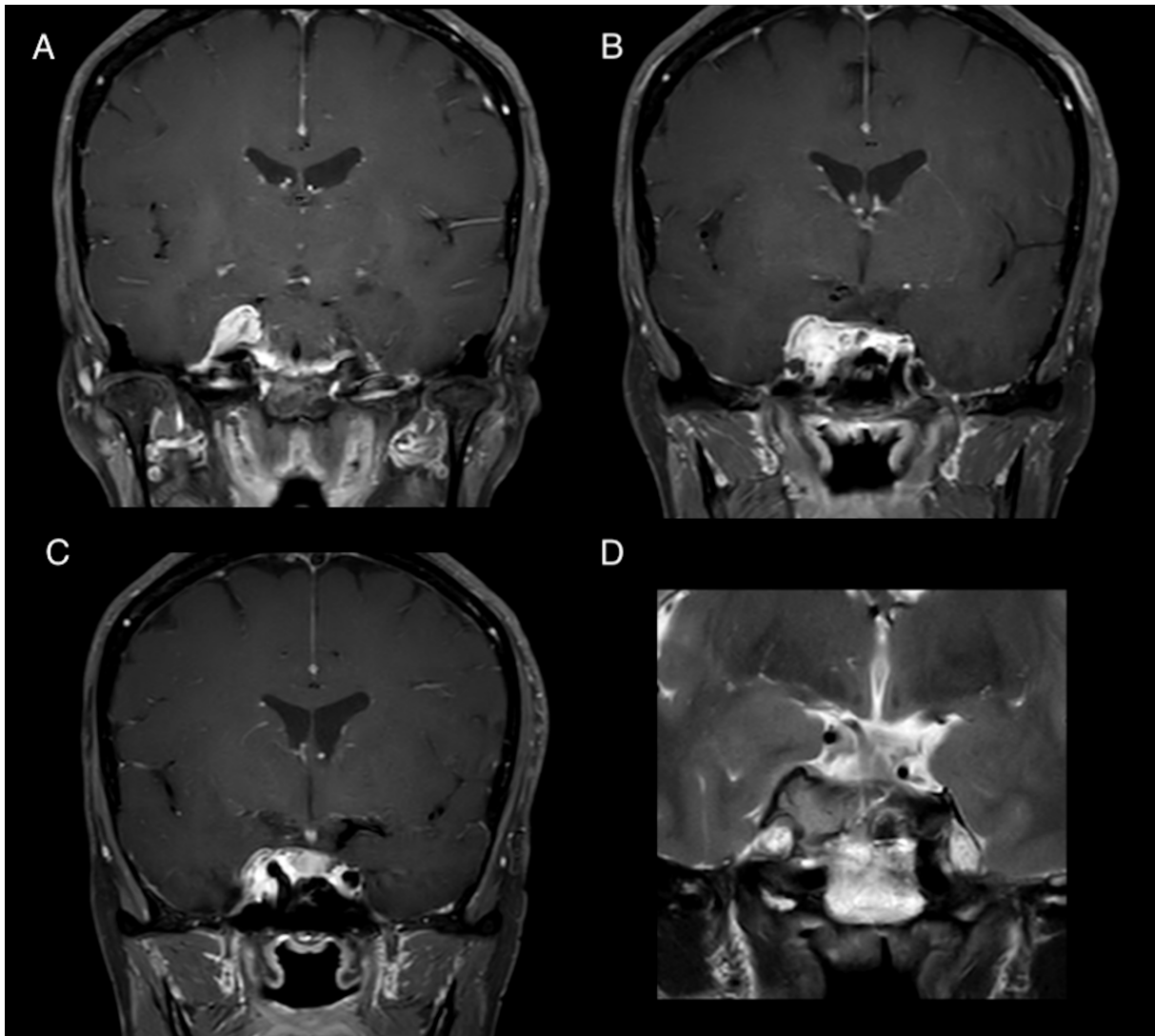


Figure 6. Coronal view of a cerebral MRI showing a meningioma in the right CS. The asymmetry between the row cavernous sinuses is evident and the lesion present a strong contrast enhancement after gadolinium administration (A-C). The relationships between the meningioma and the lateral wall of the CS and the optic apparatus are better defined through the analysis of T2-weighted sequences (D). CS: cavernous sinus

the optic canal and the superior orbital fissure, as well as rotundum, ovale, and lacerum foramina, should be checked for, as well as the potential invasion of the sphenoid sinus. The presence of osteolysis or bone reactive hypertrophy should be carefully evaluated. The latter in particular could reflect tumoral infiltration and may be the target for extensive drilling.

While angio-MRI and angio-CT have progressively lessened the need for digital subtraction angiography, this may be useful to evaluate the collateral network, particularly in case of ICA narrowing using balloon occlusion tests.

SURGICAL TECHNIQUE

The endonasal approach to address CS meningiomas has the advantage of avoiding brain retraction and manipulation, with a straightforward access to decompress the optic nerve, pituitary gland, and cranial nerves. The endoscope allows a panoramic visualization and a more lateral exposure when compared to

microscopic endonasal approaches^[27]. This permits the performance of a precise bony decompression around the sella, the medial cavernous sinus, the optic canal, and, if necessary, of the clivus and Meckel's cave^[17]. Furthermore, this approach allows the positioning of autograft fat between the tumor and radiosensitive structures for further treatments^[28].

After induction of general anesthesia, the endotracheal tube is positioned on the left of the patient and the head should be slightly tilted to the left, turned to the right, and slightly flexed as for a standard endoscopic endonasal transsphenoidal approach. The neuronavigation system is positioned to guide the procedure and the volumetric MRI is fused with the bone-window CT to increase the precision of target definition. Intraoperative monitoring is useful to monitor the function of the oculomotor and trigeminal nerves. The face, the right periumbilical area, and/or the thigh are draped for graft harvesting if necessary.

In general, a binostril bimanual technique is preferred to obtain a wider range of movement. The primary surgeon operates with dissecting instruments and the drill from the right nostril, while the assistant surgeon manages the endoscope in the right nostril and the suction in the left nostril to keep the surgical field clear. Alternatively, a contralateral uninostril approach can also be an option. The right middle turbinate can be resected to widen access if needed during the procedure. Once the sphenoid ostium is identified medial to the superior turbinate and superior to the choana, a wide sphenoidotomy is performed with a posterior septostomy. A large exposition of the sphenoid sinus is necessary to identify the posterior wall landmarks, including the tuberculum, sellar floor, and clival recess in the midline, as well as the optic canals, carotid prominences, and optico-carotid recesses laterally.

A key part of the procedure is bony decompression of the sella, cavernous sinus, optic canal superiorly, and upper clivus when necessary. The bone is generally removed with a high-speed diamond burr and the ultimate eggshell layer is removed with a Kerrison rongeur to safely expose the dura. Constant irrigation should be performed during the drilling to avoid thermic lesions to delicate neuro-vascular structures. The medial and the anterior wall of the cavernous sinus are exposed after the ipsilateral side of the sella is exposed. The medial optico-carotid recess is then progressively exposed. The optic canal unroofing is one of the most important steps, which should be carefully performed as this could induce visual deterioration^[29]. This part of the procedure is necessary when there is a reduction in the caliber of the optic canal and/or when the patient presents with an optic neuropathy. Doppler ultrasound and neuronavigation are useful to localize the ICA during the osseous decompression and before dural opening. Tumor removal should be performed selectively with the goal of decompressing the optic nerve, the pituitary gland, and the cranial nerves into the cavernous sinus. The medial portion of the tumor invading the sella should be initially removed [Figure 7].

Subsequently, the dura over the cavernous sinus can be opened in a lateral to medial direction to avoid injury of the ICA. Brisk venous bleeding is common after tumor removal and can be controlled with hemostatic agents and temporary mechanical packing. A nerve stimulator is used to localize the course of VI cranial nerve once the CS is entered. Visualization of cranial nerves is not necessary and often dangerous. Electrocautery in the area should be avoided to prevent thermal injuries. Excision of the tumor is done in a piecemeal fashion with curettes and ultrasonic aspiration (particularly useful with fibrous tumors). The integrity of the lateral wall and the roof of the cavernous sinus should be respected. At the end of the resection, a hypophysopexy is performed with the positioning of small pieces of fat between the residual tumor and the pituitary gland to fill the dead space created by tumor removal and to better delineate the target and provide a margin for adjuvant radiosurgery in order to protect radiosensitive structures. In general, when a biopsy is performed for purely intracavernous lesions, there is no CSF leakage. An artificial dural substitute or fascia lata from the thigh and glue are sufficient for skull base reconstruction. A nasoseptal flap is rarely required. An endocrinological assessment should be performed in the postoperative period and records are kept for fluid intake and urine output.

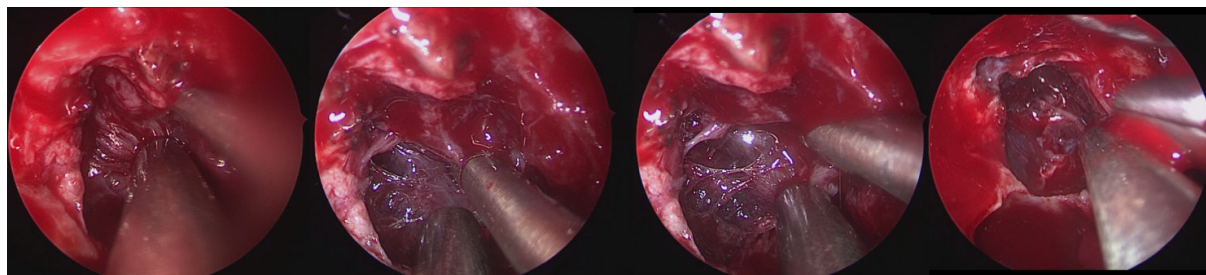


Figure 7. Intraoperative pictures showing the endoscopic resection of an infradiaphragmatic meningioma invading the right cavernous sinus. The resection should start from the intrasellar portion and then proceed towards the cavernous sinus. A complete removal of the meningioma invading the medial portion of the cavernous sinus was possible in this case

REVIEW OF REPORTED SURGICAL SERIES

We performed a literature review on PubMed database up to April 2020 to summarize the surgical series treating patients with CS meningiomas through endoscopic surgery followed or not by adjuvant radiotherapy. The articles were identified using Boolean searches with the keywords “endoscopy” AND “cavernous sinus” AND “meningioma”. Table 2 shows in detail the surgical results and the final outcome. Nine series published between 2009 and 2020 gathered 106 patients in whom an endoscopic endonasal approach was performed for CS meningiomas^[18,28,30-36]. In most of cases, the aim was to perform a tissue biopsy and decompression of cranial nerves in the CS or optic nerve. gross total resection was performed only in rare cases^[18,33-35].

In only nine cases (8.5%), a worsening of the cranial nerve palsy was recorded, while in three out of 97 cases (3%) a new endocrinological deficit occurred. The surgical complications reported were: CSF leakage in three cases, one case needed a ventriculoperitoneal shunt but he was operated through a combined approach (endoscopic and transcranial), and two patients experienced an ICA injury (one died from a hemispheric infarct). Forty-three out of 64 patients (67%) reported an improvement in CN palsy in the postoperative period and 22/41 (53.6%) had an improvement in their pituitary function. Adjuvant radiation therapy was administered in 43/78 patients (55%). The protocols of radiation therapy administered varied from stereotactic radiotherapy (RT) to radiosurgery or particle beam irradiation and when specified the tumor control was excellent at a mean follow-up of 39 months. Only one complication of stereotactic RT was reported with the development of a pituitary insufficiency after the treatment.

Endoscopy might enhance the efficacy and safety of stereotactic radiotherapy or radiosurgery. This might be due to the fact that during surgery an adequate distance can be created between the tumor and the pituitary through the resection of the meningioma, thus allowing a safer irradiation. Furthermore, the interposition of abdominal fat (hypophysopexy) between the meningioma and the pituitary gland may limit the risk of post-radiation endocrinopathies.

In summary, from these studies, we can conclude that a biopsy or planned partial tumor removal may be safely performed, coupled with bony decompression, to improve the visual symptoms and obtain a decompression of the cavernous sinus. Better results in terms of symptomatic improvement were obtained in the cohort of previously untreated patients^[28].

Furthermore, endoscopy may improve or stabilize pre-existent cranial neuropathy and endocrinopathy (67% of patients in Lobo’s series improved their endocrinopathy and 42% of patient improved or resolved their cranial neuropathy)^[32].

Table 2. Summary of the surgical series reporting an endoscopic management of patients with cavernous sinus meningiomas

	No. pts	Treatment plan	Postop new CN palsies	Postop new CN endocrinopathies	Other complications	CN palsy improvement	Endocrinological improvement	RT protocol	Mean FU	Tumor control
Akutsu et al. ^[30] 2009	21	17 Surgery + RT 4 only surgery	0	1	0	15/17 (88.2%) Or 32/34 (94%)	16/28 (57%)	13 SRT 2 SRS 2 PBRT	71 mo	100%
Liu et al. ^[36] 2009	2	Surgery +/- RT	0	0	1 CSF leakage	NS	NS	1 RT	NS	NS
Grailion et al. ^[31] 2014	2	STR + SRS	0	0	0	2	NS	SRS	18 mo	2 (100%)
Khan et al. ^[33] 2014	9	8 STR 1 GTR	1/7 (14%)	NS	1 VP shunt and 1 meningitis (also transcranial approach performed)	5/7 (71%)	NS	6 RT	14 mo	NS
Zhang et al. ^[18] 2014	6	4 GTR 2 STR	0	0	0	NS	NS	None	37 mo	NS
Lobo ^[32] 2015	15	9 surgery 6 surgery + RT	1	0 (1 after SRT)	NS	8/15 6 stable	4/6 (67%)	6 SRT	21 mo	10 controlled (6/6 or 100% pts with surgery + SRT) 5 progression NS
Koutourouliou ^[35] 2017	28	2 GTR 14 STR	4 (14.3%)	2 (7.1%)	1 CSF leak 1 DVT (3.8%) 2 ICA injuries (7.1%; 1 died)	NS	NS	NS	NS	NS
Sivakumar ^[28] 2019	20 (6 previous TT)	Surgery + SRT if no previous RT and growth at FU	1 immediate 2 delayed TOT 3/8 (38%)	0	1 CSF leak and meningitis	8/14 (57%) 2/6 (33%) 4/6 pts with ON decompression had improvement (66%)	2/7	SRT 54Gy in 30fr 11/14	57 mo	14/14 pts with no previous RT (100%) 2/6 with previous TT controlled tumor 2/6 died 3 (100%)
Zhang ^[34] 2019	3	Only surgery 1 GTR 2 STR	0	0	0	3	NS	None	54 mo	3 (100%)

CN: cranial nerve; CSF: cerebrospinal fluid; DVT: deep venous thrombosis; GTR: gross total resection; PBRT: proton beam radiotherapy; fr: fractions; FU: follow-up; Gy: gray; NS: not specified; ON: optic nerve; RT: radiotherapy; SRS: stereotactic radiosurgery; STR: stereotactic radiotherapy; SRT: stereotactic resection; TOT: total; T: treatments; VP: ventriculoperitoneal

COMBINED AND ADJUVANT STRATEGIES

From a radiobiological point of view, meningiomas are considered as late responding tumors and they can be better controlled with a higher dose/fraction rather than conventional fractionation, as explained in the meta-analysis performed by Leroy et al.^[37], where radiosurgery (RS) achieved a twice-higher rate of tumor volume regression than fractionated radiotherapy. This explains why the use of Gamma Knife or dedicated Linac/Cyberknife systems may offer the possibility to obtain excellent outcomes in terms of local control with reduction of treatment associated risks^[37]. Precise delineation of target volumes (TV) with selective coverage and steep radiation falloff with sparing of normal tissues are the keys to a successful treatment.

RS can be considered as first line treatment for small symptomatic CS meningiomas if they present a safe distance from the optic pathway^[38-43]. For large meningiomas, a single fraction RS may be problematic as the risk of damaging healthy tissues is high and a complication rate of 21% *vs.* 3% was reported for meningiomas larger than 10 cm³ *vs.* smaller lesions respectively^[44]. Furthermore, the distance between the optic apparatus and the tumor should be carefully considered before choosing the primary treatment: a distance of at least 5 mm between the meningioma and the optic nerve is considered safe^[45,46]. Thus, when the meningioma is large or too close to the optic pathways, a combined approach with a surgical partial decompression followed by adjuvant radiation therapy should be preferred.

Whether RS should be routinely performed in the months after surgery or only in cases of postoperative tumor progression is still a matter of debate. Considering the natural history of meningiomas, we know that they have a slow tendency to grow but about one fourth of all the meningiomas, in particular those calcified, do not seem to grow^[47]. In common practice, the irradiation is generally performed 3-6 months after surgery, while, for minimal residual tumors, radiation is performed when a growth is visible on follow-up images. This waiting time should help in the recovery of cranial nerves and pituitary gland surgical manipulation^[32]. For atypical meningiomas or meningiomas showing an aggressive behavior with a higher growth rate, radiotherapy should be performed in a shorter period of time^[32]. Beside the histological grade, the previous treatments performed should also be taken into account before planning the treatment. The inclusion of the dural tail in the TV is matter of debate, and, when an irregular shape is present, the dose distribution should be accurately checked^[48-50].

For radiosurgical treatments, the dose recommended is between 12 and 15 Gy, which allows a good compromise between tumor growth control and local neurotoxicity. The risk of damaging the optic apparatus exists when the dose (to nerve) received is more than 8 Gy. The oculomotor nerve in the cavernous sinus tolerates doses greater than 20 Gy while the trigeminal nerve is at risk with doses beyond 19 Gy. However, in common practice, the lateral wall of the cavernous sinus, the pituitary gland, and stalk, the hypothalamus and brainstem should not receive more than 15 Gy.

In their review of the outcomes of large radiosurgical series, Fariselli *et al.*^[51] showed progression free survival at 5 and 10 years of 80%-100% and 73%-98%, respectively, and a radiological volume reduction was observed in 29-69% of cases. No mortality was described as secondary to radiation therapy, while the reported morbidity included new neurologic symptoms or symptoms of neurotoxicity (optic neuropathy, pituitary dysfunction, diplopia, and radiation-induced edema), which ranged from 6% to 27.5%^[52-55]. A meta-analysis comparing primary RS *vs.* surgery followed by adjuvant RS showed a lesser rate of neurological morbidity in the primary RS group (27.5% *vs.* 59.6%)^[55]. Kano *et al.*^[56] reported that improvement in cranial nerve palsies was less likely to occur in patients who had undergone previous surgery when compared to those treated with radiosurgery alone (14% *vs.* 39%). One explanation may be that operated patients had permanently damaged cranial nerves as a result of the surgery. It is well described that about 75% of recurrences occur outside the treatment field and this reflects the paramount importance that needs to be placed on the contouring phase of the treatment^[57].

For recurrent meningiomas, data on the efficacy of repeated RS are limited. Mifepristone and bevacizumab have been described as promising agents for recurrent tumors, but these results still need to be validated in larger studies. Nonetheless, these drugs, which target tumor receptors, highlight the importance of obtaining a histological diagnosis and genomic profiling before their introduction to select effective targeted therapies^[58,59].

CONCLUSION

The management of CS meningiomas depends on the size and extension of the tumor and on the clinical manifestations of the patient. The treatment decision varies among a simple annual clinico-radiological

follow-up, transcranial or endoscopic surgery according to the extension of the tumor, radiation therapy, or the combination of both. The main goal of the treatment is to prevent growth and to avoid or prevent neurological deficits. For symptomatic meningiomas extending into the antero-inferior portion of the cavernous sinus, a direct endoscopic transcavernous approach should be preferred. It represents a safe procedure, with a very low complication rate when patients are carefully selected in a tertiary level center, with good improvement rates or at least stabilization of cranial neuropathies and endocrinopathy. Multidisciplinary recommendations for a specific treatment carries an important ethical responsibility and it is the duty of each surgeon to propose the best management to each patient keeping in mind the risk-benefit analysis.

TRICKS

1. An endoscopic transcavernous biopsy/partial removal is easily performed when the meningioma is located in the antero-inferior portion of the CS.
2. Intraoperative neuronavigation and careful understanding of preoperative anatomy are key factors in safely performing the procedure.
3. Fully endoscopic procedures should be preferred to microscopic procedures performed under endoscopic assistance for the better panoramic view allowed by the endoscope.
4. Doppler ultrasound is invaluable in localizing the carotid artery inside the tumor and guide tumor removal.
5. Bony decompression of the optic canal is a key step of the procedure to increase the chance of visual improvement.
6. Autologous fat can be interposed between the residual tumor and the pituitary gland to limit the risks of hypopituitarism after adjuvant radiation therapy.
7. A careful reconstruction should be performed to avoid postoperative CSF leakage.
8. Meningiomas better respond to higher dose/fraction of radiation therapy, and a gamma knife/Cyberknife/Linac treatment should be preferred.

DECLARATIONS

Authors' contributions

Made substantial contributions to conception and design of the study and performed data analysis: Cossu G, Berhouma M, Messerer M

Performed data acquisition, as well as provided administrative, technical, and material support: Abarca J, Levivier M, Starnoni D, Daniel RT

Availability of data and materials

Not applicable.

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Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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