

Review of Surgical Anatomy of the Tumors Involving Cavernous Sinus

Abstract

The lesions involving cavernous sinus (CS) and lateral sellar region includes tumors, vascular lesions, infection, inflammation, and trauma. Tumors associated with CS cause significant distortion of the microanatomy posing an additional surgical challenge to the neurosurgeons. The surgical approach and microsurgical anatomy with respect to the origin and growth of the tumor within the CS region have not been comprehensively described in recent years. We conducted a review of literature concerning CS and associated tumors, compiled through MEDLINE/OVID and using cross-references of articles on PubMed with the keywords cavernous sinus, CS tumors, pituitary adenoma, meningioma, schwannoma, chordoma, CS hemangiomas, extradural, interdural, intradural, skull base, gamma knife radiosurgery, endoscopic endonasal approach. Based on the tumor origin and growth pattern, the tumors associated with CS can be classified into three categories: Type-I: tumor originating from CS, Type-II: originating from lateral wall of CS, and Type-III: extraneous origin and occupying CS. The review focuses on approach to a tumor within each type of tumor in the CS region. The emphasis is that the tumor growth pattern and significant distortion of the CS anatomy caused by the tumor growth should be considered while planning the optimal surgical approach for tumors in this region to ensure complete tumor resection with minimal neurovascular morbidity.

Keywords: *Anatomy, cavernous sinus, meningioma, tumors*

Introduction

Since the seminal description of cavernous sinus (CS) as the “anatomical jewel box” and surgical “no man’s land,” numerous studies have contributed to the understanding of microsurgical anatomy of CS.^[1] The normal microsurgical anatomy of CS and the triangular corridors to approach the CS are well described in literature.^[1-6] The understanding of the borders and walls that contains the CS is vital to determine the accurate orientation of tumor in relation to the surrounding neurovascular structures. The anterior CS border consists of anterior clinoid and superior orbital fissure, posteriorly the petrous tip and posterior clinoid, medial extent is to the sella and sphenoid body, and lateral extent is the junction of the greater wing of sphenoid. The wall containing CS includes anterior, lateral, medial, posterior, and inferior walls.^[6] The medial wall of CS can be divided into sellar and sphenoidal part. The description of the medial CS wall in literature varies.^[7,8] Some authors describe medial wall as a single meager

membrane, others described the medial wall as a distinct dural layer, composed of the loosely arranged collagen fibers with mean thickness of 0.195 ± 0.066 mm^[9] while in our previous study, we found it to be a bilayered membrane with lateral part of the pituitary capsule and the fibrous layer forming the two layers, thus making medial wall a double-membrane structure rather than double dural structure.^[10] The lateral CS wall is described as a two-dural layer with the cranial nerves (CNs) III, IV, and VI traversing between these layers.^[6,11-13] Janjua *et al.*^[14] have described an intermediate layer (fibrous contribution to the meningeal dura) that decreases in thickness posteriorly and laterally. The authors recommended that choosing the dissection plane between meningeal dura and intermediate layer for an extradural exposure might yield additional protection to the CNs in membranous layer. These anatomical layers are basis of planning the surgical approach to the lesions in and around CS.

The pioneer description of surgical entry point into CS by Parkinson and West and Dolenc has been adopted by most

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neurosurgeons operating in this region.^[3,11] The approach selection is mainly based on exact location of lesion in and around the CS. The lesions affecting CS include vascular, neoplastic, infective, and inflammatory lesions arising in the CS proper or through extension from adjacent intra- and extra-cranial regions. The lesions such as intracavernous aneurysm and arteriovenous fistulae are generally smaller and do not cause significant distortion; hence, direct approach to these lesions based on the triangular corridors and anatomical dural layers is feasible.^[15] However, the tumors involving CS, when reach a certain size, might develop a large degree of anatomical distortion making the identification of anatomy and optimal surgical planes difficult. Therefore, understanding the surgical anatomy with respect to the tumor origin and growth pattern is important. The tumors in the CS region can be classified based on the origin, growth pattern, and concept of membrane structures forming CS wall. In the present review, we discuss the tumors based on their origin and invasion into CS and discuss pertinent surgical approaches as well as current concepts on management strategy for tumors originating and/or invading the CS.

Methods

We conducted a review of literature concerning CS and associated tumors, compiled through MEDLINE/OVID and using cross-references of articles on PubMed with the keywords cavernous sinus, cavernous sinus tumors, pituitary adenoma, meningioma, schwannoma, chordoma, CS hemangiomas, extradural, interdural, intradural, skull base, gamma knife radiosurgery, and endoscopic endonasal approach.

Results

Based on the tumor origin and growth pattern, the tumors associated with CS can be classified into three categories: Type-I: tumor originating from CS, Type-II: originating from lateral wall of CS, and Type-III: extraneous origin and occupying CS. The review focuses on approach to a tumor within each type of tumor in the CS region.

Discussion

CS tumors can be divided into three types [Figure 1]:^[16,17] Type-I: tumor originating from CS [Figure 2a-c], Type-II: originating from lateral wall of CS [Figure 2d], and Type-III: extraneous origin and occupying CS [Figure 2e and f].

Type-I: Tumor originating from the cavernous sinus

a. CS cavernous hemangiomas are benign and the only primary intracavernous tumor; accounting for 13% of all intracranial cavernous hemangioma, 3% of benign tumors of the CS area, 2% of all tumors within the CS area, and 0.4%–2% of intracranial vascular malformations.^[18,19] Complete or partial resection of

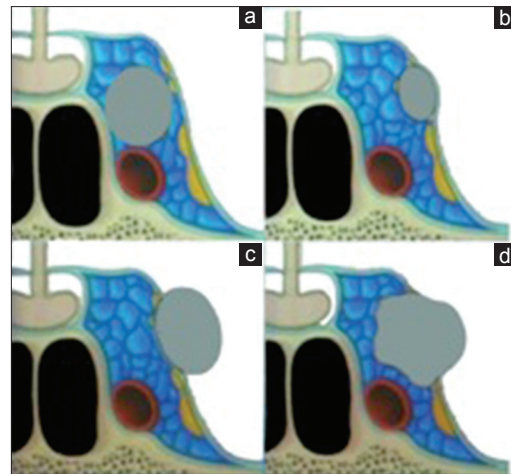


Figure 1: Cavernous sinus tumors can be divided into three types: (a) Type-I: The tumor originating from the cavernous sinus area, (b) Type-II: From the lateral wall of cavernous sinus, (c and d) Type-III: Extraneous origin and compressing the cavernous sinus, and (d) invading the cavernous sinus wall

cavernous hemangioma is the preferred treatment option; due to vascular nature of these lesions and complex neurovascular relations, complete excision is a challenge. A variety of surgical approaches to the CS hemangiomas have been described; type of craniotomy varies depending on location of tumor and local invasion to the sella versus middle fossa. The modified pterional transzygomatic craniotomy and extirpation of the hemangioma by extradural approach are by far the most adopted approach. We attempt complete excision of cavernous hemangioma in all cases without dissecting the pseudocapsule. The interface between the pseudocapsule and duramater can be utilized as a barrier to protect CNs [Figure 2a]. Despite successful resections carried out, the mortality rates still remain high, owing to the eminent possibility of profuse bleeding during surgical intervention combined with potential for long-term CN deficits.

Stereotactic radiosurgery has demonstrated good postoperative results as primary and adjunct therapy.^[20,21] The radiation-induced thrombosis of tumor blood vessels reduces tumor volume which leads to reduction in size or arrest in tumor growth with resolution of the symptoms of CN compression.^[21-24] The scar formation with preoperative radiation might impede subsequent surgical resection. Treatment of small lesions with radiosurgery and large ones with fractionated stereotactic radiotherapy is still controversial. We adopt the strategy of employing stereotactic radiosurgery for small tumors (<3 cm) with CN involvement as the only presenting symptom. For tumors >3 cm in size, preoperative conventional radiation therapy is used to shrink the tumor and repress intraoperative bleeding.

b. Another group of tumors that can be classified in this group are metastasis to CS; which are associated with

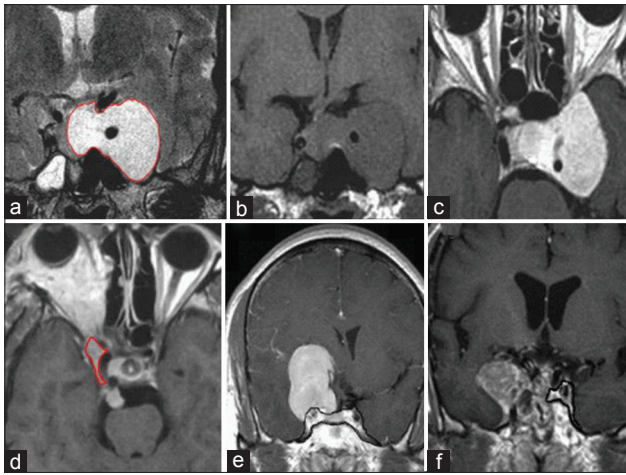


Figure 2: (a-c) T1-weighted magnetic resonance imaging demonstrating the cavernous hemangioma in cavernous sinus (Type-I), (d) T1-weighted magnetic resonance imaging demonstrating the trigeminal neurinoma extending to and between the lateral wall of cavernous sinus (Type-II), (e) sphenoid wing meningioma extending to the lateral cavernous sinus wall (Type-III), (f) nasopharyngeal carcinoma invading the cavernous sinus (Type-III)

poor prognosis and treatment is largely palliative. Radiosurgery is often used to deal with the CN compression symptoms.

Type-II: Originating from the lateral wall of cavernous sinus

Meningiomas and schwannomas constitute the most common primary tumors originating from lateral CS wall.

a. Meningioma: Kehrl *et al.*^[25] demonstrated that arachnoid granulations of CNs in lateral CS wall are the possible origin of meningioma in this region. The meningiomas originating from lateral CS wall tend to confine between outer and inner layer of the lateral wall [Figure 3b]. In this case, complete tumor resection can be achieved by working in between two dural layers. However, extension or invasion into CS or surrounding structures is not uncommon.^[26,27] Meningiomas arising from around the Meckel's cave have a tendency to invade the lateral CS wall leaving no clear dissection plane between the tumor and CNs, especially between the abducens nerve and tumor.^[28] Internal carotid artery (ICA) invasion might occur without any preoperative imaging evidence of arterial narrowing. Complete resection of such invasive meningioma can be challenging due to significant morbidity associated with the risk of ICA and CN damage. Many neurosurgeons aim at achieving subtotal resection as an effective means to achieve tumor control and symptomatic relief of compressive cranial neuropathies.^[29,30] For large meningioma that is not invasive, simple extradural dissection might not suffice; this is discussed at length in the extradural approach section in this paper. Gross-total resection of CS-associated meningioma has been reported in

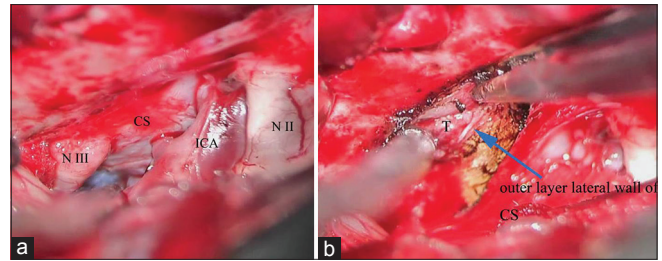


Figure 3: (a) Intraoperative view showing the lateral CS wall exposure; CN II, ICA, CN III, and lateral wall of CS, (b) meningioma (Type-II) between the outer and inner layer of the lateral CS wall; ICA – Internal carotid artery; CS – Cavernous sinus; CN III – Cranial nerve III; CN II – Cranial nerve II; T – Tumor

20%–76% of published cases.^[31,32] CN involvement has been a critical issue while attempting complete resection of CS meningiomas.^[27] DeMonte *et al.* reported postoperative improvement in 14% of preoperatively affected CNs, no change in 80% of patients, and 10 new neuropathies after the CS meningioma resection;^[33] no other report on significant improvement in postoperative CN morbidity was available for review. Sughrue *et al.* in their meta-analysis^[34] reported that primary or supplement radiation offers a successful alternative to microsurgery for meningioma involving CS

b. Trigeminal schwannomas: Trigeminal schwannoma (TS) that originates from the trigeminal ganglion in the outer layer of lateral wall and perches in the CS could be classified precisely based on the origin as Type-II [Figure 2d]. TS are positioned posteriorly within the lateral CS wall and may show extension into the posterior fossa. Historically, epidural and interdural middle fossa approaches are employed to achieve complete resection of these tumors.^[35] Schwannomas are distinctly separated from the CS by inner layer. Although large tumors tend to extend into CS, they usually do not invade venous plexus, CN, and carotid artery.^[28] Thereby, achieving complete resection of tumor while preserving major trigeminal nerve fibers and other CNs is feasible in most cases. CS involvement is treated by both surgery and radiosurgery to minimize the postoperative complications. The controversy exists on decompression followed by radiation versus primary gamma knife radiosurgery for these tumors.^[36] For the patients undergoing primary radiosurgery, additional surgical treatment after gamma knife surgery due to tumor enlargement or uncontrolled facial pain is warranted in many cases.^[36,37]

Type-III: Extraneous origin and compressing/invading the cavernous sinus

a. Pituitary adenoma: CS invasion rate for parasellar pituitary adenoma is reported in the range of 15%–20%.^[38,39] As yet, the route of pituitary adenoma invasion in parasellar region is controversial. Some researchers advocate that pituitary adenomas being

biologically benign, the parasellar infiltration is due to histological defect in medial CS wall^[8,38] while others have postulated that the biological behavior of tumor aids infiltration.^[7,40] Regardless of the route of invasion preoperative diagnosis of CS invasion has been the subject of debate in recent studies. The contemporary neuroimaging has failed to delineate the medial CS wall, which otherwise would aid in prediction of CS invasion. The distance between the two sides of the ICA is commonly used criteria to gauge the adenoma invasion. Frank and Pasquini^[39] provided the five grade endoscopic classification system for the CS invasion, where Grade 2 and over are considered as CS invasion. Ceylan *et al.*^[38] reported that the invasion of pituitary adenoma into CS is more common from medial corridors compared to lateral surgical corridors (endoscopic surgery corridors). Although, not generally accepted, another concept is that the pituitary adenoma does not actually invade CS, the tumor growth pushes covering membranes and medial wall toward the CS. The two layers of pituitary become thinner as tumor grows but separates the tumor and the CS.^[10] Based on this concept, the parasellar extension of pituitary adenoma can be resected without opening the medial CS wall. The residual or recurrent tumors are treated by radiosurgery and are characterized by high rates of local control and endocrine remission

- b. Chordoma and chordosarcomas: Another tumor extending to CS is the chordoma. Gross radical removal of chordomas and chordosarcomas involving the CS has been accomplished with an acceptable surgical morbidity.^[41] In chordomas and chordosarcomas, compression of CS is more frequently seen than its invasion [Figure 4b and c]; however, delineation

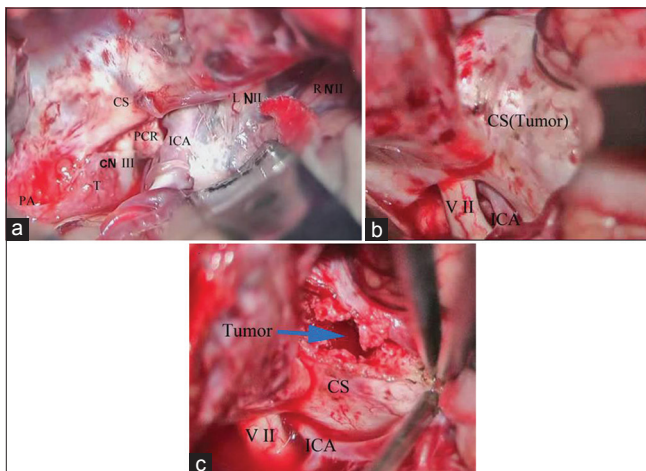


Figure 4: (a) Intraoperative view of the meningioma from the right petrous apex, compressing cavernous sinus, without invading the wall of cavernous sinus (Type-III); (b) Intraoperative view of chordoma invading the cavernous sinus through posterior cavernous sinus wall (Type-III); (c) intraoperative view showing the tumor after opening outer cavernous sinus wall; VII-Cranial nerve VII. PA – Petrous apex; T – Tumor; CN III – Cranial nerve III; PCR – Posterior clinoid region; CS – Cavernous sinus; ICA – Internal carotid artery; LN-II – Left cranial nerve II; RN-II – Right cranial nerve II

between compression and invasion is arduous. The tumor growing from skull base pushes CS wall and compresses it between the tumor and CS. This leads to thin and weakened wall, which is often missed to view and respect during surgery, which might result in direct inadvertent entry into CS. Hence, even though this tumor does not invade the CS, it might be safer to consider this as Type-I tumor. Multimodality treatment with surgical resection employing skull base approaches, endoscopic endonasal trans cavernous approach, and radiosurgery have increased the propensity of complete resection with decreased CN morbidities, especially for lateralized chordomas or when tumors intimately involve the ICA or CS.^[41-43] However, in case of recurrence, the previous radiotherapy increases the risk of mortality in both the postoperative and follow-up period^[44]

- c. Nasopharyngeal carcinoma: Nasopharyngeal carcinoma has tendency to invade the CS through inferior and lateral CS walls. These lesions invade CS by direct skull-base invasion, perineural spread along the V2 or V3, or extension through the foramen lacerum. The aim of the surgical treatment is to relieve the compressive CN symptoms, which is often achieved by partial tumor resection [Figure 2f]. Stereotactic radiosurgery performed early is deemed to be a good alternate palliative measure for improving the CN deficits^[45,46]
- d. Petroclival meningioma (PCM): PCMs are located in the anatomical complex region involving the dural folds, venous sinuses, and CNs. The surgical resection gets further challenging with extension of PCM to CS through posterior wall.^[47] PCM often tends to compress the posterior and lateral CS wall rather than invading the CS [Figure 4a]. For the residual or recurrent PCM, stereotactic radiosurgery is favorable treatment option.^[48] However, with evolving anatomical and clinical studies of tumors in this region, better outcomes with surgical resection can be anticipated. Subtemporal approach with anterior petrosectomy and extended retrosigmoid approach allow exposure of the posterior CS by dividing the dura medial to the entry point of trochlear nerve into the tentorium, which allows for the exposure of the intracavernous ICA.^[49] The accessibility to the posterior CS region through retrosigmoid approach might be further optimized by the endoscopic-assisted techniques; where entry to the middle fossa and the CS can be achieved through intradural suprameatal approach. The endoscope can be inserted parallel to the posterior surface of the petrous bone toward the Meckel's cave and the channelized to follow the cisternal anatomy to the posterior CS^[50]
- e. Finally, meningioma originating through the sphenoid ridge and invading the CS can be classified into Type-III. The characteristics of these invading meningiomas, surgical concepts, and challenges could be compared to the large aggressive meningioma originating in the lateral wall and invading the CS (Type-II).

Surgical approach selection based on the classification

The triangular spaces around the CS are natural corridors through which the intracavernous lesions might be accessed. However, tumors in the CS area make the identification of triangular anatomy very difficult. Nonetheless, the orientation of the access gained by each of these corridors is paramount to achieve direct control and visualization of the ICA and CNs. The access to roof of CS and subclinoidal segment of ICA can be achieved by drilling the anterior clinoid through clinoidal triangle. For tumors involving medial CS and for approaches to the interpeduncular fossa, the oculomotor triangle is an important access corridor. The entry through supratrochlear triangle is utilized to expose the posterior band of the intracavernous carotid artery and meningohypophyseal and inferolateral trunk. Another entry zone for the meningohypophyseal trunk is the infratrochlear or Parkinson's triangle; sixth nerve can be exposed through this triangle. This corridor provides a lateral and direct entry to the CS and has been utilized by many neurosurgeons as a safe entry zone for the lateral intradural approach to CS lesions. The four middle fossa triangles including anteromedial, anterolateral, posterolateral, and posteromedial triangles have been utilized as the natural corridor for various tumors. For instance, opening the anteromedial triangle between the V1 and V2 and displacing V1 exposes the sixth nerve, which is important to identify and preserve when dissecting the tumor invading the CS, particularly for Type-II meningiomas and Type-I cavernous hemangiomas. This anteromedial corridor is employed for the superior extradural approach. For the Type-I tumors with anterolateral extension and Type-II tumor with intracavernous extension, anterolateral middle fossa triangle can be opened. Posteromedial or Kawase's and posterolateral or Glasscock's triangles are corridors for the combined lateral and inferolateral approach to CS. The entry to posterior CS can be gained by posteromedial or Kawase's triangle. In addition, the posteromedial triangle forms boundaries for drilling the petrous apex and for entry to the posterior fossa. The approaches to the CS can be broadly classified as either extradural or intradural and combined extradural intradural approach.

A number of surgical approaches are utilized for the entry into the CS through superior, lateral, posterior, medial, and inferior walls.^[18,32,35,49-53] Orbitozygomatic approach (OZ) provides wide exposure to the entire CS with minimal cerebral retraction; for the additional posterior exposure, extended middle fossa transzygomatic approach can be used. The commonly used approaches including pterional approach (entry through superior wall), anterior subtemporal approach (through lateral wall), transpetrosal-transstentorial approach (posterior wall), contralateral pterional transsylvian approach (medial wall), and transsphenoidal approach through inferior wall are commonly used.

Extradural approach

Extradural or epidural approach to the CS for trigeminal neuroinoma was pioneered by Dolenc *et al.*, which involved peeling off the outer layer from the inner layer which allows exposure of CNs coursing in semitransparent inner layer of the lateral CS wall. As the surgical procedure is performed substantially in the interdural space, this approach is also referred as interdural approach.^[54] This approach offers advantages of complete exposure of tumor bed, swift control of intraoperative bleeding, extracavernous resection, tumor removal with CN in surgeon vicinity, minimal brain injury due to no direct brain retraction and thereby reducing the incidence of iatrogenic subarachnoid hemorrhage, and reduced possibility of intracranial infections. This extradural/interdural approach utilizes the inner wall, which not only acts as the mechanical barrier but also protects the vasa-nervosum that originates from intracavernous carotid and ascends through the inner wall. For Type-II tumors [Figure 3a and b], working in between the outer and inner lateral wall of CS enables resection of tumor without compromising the blood supply to the CNs. The CN between the layers of the lateral wall of CS is usually severely adhered to tumor and is pushed in different directions as the tumor grows. The preoperative knowledge of tumor origin and position of CNs might aid in designing the surgical approaches. For instance, if the nerves were pushed medially or superiorly, lateral wall approach can be used, while if the CNs are lateral or inferior, the approach through roof of CS can be employed. This strategy would expose the tumor first, which would allow direct control on tumor while identifying and exposing the CNs. The separation of outer layer and selecting incision site on outer layer must be based on tumor size and growth direction; for a medium to large tumor, the area that is bulged out can be safely incised with a laser knife in the direction of tumor growth.

The large tumor of Type-II, III might damage the thin inner layer; so after opening the outer layer and while working in the interdural space, the inner membrane can give way leading to direct entry into CS; then, control of bleeding is a challenge [Supplemental Video 1]. Based on this, the larger tumors of Type-II and Type-III even if do not invade the CS necessitate working within the CS and can be classified as Type-I. Conventionally, the use of thin layer of gelatin sponge and bipolar coagulation around the opening gradually controls the bleeding. Safe and effective hemostasis can be achieved with the use of microfibrillar collagen hemostat or fleece-coated fibrin glue patch applied over the opened CS with gentle compression. Fibrin glue injection between V1 and V2 obliterates the lateral CS compartment, and injection posterior to the clinoidal segment of ICA obliterates the medial compartment and thereby facilitates visualization during surgery and decreases blood loss.^[55]

In addition, the large tumors might push CNs laterally which are then first encountered, increasing the risk of CN damage. Another challenge with larger tumor might be excessive temporal lobe retraction for optimal tumor exposure, which increases the risk of injury due to increase splitting of brain tissue. Consequently, for large tumors, when the temporal lobe is required to be being elevated more than 3 cm, intradural approach could be more suitable. The ideal tumor that could be safely resected by extradural/interdural approach would be a small- to medium-sized Type-II and Type-III tumors, which either remains confined within the two layer of lateral, medial, posterior, and inferior CS wall or compress the outer layer of CS wall without significant distortion.

Intradural approach

The triangular spaces around the CS are natural corridors through which the intracavernous lesions can be accessed. The normal anatomy of CS and middle fossa triangles has been well described in literature.^[1-6] The direct access to CS through the roof can be achieved by intradural transsylvian route with drilling of the anterior clinoid process and superior wall of the optic canal and opening the optic nerve sheath. The roof is exposed at exit point of ICA from CS. This approach is traditionally used for the lesions adjacent to anterior loop of the ICA as well as those superior and/or medial to the cavernous ICA. The intradural approach from lateral wall into CS is through the Parkinson triangle or at the point of maxillary branch of trigeminal nerve on the lateral wall.^[11] The lateral approach provides optimal exposure to the lesions that are lateral and/or inferior to ICA and those posteriorly located within the CS (Type-II and III tumors). The superior and lateral approaches can be combined for lesions widely involving the CS. For Type-I tumors or larger Type-II, where the lateral wall might be enlarged and distorted and/or the CS cavity might be occupied or compressed by tumor; the intradural approach could be considered. Intradural approach allows wider field of vision and direct exposure to the tumor in CS area. However, it precludes the exact determination of CN entry points rendering partly unsighted resection. Further, the opening of dura could channelize the blood to subarachnoid space, increasing the risk of postoperative complications.

Transsphenoidal endonasal endoscopic approach

Endoscopic endonasal approach is alternative to the medial approach to CS; offering improved visualization and low morbidity compared to microscopic transsphenoidal route.^[39,56] Three different surgical approaches have been employed to access the CS: the parasagittal, middle meatal, and middle turbinectomy approaches.^[57] Although medial to lateral endonasal approach can be utilized for variety of tumors involving CS (Type-I and III), based on the consistency, site of origin of the tumor, and the risk to the patient, lateral to medial approaches (for Type-I) may be

required to control tumor growth in the lateral CS wall. Type-II lesions might not be suitable for this approach due to downward displacement of ICA and CNs. The ideal lesions for endoscopic endonasal approach are small to medium volume soft tumors with minimal chances of ICA infiltration and with a mediolateral growth leading to lateral displacement of CNs.^[56,57] The potential setbacks of this approach include complications such as CN injury, ICA rupture, cerebrospinal fluid leak, and associated steep learning curve. However, with increasing use of neuronavigation, imaging, and newer angled endoscopes with better two-dimensional and three-dimensional image acquisition, more neurosurgeons are incorporating endoscopic surgery. Another such avenue recently described in the keyhole endoscopic subtemporal approach to lateral CS; the use of which is in infantile stage for the lesions in and around CS and is limited to the cadaveric studies.^[58]

Conclusion

Classification of tumors in CS area based on their origin and growth pattern would facilitate optimal approach selection to anticipate better surgical outcomes. The membranes around the CS form a natural barrier to intracavernous neurovascular structures. Type-I tumors necessitate opening of CS; small- to medium-sized Type-II and III can be dealt with by working between the outer and inner layers of medial, lateral, superior, or inferior wall of the CS. However, large and aggressive Type-II or Type-III tumors could compress and damage the thin inner layer, which might be distorted at the beginning or give way while working in between the two layers. Therefore, the large Type-II and Type-III tumors can be treated as Type-I tumor.

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Conflicts of interest

There are no conflicts of interest.

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