Endoscopic transorbital approach to the cavernous sinus: Cadaveric anatomy study and clinical application (SevEN-009)

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Objective: Cavernous sinus (CS) invasion is frequently encountered in the management of skull base tumors. Surgical treatment of tumors in the CS is technically demanding, and selection of an optimal surgical approach is critical for maximal tumor removal and patient safety. We aimed to evaluate the feasibility of an endoscopic transorbital approach (ETOA) to the CS based on a cadaveric study.

Methods: Five cadaveric heads were used for dissection under the ETOA in the comparison with the endoscopic endonasal approach (EEA) and the microscopic transcranial approach (TCA). The CS was exposed, accessed, and explored, first using the ETOA, followed by the EEA and TCA. A dedicated endoscopic system aided by neuronavigation guidance was used for the procedures. During the ETOA, neurovascular structures inside the CS were approached through different surgical triangles.

Results: After completing the ETOA with interdural dissection, the lateral wall of the CS was fully exposed. The lateral and posterior compartments of the CS, of which accessibility is greatly limited under the EEA, were effectively approached and explored under the ETOA. The anteromedial triangle was the largest window via which most of the lateral compartment was freely approached. The internal carotid artery and abducens nerve were also observed through the anteromedial triangle and just behind V1. During the ETOA, the approaching view through the supratrochlear and infratrochlear triangles was more directed towards the posterior compartment. After validation of the feasibility and safety based on the cadaveric study, ETOA...
was successfully performed in a patient with a pituitary adenoma with extensive CS invasion.

**Conclusions:** Based on the cadaveric study, we demonstrated that the lateral CS wall was reliably accessed under the ETOA. The lateral and posterior compartments of the CS were effectively explored via surgical triangles under the ETOA. ETOA provides a unique and valuable surgical route to the CS with a promising synergy when used with EEA and TCA. Our experience with a clinical case convinces us of the efficacy of the ETOA during surgical management of skull base tumors with CS-invasion.

**KEYWORDS**
cavernous sinus, endoscope, lateral compartment, skull base tumor, transorbital

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**Introduction**

The cavernous sinus (CS) is a venous sinus deep-seated in the central skull base. Radical surgical resection is not generally feasible because CS exploration involves potential risks of complications such as massive venous bleeding, cranial neuropathy, and internal carotid artery (ICA) injury. However, cavernous sinus exploration is often necessary, especially during treatment of various skull base tumors such as endocrine-active pituitary adenomas, chordomas, meningiomas and, at the least, for debulking non-functioning adenomas. Surgeons should be prepared to have a comprehensive anatomical understanding and delicate surgical technique when they access the CS (1–4).

The transcranial approach (TCA) has been a mainstay of cavernous sinus exploration for various conditions such as aneurysms, meningiomas, and pituitary adenomas (5–7). The TCA is basically a lateral-to-medial approach and intracavernous neurovascular structures are accessed through several windows between each cranial nerve in the lateral CS wall. Therefore, a certain degree of cranial nerve violation is inevitable. Also, access to the medial compartment of the CS is limited (2, 3). Extensive loss of bony structure, excessive brain retraction, and long operation times are additional disadvantages of the TCA.

The transnasal corridor (EEA) is another major surgical approach to the CS. Especially during surgery for pituitary adenomas, where the EEA is the choice of surgical corridor in most cases, CS can be explored with various modifications (8, 9). The transnasal corridor is basically an anteromedial-to-posterolateral approach. Because neurovascular structures are less crowded in the medial compartment, surgical morbidity is lower for the EEA than for the TCA. However, access to the lateral compartment is greatly limited by tortuous course of the ICA (Figure 1) (8, 10–12).

Recently, endoscopic trans orbital approach (ETOA) has been proposed as an alternative route to access various skull base regions. Especially, it has been proved that the medial temporal lobe is effectively approached by ETOA in many studies, which suggests it is a promising surgical corridor to access the CS (4). However, the potential benefits of CS exploration using the ETOA have not been fully investigated. We postulated that the ETOA is an effective alternative to access the lateral compartment of the CS. We aimed to evaluate the feasibility of the ETOA for access to the CS, compared with the TCA and EEA.

**Materials and methods**

Five human cadaveric heads provided by the Surgical Anatomy Education Center of Yonsei University College of Medicine were used for this study. Three cadaveric heads were prepared using Thiel embalming and ethanol-glycerin fixation, and two were fresh cadavers. All cadaveric heads were injected with silicone rubber compounds (MICROFIL®; Flow Tech, Inc., Carver, MA, USA) to fill and opacify the vessels. Before starting dissection, the cadaveric heads were examined using computed tomography (CT) scans to obtain images that were used by the neuro-navigation system (Stryker navigation system, Kalamazoo, MI) during dissection. For cadaveric dissection under ETOA and EEA, a rigid endoscope 4 mm in diameter and 18 cm in length with 0° and 30° optic lenses was used (Stryker neuroendoscopy, Kalamazoo, MI, and Arthrex Synergy UHD4 endoscopy, Naples, FL). During the TCA, a conventional skull base approach was performed, aided by a surgical microscope (Carl Zeiss, Oberkochen, Germany) with a 2D medical camera system (3D Medivision, Seoul, Republic of Korea). The cadaveric study committee of the Yonsei
University of Medicine and the Institutional Review Board of Severance Hospital, Yonsei University College of Medicine approved this study. After testing feasibility and safety based on this cadaveric study, combined EEA and ETOA was performed to treat a patient with a recurrent invasive pituitary adenoma.

Endoscopic transorbital approach

Dissection under ETOA was performed as previously described (4, 13, 14). A superior eyelid incision was made along the superior eyelid and was laterally extended (Figure 2). After making an incision on the orbicularis muscle and periorbitum, the superolateral orbital rim was exposed. Subperiosteal dissection was extended towards the orbital apex while the orbital contents were medially retracted using a malleable retractor without violating the periorbital layer. The pyramid of sphenoid was drilled out. The meningolacrimal artery was identified and cut. After the meningoorbital band was fully exposed and cut, which facilitated medial retraction of the periorbita and lateral retraction of the temporal lobe dura, the greater and lesser wings of the sphenoid were further removed until full exposure of the superior orbital fissure (SOF) was achieved. The CS membrane consists of two dural layers; the outer layer dura propria continues with the frontotemporal dura and the inner layer, the true cavernous membrane, continues intraorbitally as the epineurium of the cranial nerves. Similar to the conventional transcranial CS approach, sharp and gentle interdural dissection was performed in the anterior-to-posterior direction to achieve wide exposure of the lateral CS wall (4, 15). Immediately after beginning the interdural dissection, ophthalmic (V1) and maxillary (V2) branches of the trigeminal nerve were identified at the front. After dissecting the space around these two large cranial nerve branches, the oculomotor and trochlear nerves were identified just above V1; the mandibular nerve (V3) and middle meningeal artery were identified just posterior to V2. After complete exposure of the lateral CS wall, the CS was explored though each surgical triangle and neurovascular structures inside the CS were identified (Figures 3A, B).

Endoscopic endonasal approach

The endonasal approach to the CS was performed in a standard manner using a two-surgeon binostil technique. The turbinates on the opposite side of the target CS were pushed to the lateral side. The middle turbinate, superior turbinate, and uncinate processes were removed. The posterior nasal septum was removed, and the sphenoid rostrum and the ostia were removed. Then, the anterior wall of the sphenoid sinus and septum inside the sinus were removed to fully expose the sellar floor. Ipsilateral posterior ethmoidectomy was performed to enhance lateral access to the CS. Sellar floor bone was removed which extended to the level of the tuberculum sellae. The inferior compartment of the CS was accessed by removing the shell covering the carotid protuberance. The anterior and medial dural layer of the CS was removed to allow full exposure of intracavernous structures, including the ICA and cranial nerves (Figures 3C, D).

Microscopic transcranial approach

The frontotemporal craniotomy was performed in a conventional manner. After curvilinear scalp incision, the temporalis muscle was incised and retracted inferiorly with interfascial dissection until the zygomatic arch was fully exposed. The zygomatic arch was removed and a routine frontotemporal craniotomy was performed. The temporal skull
base was fully exposed with dural retraction of the temporal lobe and was further flattened with drilling. The sphenoid lesser wing was removed using a high-speed drill until the meningoorbital band was identified. After the meningoorbital band was cut, the temporal dura was further retracted until the SOF entry point was exposed. The temporal dural layer was further dissected and separated from the temporal skull base circumferentially, and the foramen rotundum and foramen ovale were exposed after cutting the middle meningeal artery at the level of the foramen spinosum. During dissection, the greater superficial petrosal nerve was identified and preserved. Then, the dural layer covering the trigeminal nerve was cut and the outer layer of the CS was separated from the inner layer while preserving the cranial nerves within the lateral CS wall. The CS was then explored via the various surgical triangles demarcated by each cranial nerve (Figures 3E, F).

We generated three-dimensional models of the CS that were based on the cadaveric dissection results of the three approaches to the CS. A three-dimensional model of anatomical structures including the skull, ICA, and cranial nerves, was reconstructed using Visible Korean data from Department of Anatomy, Ajou University School of Medicine. Using the three-dimensional model, the final views of the transorbital approach, transnasal approach, and transcranial approach were rendered. (Figures 1, 3B, D, F).

**Results**

Accessibility to the lateral compartment of the CS under the EEA was extremely limited mainly because of the tortuous ICA inside the CS. On the other hand, after the entire lateral wall of CS was exposed under ETOA, the oculomotor nerve, trochlear nerve, trigeminal nerve and its branches, which constitute the lateral wall of the CS, were easily identified and further dissected. The angle of attack under ETOA naturally aims towards the...
temporal lobe rather than frontal lobe, while providing a looking-down view. Thus, the viewing angle of the ETOA was very different from that of the EEA, which was obtained using a rather looking-up angle. The middle meningeal artery was seen lateral to V3. The anteromedial triangle demarcated by V1 and V2 was reached earlier during the ETOA, which provided a more spacious surgical window to enter the CS, compared with the surgical windows. As dissection was extended postero-superiorly, the oculomotor and trochlear nerves were identified above V1. Two surgical windows were identified and demarcated by the oculomotor nerve, trochlear nerve, and V1: the supratrochlear and infratrochlear triangles. The anterolateral triangle was also identified between V2 and V3, which did not provide a route into the CS. Using the three triangles, the lateral compartment of the CS was fully explored without damaging cranial nerves. The different trajectories towards the clinoid...
triangle, supratrochlear triangle, infratrochlear triangle, and anteromedial triangle were compared between the surgical approaches (Figure 4). It was difficult to visualize the cavernous segment of the ICA from outside the CS, which was covered by V1 during the ETOA. The abducens nerve was located between ICA and V1, running along medially to V1.

When the endoscope tip was advanced through each surgical triangle into the CS, different CS regions with different neurovascular structures were visualized (Figure 5). The anteromedial triangle was the largest window where most of the lateral compartment was freely approached. The ICA and abducens nerve were also observed through the anteromedial triangle and just behind V1. Because the CS was accessed from

|              | Medial-to-lateral | Lateral-to-medial |
|--------------|-------------------|------------------|
| **Orientation** |                   |                  |
| **Clinoidal Triangle** | ![Image](image1.png) | ![Image](image2.png) |
| **Supratrochlear Triangle** | ![Image](image3.png) | ![Image](image4.png) |
| **Infratrochlear Triangle (Parkinson’s Triangle)** | ![Image](image5.png) | ![Image](image6.png) |
| **Anteromedial Triangle** | ![Image](image7.png) | ![Image](image8.png) |

**FIGURE 4**
Surgical triangles of cavernous sinus with different approaches. Using a fresh cadaveric head, the surgical triangles to enter the cavernous sinus were simultaneously observed through an endoscopic endonasal approach (EEA), an endoscopic transorbital approach (ETOA), and a microscopic transcranial approach (TCA). The clinoidal triangle was made by removing the anterior clinoid process. The supratrochlear triangle consists of the oculomotor and trochlear nerves while the infratrochlear triangle, so called Parkinson’s triangle, was demarcated by trochlear nerve and ophthalmic branch of a trigeminal nerve. The anteromedial triangle indicated the space between the ophthalmic and maxillary branches of trigeminal nerve. After inserting an indicator (white arrowheads) into each triangle under TCA, the indicator’s location and angle were checked under EES and ETOA to enhance the understanding of surgical orientation in each approach.
the anterolateral side, it provided excellent accessibility to the trigeminal ganglion, the proximal part of cranial nerves, and even the tentorial incisura, whose accessibility was otherwise greatly limited under EEA. Compared with the TCA with a lateral-to-medial view, the ETOA visualized all these structures using less retraction of the temporal lobe. When the endoscope was directed inferiorly towards V2, the inferior compartment was also safely accessed through anteromedial triangle. ACA, anterior cerebral artery; AM Tr, anteromedial triangle; ICA, internal cerebral artery; II, optic nerve; III, oculomotor nerve; IT Tr, Inferior trochlear triangle; IV, trochlear nerve; GSPN, greater superficial petrosal nerve; MCA, middle cerebral artery; PCA, posterior cerebral artery; PCP, posterior clinoid process; PG, pituitary gland; PO, periorbita; SCA, superior cerebellar artery; V1, ophthalmic branch of trigeminal nerve; V2, maxillary branch of trigeminal nerve; V3, mandibular branch of trigeminal nerve.

Case illustration

A 57-year-old male patient presented visual discomfort and diplopia caused by a recurred pituitary adenoma. The tumor was previously treated three times using surgery and two times using gamma knife radiosurgery (GKS), until the tumor became large enough to cause neurological symptoms. Magnetic resonance imaging revealed a huge invasive pituitary adenoma (Figure 6). The optic apparatus was compressed by the suprasellar part of the tumor. The tumor extensively invaded the right CS and completely encased the ICA. Because the tumor in the lateral compartment of CS was too large to be treated by radiation alone and it was expected to adhere to neurovascular structures inside CS, the EEA alone was thought to be insufficient to access the tumor in the lateral compartment. It was decided to remove the tumor using a combined EEA and ETOA. Before surgery, we performed volume rendering of the tumor and the surrounding normal neurovascular structures using the Smartbrush® of the Brainlab neuronavigation system (Brainlab AG, Munich, Germany), which greatly helped the surgeons understand the three-dimensional orientation of the target structure and thus simulated the surgical view under EEA and ETOA.

An extended transsphenoidal approach was performed in a standard fashion using a rigid endoscope 4 mm in diameter and 18 cm in length with 0° and 30° optic lenses (Karl Storz Endoscopy-America, Inc., Culver City, CA). Due to repeated previous surgical and radiosurgical treatments, the tumor was very hard and adhesive to surrounding structures and thus it was very difficult to identify clean dissection planes. Simple curettage was not effective to remove the hard tumor tissue, so it was forcefully removed in a piecemeal fashion using cup forceps. Consequently, it was very difficult and dangerous to explore the right side CS far laterally EEA. Especially, intracavernous ICA
greatly limited accessibility to the lateral compartment of the CS under EEA.

After completion of the EEA, the extent and size of the remaining tumor was visualized using an intraoperative CT scan (AIRO mobile intraoperative CT; Brainlab AG, Munich, Germany). As majority of the tumor inside the right CS was not accessed by EEA and thus remained, the ETOA was then used. About a 3 cm-length eyelid incision was made with lateral extension, and the oculi muscle was incised and retracted. Using subperiosteal dissection, the periorbita was separated from the lateral orbital wall. The temporalis muscle was also dissected from the orbital lateral wall. Then, a piece of lateral orbital rim was removed creating a spacious...
window for the ETOA. Obviously, removal of the lateral orbital rim was not an essential procedure for ETOA, however, it provided greater surgical freedom with less orbital retraction. The right eyeball was covered with a corneal protector and the periorbita was gently retracted medially. After the endoscope was introduced to the surgical field, the greater and lesser wings of the sphenoid were drilled out until sufficient exposure of the frontal and temporal dural surfaces was achieved. Because of the dense fibrosis caused by previous TCA and repeated GKS, clean interdural dissection was not possible. Instead, the anteromedial triangle demarcated by V1 and V2 was roughly localized and opened. The tumor inside the lateral compartment of CS was exposed and removed in a piecemeal fashion. Although a tumor-free margin was not obtained because of severe fibrosis, tumor tissue lateral to the ICA was more effectively explored under ETOA than the EEA, as previously demonstrated the cadaveric dissection. During dissection, the oculomotor and abducens nerves were localized using triggered electooculography (16). Sensory fibers of the trigeminal nerve were monitored by checking the blink reflex (17) and motor fibers (V3) were localized using electromyography. The ICA was frequently localized using Doppler ultrasonography during the tumor removal. Although small remnant tumors were left to avoid permanent damage of these critical neurovascular structures inside the CS, most of the tumor mass was successfully removed using the combination of the EEA and ETOA. The pathological examination revealed the diagnosis of a pituitary adenoma with 2% of the Ki-67 labeling index. Immunohistochemistry was positive only for SF-1 (steroidogenic factor 1) which was suggestive of a gonadotroph adenoma. The patient experienced transient right oculomotor palsy that resolved 3 months after surgery. After palliative re-resection for the remnant tumor, patient has been followed up for 14 months without an evidence of further progression.

Discussion

Surgical resection of CS tumors has been challenging for neurosurgeons. Because the CS is a complicated region surrounded and crowded by many neurovascular structures, various surgical approaches have been proposed; using them in combination is often required for large and extensive tumors (10, 18–21). For pituitary adenomas with extensive CS invasion, both transphenoidal and transcranial surgery can be considered for tumor removal, and radiation and receptor-based pharmacotherapy are also a useful adjunctive treatment option for tumor control (19–23). The ETOA is an emerging surgical corridor and provides access to various skull base regions. Trigeminal schwannomas, medial temporal lobe structures such as the amygdala and hippocampus, and sphenoid ridge meningiomas have been proposed as ideal targets of this novel approach (24–26). However, the CS has not attracted as much interest as other popular destinations of the ETOA. In this study, we conducted a cadaveric study to evaluate the feasibility of ETOA for access to the CS. Using previously reported interdural technique (4, 13), we found the CS lateral wall was effectively exposed under ETOA. Our study aimed not only to expose the lateral wall of the CS, but also to evaluate whether it was possible to access and explore the CS through the surgical triangles of the lateral wall.

Until the ETOA was proposed, TCA was the only surgical route used to explore the lateral compartment of the CS. Compared with the TCA, the ETOA has many advantages, such as a smaller skin incision, better cosmetic results, avoidance of temporal branch of the facial nerve palsy, no temporalis muscle atrophy, and less brain retraction (27–30). The approaching angle of the ETOA to the CS is quite different from the classical cavernous sinus approach used during the TCA, which has added a unique value to surgical routes to the CS. Because the ETOA aims more posteriorly along most of the cranial nerves, the Gasserian ganglion, the proximal part of the cranial nerves near the brain stem, and even the tentorial incisura were approached more easily. However, a narrow surgical corridor is a major limitation of the ETOA. Unlike the EEA where surgeons use two nostrils as external entry points providing a spacious surgical corridor for the endoscope and instruments, the ETOA generally allows only one external entry point. Therefore, during the ETOA, surgical freedom is profoundly limited when the retractor and endoscopic instruments are inserted altogether although several solutions are suggested to overcome this limitation (31, 32). Because the ETOA is a basically lateral-to-medial approach, a certain degree of cranial nerve manipulation in the lateral CS wall is inevitable. In addition, whereas the ICA is identified during the earlier phase of surgery under EEA, most of the cavernous ICA is concealed behind V1 which may impede identification of the ICA.

The CS is the region frequently invaded by pituitary adenoma. Although radiation is very effective for tumor control during pituitary adenoma management (21), CS exploration is often required for patients with large tumors inside the CS, patients with endocrine-active tumors such as acromegaly and Cushing’s disease, and patients with tumors refractory to radiation or pharmacotherapy. Because tumor consistency is often very soft and friable, surgical removal is more feasible with less chance of morbidity than other tumors such as meningiomas, chordomas, and nasopharyngeal malignancies. Most tumors medial to the ICA can be reliably approached and removed under EEA. However, it is not uncommon that tumors completely encase the ICA and certain parts of the CS cannot be visualized and accessed using the EEA. Especially when the tumor is very solid and thus not easily removed by simple curettage, a direct lateral-to-medial approach to hidden CS regions is necessary. Fernandez-Miranda et al. divided the CS into four compartments based on spatial relationships (i.e., superior, posterior, inferior, and lateral) (33). Because the EEA results in a view from the inferomedial side of
the CS, it is difficult to reach the superior compartment and the lateral compartment blocked by the cavernous ICA. In contrast, when it is accessed via the supratrochlear, infratrochlear, and anteromedial triangles under ETOA, the lateral CS compartment located on the lateral side of the ICA can be easily reached. When it is directed more posteriorly through the supratrochlear and infratrochlear triangles, the superior CS compartment located above the horizontal ICA is directly approached. For the cases with tumor invasion into the clivus and tentorium, the supratrochlear and infratrochlear triangles provide a unique and valuable surgical route to these regions.

It is obvious that ETOA is now adopted to access various surgical regions, however, the advantages and risks should be individually discussed. Under the belief that each surgical region should be differentiated, Di Somma et al. recently proposed a staging system that categorizes various surgical regions based on the levels of difficulty in the ETOA. According to this scheme, the CS approach is a Stage 4 procedure and is considered to be one of the most technically demanding (34). Although the ETOA is obviously advantageous to provide a unique surgical route to the CS with a different angle of attack visualizing different CS regions distinguished from the EEA and TCA, it should not be adopted as the first line surgical corridor to the lateral compartment of CS. Because all these surgical approaches are complementary, the three-dimensional orientations of anatomical structures using these three different approaches is critical to consider during preoperative planning. The three-dimensional model of the CS developed during this study helped to enhance the surgeon’s understanding and thus can be used to improve surgical outcomes in the management of various skull base tumors.

Conclusions

A cadaveric study found that the lateral CS wall was reliably accessed using the ETOA. Most of the lateral compartment was effectively explored through the anteromedial triangle; the infratrochlear and supratrochlear triangles provided a reliable entry point to the posterior compartment of the CS. We believe the ETOA provides a unique and valuable surgical route to the CS, with promising synergy when used with EEA and TCA. Our early experience with a clinical case convinces us of the efficacy of the ETOA for surgical management of CS-invading skull base tumors.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.
organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

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