REVIEW

Vestibular Schwannoma Surgical Treatment

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SUMMARY

Neurosurgical intervention remains the main step in the effective management of vestibular schwannomas. Extensive studies on vestibular schwannoma treatment have placed emphasis on preserving quality of life and neurological functions, particularly of the facial and vestibulocochlear nerves. Facial nerve preservation and hearing preservation have been achieved by significant advances in skull base microsurgical techniques and intraoperative neuromonitoring. Diffusion tensor imaging is a powerful and accurate method for preoperatively identifying the facial nerve in relation to vestibular schwannomas. Endoscopy offers excellent illumination of the anatomical structures and provides panoramic vision inside the surgical area. In this report, we focused on facial nerve and vestibulocochlear nerve preservation and analyzed the major techniques used for identifying the nerve–tumor relationship.

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Introduction

Vestibular schwannomas, also known as acoustic neurinomas, are benign neoplasms of Schwann cell origin. These tumors, which constitute approximately 85% of all tumors in the region of the cerebellopontine angle (CPA), are located close to the facial and vestibulocochlear cranial nerves. Considering its benign nature and the potential surgical morbidity and mortality related to the complex anatomy of the CPA, vestibular schwannomas remain among the most technically challenging of tumors to remove at the cranial base for neurosurgeons [1].

Over the last decade, skull base technological advancements and emphasis on functional outcomes have shifted the attention of surgeons from merely saving lives to obtaining the best possible cranial nerve outcomes, oncological control, and posttreatment quality of life for patients. Better understanding of the natural history of the tumors and the advent of stereotactic radiotherapy have increased the number of options and strategic paradigms for tumor management. However, neurosurgical intervention remains the main option for effective management. In this review, we focus on the facial nerve and vestibulocochlear nerve preservation and analyze the major techniques used in identifying the nerve–tumor relationship. These techniques include morphological patterns of the facial nerve and their corresponding microsurgical strategy, intraoperative neuromonitoring, preoperative diffusion tensor imaging (DTI), and endoscopic techniques.

Surgery Approach

The three surgical approach options (middle cranial fossa vs. retrosigmoid vs. translabyrinthine) for vestibular schwannomas and their respective patterns of postoperative cranial nerve preservation have been well described. Each approach has associated advantages and disadvantages. The middle fossa approach has long been used to expose the internal auditory canal (IAC), mainly for resection of small vestibular schwannomas located at the lip of the internal auditory meatus [2]. The retrosigmoid approach provides a panoramic visualization of the CPA [3]. We favor this approach and apply it to almost all of the vestibular schwannomas we encounter because the retrosigmoid approach is an available surgical method for tumors of any size regardless of the preoperative hearing condition. However, this approach limits the vision at the fundus of the IAC. The translabyrinthine approach offers very good visualization of the lateral IAC and fundus, thereby allowing for early identification of the facial nerve and more complete resection of tumors from these areas [4]. Thus, the translabyrinthine approach is preferred in larger tumors that grow toward to the IAC without preoperative serviceable hearing. Ansari et al. [5] conducted a systematic review of the available data (35 studies, 5064 patients) on vestibular schwannomas surgery and compared the different approaches as well as their associated complications. The results showed that the middle cranial fossa approach seems to be the safest technique to ensure hearing

preservation in patients with smaller tumors. The retrosigmoid approach seems to be the most versatile route for facial nerve preservation for most tumor sizes, but it is associated with a higher risk of postoperative pain and CSF fistula. The translabyrinthine approach is related to complete hearing loss. Incidences of residual tumor, mortality, and dysfunction of other cranial nerves were not significantly different between the three approaches.

Morphological Patterns of the Facial Nerve and their Corresponding Treatment Strategy

Vestibular schwannomas most frequently arise in the posteriorly located vestibular nerves and usually displace the facial and cochlear nerves anteriorly. Variability in the direction of the tumor growth arising from the vestibular nerves may result in the facial nerve being displaced not only directly anteriorly but also anterosuperiorly or anteroinferiorly. The most common location of the facial nerve is on the anterior middle third of the tumor capsule, regardless of tumor size. However, the morphological features of the facial nerve observed under a microscope and the anatomical relationship between the facial nerve and the tumor during surgery are complicated. We summarized our experience with 116 patients who underwent surgery using the retrosigmoid approach. Five morphological patterns of the facial nerve (Figure 1) as well as their corresponding treatment strategy for tumor resection are proposed. These findings provide more valuable information that could help achieve optimum outcomes in patients.

Normal Subtype

The normal subtype can be identified in small vestibular schwannomas and in vestibular schwannomas that grow outwards. This subtype accounts for approximately 3.4% of all vestibular schwannomas (4/116). The normal subtype grows around the IAC

without the adherence to the brainstem. The facial nerve can be easily recognized in this type. The facial nerve is usually dissected from the brainstem end to the internal auditory canal end to avoid damage.

Flat Subtype

The flat subtype comprises the majority of the facial nerve morphologies in vestibular schwannoma intraoperative findings, accounting for 72.4% (84/116) of all cases. Prior to tumor resection, grinding of the internal auditory canal posterior wall is preferred, and the facial nerve is separated from the internal auditory canal end to the brain stem end. Upon raising the medial or lateral capsular after subtotal resection, the flat facial nerve is often observed with a silvery white appearance (pale for the minority).

Membranoid Type

The membranoid subtype (18.1%, 21/116) can be detected in larger vestibular schwannomas and vestibular schwannomas that grow toward the brainstem. Considering the long-term tumor compression and blood supply insufficiency, the facial nerve appears pale yellow or gray white, similar to the tumor color. The facial nerve shows a membrane attached to the anterior portion of the tumor. Thus, the facial nerve can be easily injured if the surgeon separates the facial nerve from the internal auditory canal end or the brain stem end before tumor resection. Intracapsular tumor resection is preferably performed first followed by subdivided block resection of the tumor body. After resection of the tumor body, the facial nerve tension relaxes gradually, the color slowly turns gray or silvery white from pale yellow, and the morphology shifts to a flat shape. Then, the facial nerve becomes easy to identify and isolate. In summary, the facial nerve of this subtype should be dissected after removal of the tumor body.

Figure 1 Five morphological patterns of the facial nerve according to the relationship between the facial nerve and tumor. (A) Normal subtype; (B) Flat subtype; (C) Membranoid type; (D) Penetrating subtype; (E) Diffused subtype.

Penetrating Subtype

The rare penetrating subtype (1.7%, 2/116) is found in the lobulated tumors. Considering that tumor growth is blocked by the nerves, the vascular or the thick arachnoid, the tumor presents with lobulated expansion. The facial nerve is wrapped by the two tumor lobes; thus, it is named “false penetrating”. The facial nerve is gradually exposed with the resection of each tumor lobe. In this subtype, we recommend that facial nerve dissection be performed after removal of the bodies of the tumor lobes. Interestingly, Sampath *et al.* [6] reported the “true penetrating” relationship between the facial nerve and the tumor: The facial nerves passed through the tumor itself. The incidence of this subtype is very low, 3.4% for small tumors (smaller than 2.5 cm), 2.9% for large tumors (from 2.5 cm to 4 cm), and 3.3% for giant tumors (larger than 4 cm). Whether the tumor actually infiltrates the nerve sheath or simply enfolds it requires confirmation. In the former case, the tumor is virtually impossible to dissect away from the nerve completely without causing considerable postoperative deficit.

Diffused Subtype

The diffused subtype, which can be recognized in acoustic tumors with bizarre shapes and in recurrent tumors, accounts for 4.3% (5/116) of all subtypes. In the former case, intracranial hemorrhage or inflammation during the tumor development causes uneven tumor growth, thereby dividing the facial nerve and distributing its fractions on the tumor surface or divided leaves. In the latter case, the residual tumor that remains after the first operation results in diffuse distribution of the facial nerve. Looking for the facial nerve and ensuring its protection is more difficult in this subtype. Thus, tumor resection requires close intraoperative facial nerve monitoring with the aid of an ultrasound knife.

Intraoperative Neuromonitoring

Intraoperative neurophysiological monitoring is critical in modern vestibular schwannoma surgery [7]. The application of routine intraoperative facial and vestibulocochlear nerve monitoring has significantly decreased the incidence of facial nerve paresis and hearing loss. The use of electromyography (EMG) for monitoring facial nerve function has been well demonstrated, including free-running spontaneous EMG and evoked facial nerve EMG [8]. Spontaneous EMG activity can be used to intraoperatively monitor the corresponding nerve roots responsible for muscle innervation. Surgical manipulation such as pulling, stretching, or compression of the facial nerve produces neurotonic discharges that result in activity in the corresponding innervated muscles. Evoked facial nerve EMG is a real-time method for checking the EMG evoked by occasional and continuous direct electrical stimulations of the facial nerve during tumor excision. Facial nerve EMG not only helps determine the anatomical location and functional integrity of the facial nerve but also helps predict the postoperative functional outcome of the facial nerve. Several studies have investigated the correlation between intraoperative facial nerve EMG monitoring parameters (e.g., stimulus threshold,

response amplitude, proximal-to-distal-amplitude ratio, and so on) and their abilities to predict facial nerve outcomes [9,10].

Current vestibulocochlear nerve preservation rates are not as satisfactory compared with the favorable outcomes observed for the facial nerve. Large tumors are more highly associated with postoperative neurological deficits, and tumors with extensive infiltration into CPA render hearing preservation a challenging task. Intraoperative monitoring of the vestibulocochlear nerve mainly includes brainstem auditory evoked potentials (BAEP), compound nerve action potential (CNAP), and electrocochleography (ECOG) [7]. Minimally invasive BAEP is the most widely used monitoring modality to date. However, BAEP, which features a poor signal-to-noise ratio and poor temporal resolution, is susceptible to disruption by various intraoperative procedures, including general anesthesia, body temperature, dural opening, and so on [11]. CNAP and ECOG are advantageous as near-field techniques, in which electrodes are placed close to the vestibulocochlear nerve [12,13]. Larger amplitude signal acquisition takes less time to allow real-time feedback to the surgeon, thus providing reliable, stable and reproducible monitoring of the auditory function.

Preoperative Imaging

Preoperative identification of the facial nerve could help prevent nerve injury during tumor resection. Unfortunately, as these tumors enlarge and compress the facial nerve, preoperative identification using magnetic resonance imaging (MRI) becomes difficult and urgent. Standard MRI of CPA tumors, including T1-weighted sequences and T2-weighted sequences obtained both before and after contrast administration, offers 2D resolution of distinct structures but lacks the ability to precisely reveal spatial relationships. Diffusion tensor imaging (DTI) has emerged as a powerful technique for 3D tract reconstruction and imaging of white matter fibers. Hodaie *et al.* investigated the cranial nerve map of healthy individuals using DTI-based tractography [14]. The whole course of cranial nerves II, III, and V were imaged in great detail and lower cranial nerves (nerves IX, XI, and XII) could not be imaged well. The facial/vestibular complex in the internal auditory meatus primarily showed the cisternal segment of the nerves. Moreover, the facial, vestibular, and cochlear components could not be clearly differentiated. Taoka *et al.* demonstrated for the first time that the agreement between the preoperative DTI reconstruction and the intraoperative location of the facial nerve in relation to vestibular schwannoma is 62.5% (5/8 patients), indicating that DTI could be a useful tool for preoperatively predicting facial nerve displacement in vestibular schwannomas [15]. Recently, Gerganov *et al.* who successfully validated the reliability of facial nerve DTI-based fiber tracking in a series of patients with large vestibular schwannomas, further found that the five typical locations of the CPA segment of the facial nerve are depicted with DTI-based fiber tracking in relation to the tumor; these locations include the anterior middle third, anterior inferior third, anterior superior third, inferior surface, and superior surface of the lesion [16]. As such, DTI method has proven to be a powerful and accurate method for preoperatively identifying the facial nerve in relation to vestibular schwannomas.

The Endoscopic Technique

The endoscopic technique is an established component of contemporary brain tumor surgery approaches and is widely used in various skull base surgeries, especially pituitary adenomas [17,18]. This technique allows direct viewing under high magnification and visualization under angle and is minimally invasive and team surgery [19]. The endoscopic approach offers excellent illumination of the anatomical structures using the high-quality optics and a high-definition digital setup. The application of angled endoscopes allows access to areas that would have otherwise been impossible to assess with the direct, linear view afforded by a microscope. Moreover, the entry is much smaller in comparison with microsurgical approaches. Collaboration between two surgeons is also required: one surgeon holds the endoscope and provides traction, while the other handles two surgical instruments inside the surgical field.

The application of the endoscopy is currently expanding in the case of CPA-located lesions [20,21]. In vestibular schwannomas, the whole IAC and tumor residual fractions can be easily visualized using the endoscopy. Shahinian et al. [22] reported a series of 527 patients with unilateral vestibular schwannomas who underwent fully endoscopic resections. Utilization of the fully endoscopic technique resulted in complete removal of 94% of the tumors through 2.0-cm “keyhole” retrosigmoid craniotomies. Anatomical preservation of the facial nerve was achieved in all of the patients and measurable hearing was preserved in 57% of the cases. These results indicate that the endoscope can be a minimally invasive approach for the resection of vestibular schwannomas. However, considering that the application of endoscopes remains limited, the actual significance is dependent on the particular surgical technique and the experience of the surgeon. Surgeons lack an overview of the entire CPA and accurate estimation of the real distance between the tip of the endoscope and the visualized structures may be difficult to achieve. Surgeons must further anticipate possible endoscopy outcomes, such as potential arterial bleeding and complicated reconstruction requirements. As such, in our experience, we consistently propose endoscope-assisted microsurgery (EAM), which combines the advantages of classical microneurosurgery and endoscopy. EAM allows the possibility of identifying various structures at an early stage and searching for hidden tumor fractions.

Intraoperative Fluorescence-Guided Surgery

In typical vestibular schwannomas surgery, surgeons rely mainly on preoperative images and visual inspection for the tumor and the nerves identification. Optical imaging using fluorescence is a novel technique that can be used to visualize structures in real time during surgery. To date, no intraoperative fluorescence-guided resection has yet been applied in vestibular schwannomas surgery. However, intraoperative fluorescence-guided glioma resection outcomes can provide valuable references for vestibular schwannomas.

Aminolevulinic acid (ALA), which is an orally administered prodrug that passes through the intact blood–brain barrier, is metabolized to form the fluorescent molecule protoporphyrin IX [23]. Protoporphyrin IX accumulates preferentially in neoplastic tissues and induces visible (635-nm) red fluorescence when excited with ultraviolet (400-nm) light [24]. Stummer and the ALA-Glioma Study Group have described the most extensive and most significant intraoperative fluorescence resection of malignant glioma using ALA (phase IIIa clinical trial) [25]. Tumors were removed completely in 90 (65%) of 139 patients who were assigned ALA compared with 47 (36%) of 131 who were assigned white light ($P < 0.0001$). Patients who were allocated ALA had higher 6-month progression-free survival rates than those allocated white light (41.0% vs. 21.1%, $P = 0.0003$). Therefore, tumor fluorescence derived from ALA results in more complete resections, leading to improved progression-free survival in patients with malignant glioma.

Nerve image-guided surgery could potentially be of great value for avoiding the nerve damage [26]. However, all of the intraoperative fluorescence-guided resections performed to date are based on tumor fluorescence image-guided surgery. GE Global Research synthesized a myelin-targeting fluorophore, named GE3111, which is characterized by its optical and myelin-binding properties using purified myelin basic protein. Following intravenous injection, central and peripheral nerves were visualized *in vitro* and *in vivo* using a dedicated compact imaging device [27]. Thus, nerve-highlighting contrast agents that can be used for nerve image-guided surgery require further investigation.

Conclusion

The ultimate goals of vestibular schwannoma surgery are safe and accurate total tumor resection, facial nerve preservation, and hearing preservation. For the neurosurgical oncologist, vestibular schwannoma resections using available microsurgery strategy, intraoperative neuromonitoring, preoperative DTI and endoscopy are associated with fewer neurological deficits and more extensive resection. Beyond these techniques described above, emerging intraoperative options, such as intraoperative fluorescence-guided surgery, and postoperative novel medical treatments may represent the next evolutionary step in the treatment for vestibular schwannoma.

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Conflict of Interest

The authors declare no conflict of interest.

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