NARRATIVE REVIEW

Consensus guidelines for the management of vestibular schwannoma for low- and middle-income countries

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Abstract

Vestibular Schwannoma (VS), previously known as acoustic neuroma, constitutes the majority of tumours found in the cerebellopontine angle (CPA). Most guidelines for managing CPA tumours have been developed by high-income countries (HICs). However, these guidelines often fall short in addressing the unique challenges encountered in low- and middle-income countries (LMICs), such as Pakistan. In LMICs, issues related to a limited healthcare workforce, inadequate infrastructure, and constrained financial resources hinder the effective implementation of these HIC-derived guidelines. Additionally, it has been observed that VS tends to present at a larger size in LMICs compared to HICs. Given that VS is the predominant type of CPA tumour and other types are covered under separate guidelines, this article aims to provide practical, context-specific recommendations for the screening, diagnosis, and management of Vestibular Schwannoma in LMIC settings. Our focus is to bridge the gap in care strategies and adapt them to the resource constraints and clinical realities of LMICs.

Keywords: Neuroma, acoustic, cerebellopontine angle, health care, vestibular schwannoma, radiosurgery, tumours

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Introduction

The cerebellopontine angle (CPA), located in the posterior cranial fossa, forms a triangular space that houses cranial nerves V, VI, VII, VIII, along with the anterior inferior cerebellar artery, making it a key anatomical landmark. Notably, CPA tumours account for 5 to 10% of all intracranial tumours. Among these, vestibular schwannomas (VS) represent the majority (75 to 85%), followed by meningiomas (10–15%) and epidermoid (7–8%).[1–3]

Patients with VS commonly experience unilateral sensorineural hearing loss (94%) and tinnitus (83%), with vertigo and unsteadiness also reported in 17–75% of cases.[4] The diagnostic process for CPA tumours involves a thorough medical history, physical examination, audiometric testing, and radiographic assessment. The contrast-enhanced T1-weighted MRI sequence stands as the diagnostic gold standard, supplemented by preoperative CT scans for detailed evaluation of the petrous bone's anatomy.[5–7]

The management of VS, a comparatively rare condition, poses significant challenges to neurosurgeons and otologists.[8] Emphasizing early detection and a multidisciplinary treatment approach has been linked to improved outcomes.[9] However, a study in Pakistan reveals that advanced stage tumours, indicative of delayed presentation, are quite prevalent, often hindering the possibility of curative resection. Moreover, patients with tumours larger than 4 cm exhibit significantly higher postoperative morbidity.[10]

Given the significant impact of VS and the current lack of consensus on treatment modalities, this paper advocates for the development of evidence-based guidelines for the diagnosis and management of VS, particularly tailored to the resource constraints of low- and middle-income countries (LMICs). The primary goal is to establish practical, evidence-based management protocols adaptable to the healthcare systems in these regions, keeping in mind the challenges of late presentation and associated complications in such settings.

Methodology

The literature search for high-quality data on vestibular schwannoma was done on different databases, including PubMed, Google Scholar, Scopus, and Embase. The most relevant and high-quality studies were analyzed to develop evidence-based recommendations. An expert panel was convened consisting of specialists and leading

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experts within the field of neuro-oncology to identify the gaps in diagnosis and management of vestibular schwannoma within Pakistan. This group was tasked with identifying best-practice recommendations and their application within the context of Pakistan as an LMIC. Recommendations were collated, reviewed, and debated regarding utility and evidence-based practices in a process that has been previously detailed.[11]

Initial evaluation

MRI is recommended for screening of asymmetrical sensorineural hearing loss (with ≥ 10 dB of interaural difference at 2 or more consecutive frequencies or ≥15 dB at one frequency) subjective asymmetric tinnitus, and sudden SNHL (Sensorineural Hearing Loss).[5,8,12] However, screening with MRI is not always feasible in LMICs owing to limited resources, workforce, infrastructure, and financing. If MRI scan is accessible, we recommend using it for screening. Nevertheless, if accessibility or affordability are barriers, we suggest using the auditory brainstem response (ABR) or fast-spin echo MRI as a substitute for screening of VS. ABR (sensitivity of 100% and specificity of 61.9%) and fast-spin echo MRI (sensitivity of 100% and a specificity of 100%) are widely available and cost-effective tools.[13–15]

The recommended modality of choice for the diagnosis of VS is MRI (contrast-enhanced T1-weighted and high-resolution T2-weighted. The tumour can be found using standard T1, T2, FLAIR, and DWI MR sequences acquired in the axial, coronal, and sagittal planes.[16] To assess the preoperative anatomy of the petrous bone, a complementary CT scan might be used.[17] We recommend MRI (contrast-enhanced T1-weighted and high-resolution T2-weighted MRI) and CT scan for the preoperative detection of VS. If an MRI scan is unavailable or not possible then then as the bare minimum, we suggest a high-resolution CT scan with or without contrast.

Surgical management

Observation is recommended in cases of small, asymptomatic tumours with normal cranial nerve function. If a watch and wait approach is taken, MRI should be obtained annually for 5 years, with the interval lengthening after that if the tumor is stable. SRS can be used as an alternative to observation to stop tumor growth and maintain long-term nerve function. However, there is still a negligible chance of nerve function or quality of life deteriorating. Surgery is also an option if the primary goal of management is the long-term preservation of nerve function, but there is a considerable risk of functional decline, up to 50%. Therefore, we recommend against operating on these patients. Therapy option should be discussed with patient to prevent further deterioration of small tumours exhibiting vestibular and/or auditory symptoms. In these contexts, SRS provides a higher rate of hearing preservation and a lower risk for facial paresis than surgery. The goal of therapy can be the cure or tumour control while maintaining facial nerve function in patients with small tumours and total hearing loss. In these cases, any option is acceptable. Since no function is ever really jeopardized, observation is typically the best course of action. SRS or surgery both have a low chance of causing facial nerve injury and may offer long-term control or a cure. SRS is the primary choice if tumor control is deemed sufficient by the patient since it preserves facial nerve function and has a lower risk profile than surgery.[8,16]

Patients with medium-sized tumours (<3 cm), surgery or radiosurgery can be recommended at a reasonably similar level. SRS has a better risk profile than surgery, albeit surgery can remove the tumor completely. All possibilities should be carefully explained to the patients.[8]

In a retrospective bicentric cohort study, Tatagiba et al,18 compared SRS and microsurgical for treating sporadic VS in two specialized neurosurgical centres, using data from 901 patients treated between 2005 and 2011. The study utilised the Koos classification to categorize the tumours: Koos I indicates an intracanalicular tumour, Koos II represents a tumour extending into the cistern but not reaching the brainstem, Koos III denotes a tumour reaching the brainstem surface, and Koos IV describes a tumour deforming the brainstem surface and shifting the fourth ventricle. The findings showed that overall, microsurgery had superior tumour control with a 7% recurrence rate, compared to 11% for SRS. In smaller tumours, classified as Koos I (intracanalicular) and II (extending into the cistern), both treatments were equally effective. However, in larger VS, classified as Koos III (reaching the brainstem surface) and IV (deforming the brainstem surface), microsurgery was more effective, with a clear correlation between the extent of resection and recurrence-free survival. While facial and hearing deterioration were similar for both treatments in smaller tumours (Koos I and II), these side effects were more pronounced in microsurgery for larger tumours (Koos III and IV). Additionally, microsurgery was more effective in improving symptoms like tinnitus, vertigo, imbalance, and trigeminal issues in these larger tumours. The study concludes that SRS is comparable to microsurgery in smaller VS (Koos I and II) but less effective in larger ones (Koos III and IV), suggesting that combination therapy should be limited to residual tumours not exceeding Koos II size.[18]

Patients with larger sporadic VS tumour sizes should be warned about the higher-than-average risk of loss of serviceable hearing when undergoing microsurgical resection.[19] Long-lasting eighth cranial nerve symptoms are frequent in patients with large tumours with brainstem compression (>3 cm). These patients frequently also exhibit other symptoms such as facial nerve paresis and gait ataxia. Surgery is the only treatment that can decompress the brainstem and stretched cranial nerves, which is the main goal of therapy. A sizeable risk of loss or impairment of cranial nerve function is associated with surgery for large tumours. For this reason, subtotal resection (maximal safe resection) of the tumour followed by SRS or observation to reduce the tumour bulk is a viable approach.[8, 19]

In small, asymptomatic VS (<2.5cm), we recommend observation with an annual MRI for 5 years, and the interval lengthening after that if the tumour is stable. In small VS with auditory or vestibular symptoms, we suggest SRS owing to its higher rate of hearing and facial nerve preservation. If SRS facilities and expertise are not available, then we advise surgery. In cases of medium-sized VS (<3 cm), we propose SRS or surgery depending on the patient's preference, centre resources, and neurosurgeon expertise. For patients with large sporadic VS, we recommend subtotal resection (maximal safe resection) and postop SRS due to the high rate of hearing and facial nerve preservation (95% and 60%) with limited regrowth of tumour (5%).[20] The surgical approach depends upon the surgeon´s preference. The most often surgical approach used is the retro sigmoid craniotomy and intracapsular maximal safe resection. The other surgical approaches include presigmoid translabyrinthine and sigmoid retrolabyrinthine. The translabyrinthine approach is suitable for patients with no functional baseline hearing as it would result in permanent hearing loss. However, sigmoid retro-labyrinthine can provide excellent visualization and control over the tumour without significantly compromising functional hearing.

Intraoperative cranial nerve monitoring

To enhance long-term facial nerve function following vestibular Schwannoma surgery routine use of intraoperative cranial nerve monitoring is required. Monitoring of the facial nerve consisting of direct electrical stimulation, and free-running electromyography to increase the rate of functional preservation. Evoked facial motor potentials are currently being examined.[8,21] When attempting to preserve hearing, brainstem auditory evoked responses are recommended.[19] Electromyography of the lower cranial nerves is suggested in cases of large lesions.[8,22] We recommend Intraoperative cranial nerves monitoring if the center has the relevant modalities and trained workforce.

Pathologic assessment

Histopathologic evaluation is relatively straightforward and relies upon the examination of haematoxylin and eosin (H&E) preparation. Immunohistochemical stains may be performed to distinguish from spindle cell meningioma, which can occasionally be present in this location. There is no recommendation on the prognostic significance of Antoni A versus B histologic patterns and mitotic figures due to the paucity of adequate data. Similarly, recommendations cannot be framed for the prediction of the clinical behaviour of VS in terms of light microscopic features (other than Antoni A versus B), KI-67 labelling index, proliferating cell nuclear antigen labelling index, and degree of vascular endothelial growth factor expression due to a scarcity of able data.[23]

Radiation therapy

The International Stereotactic Radiosurgery Society (ISRS) recommends an option of single fraction radiosurgery (11-14 Gy) or fractionated stereotactic radiotherapy for small to moderate size VS without significant mass effect.[24] Since there is no difference in radiographic control with different doses, it is recommended to use (<13Gy, range 12-14 Gy) for single fraction SRS doses in order to preserve hearing and mitigate the risk of developing new cranial nerve deficits.[25]

VS is among the rare pathologies that do not necessitate a histopathological diagnosis prior to stereotactic radiosurgery (SRS). The presence of an intracanalicular extension into the internal auditory canal, accompanied by contrast enhancement on imaging, is a definitive indicator of VS. In cases of small VS, particularly when there is no evident mass effect on the brainstem, SRS can be confidently administered based solely on MRI findings.

There are no studies that compare the differences in the outcomes between Gamma Knife (GK), LINAC-based radiosurgery, CyberKnife, and proton beam.[25] Ideally, the time frame for follow-up imaging following SRS should consider clinical indications, a patient's unique situation, and institutional guidelines. The evaluation of recurrence over a long period of time with repeated MRIs is recommended. Regarding the time frame for these investigations, no recommendations are proposed. [25]

Hearing reservation

The likelihood of successful hearing preservation should be discussed with patients who had functional hearing in the ipsilateral ear and are considering stereotactic

Table-1: Summary of Recommendations for Vestibular Schwannoma.

Radiology	• MRI brain with and without contrast. • 'Minimum required' MRI protocol: o Imaging on at least 0.5T. o Sequences: Axial T2 and coronal or axial FLAIR sequence; pre-contrast T1 and contrast-enhanced T1. • Tumor location, size, margins, enhancement pattern, relation with critical neurovascular structures, and presence of hemorrhage/mineralization. • First postoperative MRI is recommended after 3 months. o To identify the extent of resection. o To have a baseline to compare successive imaging.
Neurosurgery and Radiation Oncology	• Small (<2.5cm) asymptomatic VS: Observation and serial follow-up with imaging and hearing assessment. •Small (<2.5cm) symptomatic VS: SRS/surgery/observation based on multiple factors (availability of expertise, risk assessment, baseline hearing status, patient's perception, social situation, financial considerations, and support system). •Symptomatic large VS (>2.5cm): Maximal safe resection followed by postop SRS/SRT/ Fractionated SRT/observation. • For Patients with good baseline hearing undergoing SRS, a single fraction (<13 Gy) is recommended to preserve hearing and avoid facial palsy. • Intraoperative cranial nerve monitoring is recommended for patients undergoing surgical resection. • Cases need to be managed in centres with site-specific clinical expertise and high volume.
Neuropathology	• Hematoxylin and eosin (H&E) preparation. • Immunohistochemical stain GFAP, S-100 and/or SOX-10 if histology is not characteristic.
Follow-up	• First follow-up at post-op day 10 for wound assessment, stitch removal, and discussion related to histopathology/NOTB recommendations. • MRI every six months for the first year, and thereafter annually or biannually based on clinical signs and symptoms for 10 years and every 2-3 years. • Redo surgery can be considered in case of recurrence/disease progression after risk stratification in NOTB.

MRI: Magnetic resonance imaging, FLAIR: Fluid-attenuated inversion recovery, VS: Vestibular Schwannoma, SRS: Stereotactic radiosurgery, SRT: Stereotactic Radiation Therapy, Gy: Gray, GFAP: Glial fibrillary acidic protein, NOTB: Neuro-oncology tumor board.

radiosurgery. The hearing preservation depends on good preoperative word recognition and/or pure tone thresholds with various cut-points reported, small tumour size, marginal tumour dosage ≤ 12 Gy and cochlear dose ≤ 4 Gy are the most reliable prognostic factors linked to maintenance of functional hearing. Age and gender are not reliable indicators of the success of hearing preservation. [7]

Post-operative management and prognosis

During surgery, lower cranial nerves are more prone to damage, specifically IX, X, XI, and XII, which will lead to difficulty in swallowing, stridor, and inability to protect the airway postoperatively. If the stridor is so severe that it causes respiratory distress, then endotracheal intubation is recommended. Emergency tracheostomy and cricothyrotomy can also be used as alternative techniques in patients with difficult endotracheal intubation. Tracheostomy is considered the long-term management in persistent stridor postoperatively.[26]

The recurrence rate of VS ranges from 0.51% to 9.2%. Long-term follow-up is necessary after the resection of the tumour, an MRI study reported 22 months as doubling time for residual fragments of the tumour. Moreover, tumour recurrence happens after a decade in the case of gross total resection (GTR), and recurrence is seen after 2.7 years in the case of subtotal resection (STR). The study revealed recurrence occurs when the post-operatively latest MRI image shows a>5mm increase in the size of the residual tumour.[27]

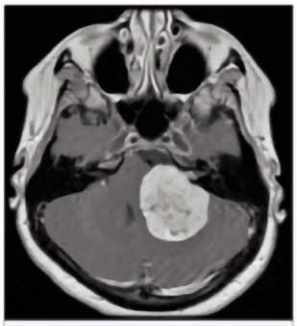
Emerging therapies for the treatment

Bevacizumab has a favourable impact on hearing and tumour growth and is a promising therapy option for patients with bilateral (NF2) or unilateral VS.[28–30] Lapatinib can be used in NF2 to improve hearing and reduce the size of the VS. However, the use of erlotinib or everolimus is not recommended in NF2. To improve postoperative facial nerve outcomes, nimodipine perioperative therapy should be taken into consideration (or hydroxyethyl starch may be added).[31]

Conclusion

Created to assist healthcare professionals operating in areas with limited resources, these guidelines offer a practical framework derived from valuable insights (refer to Table 1 and Figure 1). By putting these guidelines into practice, there is substantial potential for enhancing specific outcomes and fostering a greater focus on collaborative healthcare in low- and middle-income countries (LMICs), like Pakistan.

Knowledge gaps: One of the most common issues



MRI suggestive of vestibular schwannoma[a]

CSF diversion before urgent referral in case of a clinical emergency where expertise is not available

Hearing assessment (pure tone audiometry and speech discrimination; subject to availability)

Asymptomatic (small)

Symptomatic

<2.5 cm

> 2.5 cm

SRS/surgery/observation based on multiple factors[b]

MSR with facial nerve monitoring

MRI after 6 weeks

Significant residual with LMIC limitations[c]

GTR/minimal residual

Surveillance with MRI 6 monthly for 2 years then annually

Disease progression

Surveillance with serial imaging and hearing assessment

Radiaton[d]

NOTB

MRI: Magnetic resonance imaging, CSF: Cerebrospinal fluid, MSR: Maximal safe resection, GTR: Gross total resection, NOTB: Neuro-oncology tumor board, SRS: Stereotactic radiosurgery

[a]Vestibular schwannoma associated with NF2 does not follow this algorithm.

[b]Servicible hearing, availabilty of expertise, risk assessment, patient's perception, social situation, financial considerations, and support system

[c]LMIC limitations (cost of serial follow-ups, lost to follow, limited access to specialized health care due to distance, lack of social support)

[d]Conventional/fSRT/SRS

Figure-1: Management algorithm for Vestibular schwannoma.

faced in the LMICs is the judicious use of SRS. There are no guidelines/recommendations on the appropriate utilization of SRS and we need more efforts and prospective high-quality studies to obtain scientific evidence in this regard.

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