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 Congress of Neurological Surgeons

Congress of Neurological Surgeons Systematic Review and Evidence-Based Guidelines on the Treatment of Adults With Vestibular Schwannomas: Executive Summary

BACKGROUND: Vestibular schwannomas (VS) are uncommon lesions that are a substantial challenge to the neurosurgeons, otologists, and radiation oncologists who undertake their clinical management. A starting point to improving the current knowledge is to define the benchmarks of the current research studying VS management using evidence-based techniques in order to allow meaningful points of departure for future scientific and clinical research.

OBJECTIVE: To establish the best evidence-based management of VS, including initial otologic evaluation, imaging diagnosis, use of surgical techniques, assessment of tumor pathology, and the administration of radiation therapy.

METHODS: Multidisciplinary writing groups were identified to design questions, literature searches, and collection and classification of relevant findings. This information was then translated to recommendations based on the strength of the available literature.

RESULTS: This guideline series yielded some level 2 recommendations and a greater number of level 3 recommendations directed at the management of VS. Importantly, in some cases, a number of well-designed questions and subsequent searches did not yield information that allowed creation of a meaningful and justifiable recommendation.

CONCLUSION: This series of guidelines was constructed to assess the most current and clinically relevant evidence for the management of VS. They set a benchmark regarding the current evidence base for this type of tumor while also highlighting important key areas for future basic and clinical research, particularly on those topics for which no recommendations could be formulated.

The full guidelines can be found at: <https://www.cns.org/guidelines/guidelines-management-patients-vestibular-schwannoma>.

KEY WORDS: Acoustic neuroma, Guidelines, Radiation therapy, Surgery, Vestibular schwannoma

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Vestibular schwannomas (VS) are uncommon lesions that are a substantial challenge to the neurosurgeons, otologists, and radiation oncologists who undertake

their clinical management. Because outcomes remain imperfect, improvements in therapy are necessary. A useful starting point to improving the current knowledge base is to define the benchmarks of our current knowledge regarding VS management using evidence-based techniques in order to allow meaningful points of departure for future scientific and clinical research.

ABBREVIATIONS: **3-D**, 3-dimensional; **AANS**, American Association of Neurological Surgeons; **CISS**, constructive interference in steady state; **CNS**, Congress of Neurological Surgeons; **FIESTA**, fast imaging employing steady-state acquisition; **JGC**, Joint Guidelines Committee; **MF**, middle fossa; **MPRAGE**, magnetization prepared rapid acquisition gradient echo; **MRI**, magnetic resonance imaging; **RS**, retrosigmoid; **STR**, subtotal resection; **VS**, vestibular schwannoma.

OBJECTIVES AND GUIDELINES PANEL DEVELOPMENT

The objectives of these guidelines are to establish the best evidence-based management

of VS. The Guidelines Committee of the Joint Tumor Section recruited experts in the field as lead writers of each section. These writers, in turn, recruited experts in nonneurosurgical specialties relevant to the field of management and therapy chosen, developing a multidisciplinary task force.

TOPIC RANGE OF THIS REVIEW AND CLINICAL PRACTICE GUIDELINE

The task force designed questions to allow assessment of the literature in a manner that would provide guidance for the management of VS spanning the topics of otologic assessment, imaging, surgical resection, tumor evaluation by standard neuropathology and molecular techniques, radiation therapy, and emerging concepts and therapies.

LITERATURE EXAMINATION AND SELECTION

A wide-ranging literature search strategy was undertaken to identify all citations relevant to the management of VS. The PubMed and Embase electronic databases were searched from 1990 through 2014, with additional data being gleaned from the Cochrane Central Register of Controlled Trials, and Web of Science. The eligibility (inclusion/exclusion) criteria to screen the citations for each of the questions were determined ahead of time for each section by the respective writing group. Evidence tables, reporting the extracted study information and evidence classification, were generated for the included studies for each of the questions.

AMERICAN ASSOCIATION OF NEUROLOGICAL SURGEONS/CONGRESS OF NEUROLOGICAL SURGEONS EVIDENCE CLASSES AND LEVELS OF RECOMMENDATIONS

The evidence classifications were then used to create recommendations, the strength of which was graded according to the Joint Guidelines Committee (JGC) Guideline Development Methodology (<https://www.cns.org/guidelines/guideline-procedures-policies/guideline-development-methodology>).

GUIDELINE APPROVAL PROCESS

The completed evidence-based clinical practice guidelines for the management of VS were presented to the JGC for review. The reviewers for the JGC were vetted by *Neurosurgery* for suitability and expertise to serve as reviewers for the purposes of publication in that journal also. The final product was then approved and endorsed by the executive committees of both the American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS) prior to publication in *Neurosurgery*.

The following is a listing of the recommendations from the guidelines that provides the reader an overview of the findings

from each section. The underpinnings of these recommendations can be reviewed in at: <https://www.cns.org/guidelines/guidelines-management-patients-vestibular-schwannoma>.

RECOMMENDATIONS

Audiologic Screening

RECOMMENDATION: Level 3: On the basis of an audiogram, it is recommended that magnetic resonance imaging (MRI) screening on patients with ≥ 10 decibels (dB) of interaural difference at 2 or more contiguous frequencies or ≥ 15 dB at 1 frequency be pursued to minimize the incidence of undiagnosed VS. However, selectively screening patients with ≥ 15 dB of interaural difference at 3000 Hz alone may minimize the incidence of MRIs performed that do not diagnose a VS.

RECOMMENDATION: Level 3: It is recommended that MRI be used to evaluate patients with asymmetric tinnitus. However, this practice is low yielding in terms of VS diagnosis ($< 1\%$).

RECOMMENDATION: Level 3: It is recommended that MRI be used to evaluate patients with a sudden sensorineural hearing loss. However, this practice is low yielding in terms of VS diagnosis ($< 3\%$).

Hearing Preservation

Stereotactic Radiosurgery

RECOMMENDATION: Level 3: Individuals who meet these criteria and are considering stereotactic radiosurgery should be counseled that there is moderately high probability ($> 50\%$ - 75%) of hearing preservation at 2 yr, moderately high probability ($> 50\%$ - 75%) of hearing preservation at 5 yr, and moderately low probability ($> 25\%$ - 50%) of hearing preservation at 10 yr.

RECOMMENDATION: Level 3: Individuals who meet these criteria and are considering stereotactic radiosurgery should be counseled that there is a high probability ($> 75\%$ - 100%) of hearing preservation at 2 yr, moderately high probability ($> 50\%$ - 75%) of hearing preservation at 5 yr, and moderately low probability ($> 25\%$ - 50%) of hearing preservation at 10 yr.

RECOMMENDATION: Level 3: Individuals who meet these criteria and are considering stereotactic radiosurgery should be counseled regarding the probability of successful hearing preservation based on the following prognostic data: the most consistent prognostic features associated with the maintenance of serviceable hearing are good preoperative word recognition and/or pure tone thresholds with variable cut-points reported, smaller tumor size, marginal tumor dose ≤ 12 Gy, and cochlear dose ≤ 4 Gy. Age and sex are not strong predictors of hearing preservation outcome.

Microsurgery

RECOMMENDATION: Level 3: Individuals who meet these criteria and are considering microsurgical resection should be counseled that there is a moderately low probability ($> 25\%$ - 50%) of hearing preservation immediately following surgery,

moderately low probability (>25%-50%) of hearing preservation at 2 yr, moderately low probability (>25%-50%) of hearing preservation at 5 yr, and moderately low probability (>25%-50%) of hearing preservation at 10 yr.

RECOMMENDATION: Level 3: Individuals who meet these criteria and are considering microsurgical resection should be counseled that there is a moderately high probability (>50%-75%) of hearing preservation immediately following surgery, moderately high probability (>50%-75%) of hearing preservation at 2 yr, moderately high probability (>50%-75%) of hearing preservation at 5 yr, and moderately low probability (>25%-50%) of hearing preservation at 10 yr.

RECOMMENDATION: Level 3: Individuals who meet these criteria and are considering microsurgical resection should be counseled regarding the probability of successful hearing preservation based on the following prognostic data: the most consistent prognostic features associated with maintenance of serviceable hearing are good preoperative word recognition and/or pure tone thresholds with variable cut-points reported, smaller tumor size commonly less than 1 cm, and presence of a distal internal auditory canal cerebrospinal fluid fundal cap. Age and sex are not strong predictors of hearing preservation outcome.

Conservative Observation

RECOMMENDATION: Level 3: Individuals who meet these criteria and are considering observation should be counseled that there is a high probability (>75%-100%) of hearing preservation at 2 yr, moderately high probability (>50%-75%) of hearing preservation at 5 yr, and moderately low probability (>25%-50%) of hearing preservation at 10 yr.

RECOMMENDATION: Level 3: Individuals who meet these criteria and are considering stereotactic radiosurgery should be counseled that there is a high probability (>75%-100%) of hearing preservation at 2 yr, and moderately high probability (>50%-75%) of hearing preservation at 5 yr. Insufficient data were available to determine the probability of hearing preservation at 10 yr for this population subset.

RECOMMENDATION: Level 3: Individuals who meet these criteria and are considering observation should be counseled regarding probability of successful hearing preservation based on the following prognostic data: the most consistent prognostic features associated with maintenance of serviceable hearing are good preoperative word recognition and/or pure tone thresholds with variable cut-points reported, as well as nongrowth of the tumor. Tumor size at the time of diagnosis, age, and sex do not predict future development of nonserviceable hearing during observation.

Imaging

Initial Preoperative Evaluation

RECOMMENDATION: Level 3: Imaging used to detect VS should use high-resolution T2-weighted and contrast-enhanced T1-weighted MRI.

RECOMMENDATION: Level 3: Standard T1, T2, fluid attenuated inversion recovery, and diffusion weighted imaging MR sequences obtained in axial, coronal, and sagittal plane may be used for detection of VS.

Preoperative Surveillance

RECOMMENDATION: Level 3: Preoperative surveillance for growth of a vestibular schwannoma should be followed with either contrast-enhanced 3-dimensional (3-D) T1 magnetization prepared rapid acquisition gradient echo (MPRAGE) or high-resolution T2 (including constructive interference in steady state [CISS] or fast imaging employing steady-state acquisition [FIESTA] sequences) MRI.

Postoperative Evaluation

RECOMMENDATION: Level 2: Postoperative evaluation should be performed with postcontrast 3-D T1 MPRAGE, with nodular enhancement considered suspicious for recurrence.

RECOMMENDATION: Level 3: T2-weighted MRI may be used to augment visualization of the facial nerve course as part of preoperative evaluation.

RECOMMENDATION: Level 3: MRIs should be obtained annually for 5 yr, with interval lengthening thereafter with tumor stability.

RECOMMENDATION: Level 3: Adults with cystic VS should be Q2 counseled that their tumors may more often be associated with rapid growth, lower rates of complete resection, and facial nerve outcomes that may be inferior in the immediate postoperative period but similar to noncystic schwannomas over time.

RECOMMENDATION: Level 3: The degree of lateral internal auditory canal involvement by tumor adversely affects facial nerve and hearing outcomes and should be emphasized when interpreting imaging for preoperative planning.

RECOMMENDATION: Level 3: In general, VS associated with NF2 should be imaged (similar to sporadic schwannomas) with the following caveats:

1. More frequent imaging may be adopted in NF2 patients because of a more variable growth rate for VS, and annual imaging may ensue once the growth rate is established.
2. In NF2 patients with bilateral VS, growth rate of a VS may increase after resection of the contralateral tumor, and therefore, more frequent imaging may be indicated, based on the nonoperated tumor's historical rate of growth.
3. Careful consideration should be given to whether contrast is necessary in follow-up studies or if high-resolution T2 (including CISS or FIESTA-type sequences) MRI may adequately characterize changes in lesion size instead.

RECOMMENDATION: Level 3: For patients receiving gross total resection, a postoperative MRI may be considered to document the surgical impression and may occur as late as 1 yr after surgery. For patients not receiving gross total resection, more frequent surveillance scans are suggested; annual MRI scans

may be reasonable for 5 yr. Imaging follow-up should be adjusted accordingly for continued surveillance if any change in nodular enhancement is demonstrated.

Surgery

RECOMMENDATION: There is insufficient evidence to support the superiority of either the middle fossa (MF) or the retrosigmoid (RS) approach for complete VS resection and FN preservation when serviceable hearing is present.

RECOMMENDATION: There is insufficient evidence to support the superiority of either the RS or the TL approach for complete VS resection and FN preservation when serviceable hearing is not present.

RECOMMENDATION: Level 3: Patients with larger VS tumor size should be counseled about the greater than average risk of loss of serviceable hearing.

RECOMMENDATION: There are insufficient data to support a firm recommendation that surgery be the primary treatment for this subclass of VSs.

RECOMMENDATION: Level 3: Hearing preservation surgery via the MF or the RS approach may be attempted in patients with small tumor size (<1.5 cm) and good preoperative hearing.

RECOMMENDATION: There is insufficient evidence that surgical resection should be the initial treatment in patients with NF2.

RECOMMENDATION: There is insufficient evidence to support stating that a multidisciplinary team, usually consisting of a neurosurgeon and a neurotologist, provides superior outcomes compared to either subspecialist working alone.

RECOMMENDATION: There is insufficient evidence to support subtotal resection (STR) followed by SRS provides comparable hearing and FN preservation to patients who undergo a complete surgical resection.

RECOMMENDATION: There is insufficient evidence to support either surgical resection or SRS for treatment of preoperative balance problems.

RECOMMENDATION: Level 3: Surgical resection of VSs may be used to better relieve symptoms of trigeminal neuralgia than SRS.

RECOMMENDATION: Level 3: If microsurgical resection is necessary after SRS, it is recommended that patients be counseled that there is an increased likelihood of an STR and decreased FN function.

Intraoperative Cranial Nerve Monitoring

Facial Nerve Monitoring

RECOMMENDATION: Level 3: It is recommended that intraoperative facial nerve monitoring be routinely utilized during VS surgery to improve long-term facial nerve function.

RECOMMENDATION: Level 3: Intraoperative facial nerve can be used to accurately predict favorable long-term facial nerve function after VS surgery. Specifically, the presence of favorable testing reliably portends a good long-term facial nerve

outcome. However, the absence of favorable testing in the setting of an anatomically intact facial nerve does not reliably predict poor long-term function and therefore cannot be used to direct decision-making regarding the need for early reinnervation procedures.

RECOMMENDATION: Level 3: Poor intraoperative EMG electrical response of the facial nerve should not be used as a reliable predictor of poor long-term facial nerve function.

Cochlear Nerve Monitoring

RECOMMENDATION: Level 3: Intraoperative eighth cranial nerve monitoring should be used during VS surgery when hearing preservation is attempted.

RECOMMENDATION: Level 3: There is insufficient evidence to make a definitive recommendation.

Pathology

RECOMMENDATION: No recommendations can be made due to a lack of adequate data.

Radiosurgery and Radiation Therapy

Radiosurgery vs Observation

RECOMMENDATION: Level 3: If tinnitus is not observed at presentation, it is recommended that intracanalicular VS and small tumors (<2 cm) without tinnitus be observed as observation does not have a negative impact on tumor growth or hearing preservation compared to treatment.

Radiosurgery Technology

RECOMMENDATION: There are no studies that compare 2 or all 3 modalities. Thus, recommendations on outcome based on modality cannot be made.

Radiosurgery Technique

RECOMMENDATION: Level 3: As there is no difference in radiographic control using different doses, it is recommended that for single fraction SRS doses, <13 Gy be used to facilitate hearing preservation and minimize new onset or worsening of preexisting cranial nerve deficits.

RECOMMENDATION: As there is no difference in radiographic control and clinical outcome using single or multiple fractions, no recommendations can be given.

Radiographic Follow-up, Retreatment, and Tumorigenesis After Radiosurgery

RECOMMENDATION: Level 3: Follow-up imaging should be obtained at intervals after SRS based on clinical indications, a patient's personal circumstances, or institutional protocols.

Long-term follow-up with serial magnetic resonance imaging to evaluate for recurrence is recommended. No recommendations can be given regarding the interval of these studies.

RECOMMENDATION: Level 3: When there has been progression of tumor after SRS, SRS can be safely and effectively performed as a retreatment.

RECOMMENDATION: Level 3: Patients should be informed that there is minimal risk of malignant transformation of VS after SRS.

Neurofibromatosis Type 2

RECOMMENDATION: Level 3: Radiosurgery is a treatment option for patients with neurofibromatosis type 2 whose VS are enlarging and/or causing hearing loss.

Emerging Therapies

Medical Therapy

RECOMMENDATIONS: Level 3: It is recommended that bevacizumab be administered in order to radiographically reduce the size or prolong tumor stability in patients with NF2 without surgical options.

Level 3: It is recommended that bevacizumab be administered to improve hearing or prolong time to hearing loss in patients with NF2 without surgical options.

RECOMMENDATIONS: Level 3: Lapatinib may be considered for use in reducing VS size and improvement in hearing in NF2.

Level 3: Erlotinib is not recommended for use in reducing VS size or improvement in hearing in patients with NF2.

Level 3: Everolimus is not recommended for use in reducing VS size or improvement in hearing in NF2.

RECOMMENDATION: Level 3: It is recommended that aspirin administration may be considered for use in patients undergoing observation of their VS.

RECOMMENDATION: Level 3: Perioperative treatment with nimodipine (or with the addition of hydroxyethyl starch) should be considered to improve postoperative facial nerve outcomes and may improve hearing outcomes.

Prehabilitation

RECOMMENDATIONS: Level 3: Preoperative vestibular rehabilitation is recommended to aid in postoperative mobility after VS surgery.

Level 3: Preoperative gentamicin ablation of the vestibular apparatus should be considered to improve postoperative mobility after VS surgery.

Surgical Therapy

RECOMMENDATION: Level 3: Endoscopic assistance is a surgical technique that the surgeon may choose to use in order to aid in visualization.

CONCLUSION

This series of guidelines was constructed to assess the most current and clinically relevant evidence for management of VS in order to set a benchmark while also highlighting important key areas for future research. These recommendations are described in the 8 other articles generated from this effort.¹⁻⁸

Disclosure

These evidence-based clinical practice guidelines were funded exclusively by the Congress of Neurological Surgeons and the Tumor Section of the Congress of Neurological Surgeons and the American Association of Neurological Surgeons, which received no funding from outside commercial sources to support the development of this document.

Conflict of Interest

The Vestibular Schwannoma Guidelines Task Force members were required to report all possible COIs prior to beginning work on the guideline, using the COI disclosure form of the AANS/CNS Joint Guidelines Committee, including potential COIs that are unrelated to the topic of the guideline. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination. The CNS Guidelines Committee and Guideline Task Force Chair are given latitude to approve nominations of Task Force members with possible conflicts and address this by restricting the writing and reviewing privileges of that person to topics unrelated to the possible COIs. The conflict of interest findings are provided in detail in the full-text introduction and methods manuscript (https://www.cns.org/guidelines/guidelines-management-patients-vestibular-schwannoma/chapter_1).

Disclaimer of Liability

This clinical systematic review and evidence-based guideline was developed by a multidisciplinary physician volunteer task force and serves as an educational tool designed to provide an accurate review of the subject matter covered. These guidelines are disseminated with the understanding that the recommendations by the authors and consultants who have collaborated in their development are not meant to replace the individualized care and treatment advice from a patient's physician(s). If medical advice or assistance is required, the services of a competent physician should be sought. The proposals contained in these guidelines may not be suitable for use in all circumstances. The choice to implement any particular recommendation contained in these guidelines must be made by a managing physician in light of the situation in each particular patient and on the basis of existing resources.

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