

CONGRESS OF NEUROLOGICAL SURGEONS SYSTEMATIC REVIEW AND EVIDENCE-BASED GUIDELINES UPDATE FOR THE ROLE OF INTRAOPERATIVE CRANIAL NERVE MONITORING IN THE MANAGEMENT OF PATIENTS WITH VESTIBULAR SCHWANNOMAS

Sponsored by: Congress of Neurological Surgeons (CNS) and the Section on Tumors

Endorsement: Reviewed for evidence-based integrity and endorsed by the American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS)

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Keywords: vestibular schwannoma, acoustic neuroma, cranial nerve monitoring, facial nerve monitoring, intraoperative auditory brainstem response, functional preservation,

Running Title: *Cranial Nerve Monitoring in Vestibular Schwannoma Surgery*

Abbreviations:

ABR	Auditory brainstem response
BMI	Body mass index
BR	Blink reflex
CN	Cranial nerve

CNAP	Cochlear nerve action potential
EMG	Electromyography
FMEP	Facial motor evoked potential
FN	Facial nerve
HB	House-Brackmann
IONM	Intraoperative neuromonitoring
PICO	Population, Intervention, Comparison, Outcome
NF2	Neurofibromatosis type 2-related schwannomatosis
VS	Vestibular schwannoma
WRS	Word recognition score

No part of this manuscript has been published or submitted for publication elsewhere.

ABSTRACT

Background

Intraoperative neuromonitoring (IONM) has become vital in the management of vestibular schwannoma (VS) with the paradigm shift from tumor eradication to functional preservation. Several facial nerve (FN) monitoring strategies have been explored over the last few decades ranging from free-running electromyography (EMG), direct nerve stimulation, continuous nerve stimulation, facial motor evoked potentials (FMEP), blink reflex (BR), and others. Hearing preservation surgery is guided primarily by far-field auditory brainstem response (ABR) and real-time cochlear nerve action potentials (CNAP). Given the heterogeneity in tumor and patient factors, it remains very difficult to accurately predict FN outcomes, regardless of monitoring strategy.

Objective

Critically appraise literature regarding IONM during VS surgery and update the previous evidence-based clinical practice guideline.

Methods

Systematic review of the literature, incorporating articles from March 2015 to May 2022. Literature published prior to 2015 that would have been included in the prior CNS guideline was not searched again in this update. In contrast to the previous CNS guideline published in 2018, the key questions are presented in the PICO format (P: population, I : intervention, C: comparison, O: outcome).

Results

FN monitoring provides better functional outcomes compared to anatomical dissection alone and may guide extent of tumor resection. While FMEP s and free-running EMG can provide continuous

noninvasive FN monitoring, there are insufficient data to determine which is more strongly correlated with facial function outcome. Both electrophysiologic data and tumor size are correlated with facial function outcome. The ideal hearing monitoring strategy remains unclear as there are insufficient data comparing CNAPs to far-field ABR. All studies were graded as Class III evidence.

Conclusion

IONM should be used in all VS cases. While the optimal FN and hearing monitoring strategy remains elusive, available data support the use of a combination of strategies, including preoperative tumor size, to maximize sensitivity and specificity. There remains a significant need for high-quality comparative studies to determine which intraoperative monitoring scheme can provide intraoperative guidance and predict postoperative outcome.

RECOMMENDATIONS

FN Monitoring

Updated Questions and Recommendations

Patient Population: In patients undergoing microsurgical resection of sporadic or NF2-associated VS:

Question 1: Does the use of intraoperative FN monitoring provide superior long-term FN functional outcomes compared to anatomic dissection alone?

Recommendation: Level III: Intraoperative FN monitoring provides superior long-term FN functional outcomes compared to anatomic dissection alone.

Question 2: Is data from intraoperative FN monitoring superior to clinical and imaging information in predicting short- and long-term FN functional outcomes?

Recommendation: Level III: Electrophysiologic measures are more predictive of long-term FN functional outcomes than clinical information alone. There is insufficient evidence to determine whether electrophysiologic data is superior to clinical information in predicting short-term FN functional outcomes.

New Question and Recommendation

Question 3: Is the use of transcranial FN motor evoked potentials or BR testing superior to free-running EMG and direct FN stimulation in predicting short- and/or long-term FN functional outcomes?

Recommendation(s): There is insufficient evidence to determine whether transcranial FMEP or BR is superior to EMG-based monitoring schema in predicting FN functional outcomes.

Notable Updates to 2018 Guideline: This represents a new research question that was not addressed in the previous CNS guideline.

Cochlear Nerve Monitoring

Updated Question and Unchanged Recommendation

Question 4: Is intraoperative cochlear nerve monitoring superior to ABR monitoring in predicting short- and long-term hearing preservation outcomes?

Recommendation(s): *There is insufficient data to determine whether CNAP is superior to far-field ABR in monitoring hearing function in hearing preservation surgery for VS.*

New Question and Recommendation

Question 5: Does the monitoring of adjacent cranial nerves (cranial nerves [CN] V, IX, X, XI, and XII) provide for better preservation of their function than carrying out surgery without these CN s being monitored?

Recommendation(s): *There is insufficient evidence to determine whether monitoring of other regional CN s affects functional preservation.*

INTRODUCTION

Rationale

In the modern era of VS treatment, FN preservation, maintenance of serviceable hearing, and tumor control are the highest priorities among patients and providers alike. While these have always been considered the “goals” of treatment, falling short in one dimension was considered acceptable because of the lack of reasonable management alternatives. Early radiosurgical series reported high rates of facial palsy and hearing loss that rendered it less attractive when compared to microsurgery, which offered definitive cure. Observation was only offered to patients with very small tumors, and little was known about the rate of hearing decline over the course of observation. At present day, patients with small- to medium-sized tumors (generally considered < 1.5 cm in maximum dimension) routinely compare the risks of microsurgical treatment with the probability of FN and hearing functional preservation with nonsurgical treatment. It is well known that the risk of FN paralysis during observation is negligible. In an intention-to-treat comparative study between 167 observed tumors and 121 equivalent size surgically managed tumors, 100% of the observed cohort had HB grade I facial function at long-term (mean 62 months) follow up¹. The rates of hearing preservation over the course of observation for patients with serviceable hearing at diagnosis have also placed the risk of treatment-related hearing loss under scrutiny. Based on a recent systematic review by Khandavala et al comprising over 3,600 patients with observed VS, the estimated rate of serviceable hearing at 5 years is 60%². A more detailed summary of hearing and

FN outcomes with observation, microsurgery, and radiosurgery can be found in other areas of this Guidelines Update.

What defines tumor “management” has also evolved over time. The value of complete tumor removal is no longer high enough to warrant compromise of neurologic function. Patients are routinely willing to accept less-than-gross total tumor removal if it results in a better FN outcome or long-term hearing preservation, particularly given the knowledge that 1) the tumor remnant often does not warrant additional treatment and 2) modern radiosurgery achieves high rates of tumor control in the setting of prior sub-total resection.

These factors have changed the treatment conversation to one where patients carefully select the treatment strategy that delivers the trifecta of tumor control without the need for additional treatment, hearing preservation if hearing is serviceable at the time of diagnosis, and normal or near-normal FN function. Surgeons are therefore charged with the task of refining microsurgical techniques to match or exceed what conservative management can offer, on the basis that 1) tumor removal mitigates the risk of eventual treatment if the tumor grows and 2) tumor removal halts the progression of hearing loss from the tumor itself (regardless of growth)^{3,4}.

Objectives

This update to the “Congress of Neurological Surgeons Systematic Review and Evidence-Based Guideline on Intraoperative Cranial Nerve Monitoring in Vestibular Schwannoma Surgery” published in 2018⁵ aims to characterize the current state of intraoperative monitoring strategies. The goal is not to recapitulate the prior comprehensive guideline statement but rather to determine whether emerging data from 2015-2022 has shed light on the predictive ability of electrophysiologic measures with regard to FN and hearing outcomes among patients undergoing microsurgery for sporadic or NF2 associated VS.

METHODOLOGY

The co-authors of this guidelines update convened to determine the most salient questions on the topic of IONM in VS surgery. Through objective evaluation of the evidence and transparency in the process of making recommendations, this evidence-based clinical practice guideline was developed for the diagnosis and treatment of adult patients with VSs. These guidelines are developed for educational purposes to assist practitioners in their clinical decision-making processes. Additional information about the methods utilized in this systematic review is provided below.

Additional details of the systematic review are provided below and within the introduction and methodology chapter of the guideline (add link).

Literature Search

The members of the task force identified key search terms pertaining to intraoperative monitoring for VS. Databases included Ovid Medline and Embase. CN s of interest included the trigeminal, facial, vestibulocochlear, glossopharyngeal, vagus, accessory, and hypoglossal, and were thus included in the search strategy. Terms pertinent to ABR or cochlear nerve monitoring were used for the vestibulocochlear nerve. Only articles available in the English language were included for review. The full search strategy for each database is outlined in Appendix I.

Inclusion/Exclusion Criteria

Two co-authors were responsible for the independent review of abstracts and subsequently full text data for each article deemed relevant to the PICO questions under examination. Articles were retrieved and included only if they met specific inclusion/exclusion criteria. Inconsistencies were re-reviewed, and disagreements were resolved by consensus. To reduce bias, these criteria were specified before conducting the literature searches.

Articles that do not meet the following criteria were, for the purposes of this evidence-based clinical practice guideline, excluded.

To be included as evidence in the guideline, an article had to be a report of a study that:

- *Investigated patients with VSs who underwent microsurgery*
- *Was related to CN monitoring*
- *Was a full article report of a clinical study*
- *Appeared in a peer-reviewed publication or a registry report*
- *Enrolled a minimum of 10 patients*
- *Was of humans*
- *Was published between 1/1/2015 and 5/20/2022*
- *Quantitatively presented results*

Articles were excluded if it was determined that the article:

- *Was a case report or expert opinion paper*
- *Was a technique paper only*
- *Was a heterogenous group of tumor types where VS data could not be reliably abstracted*

- *Was a systematic review, meta-analysis, or guideline developed by others*

Systematic reviews or meta-analyses conducted by others, or guidelines developed by others were not included as evidence to support this review due to the differences in article inclusion/exclusion criteria specified compared to the criteria specified by the Guidelines Task Force.

Assessment for Risk of Bias

Articles on prognostication of CN function are affected by several potential sources of bias. Some sources of bias were particularly relevant to CN outcome studies. Bias due to lack or loss of information over time and attrition bias is relevant due to 1) varied follow up schedules, 2) patients who traveled to a center for care but conduct follow up at a local facility, and 3) the notion that individuals with absent hearing or FN function or completely normal hearing or FN function may not elect to undergo tests or evaluations as they are perceived unnecessary. Given that most articles that comprise this guidelines update are retrospective in design, there remains the risk of publication bias, bias of change in methods over time, or ascertainment bias. In addition, the data comprising the majority of included studies have variability due to the accuracy of the electronic medical record and subjectivity in assessing FN outcome (e.g. using the House-Brackmann grading scale versus alternative functional scales).

Rating Quality of Evidence

Evidence was rated in accordance with the previously published guideline on IONM in VS surgery. Specifically, a paradigm for prognostication was used with evidence classified in three classes. Additional information regarding the hierarchy classification of evidence can be located here: <https://www.cns.org/guidelines/guideline-development-methodology>.

In order to evaluate papers addressing *prognosis*, five technical criteria are applied:

- Was a well-defined representative sample of patients assembled at a common (usually early) point in the course of their disease?
- Was patient follow-up sufficiently long and complete?
- Were objective outcome criteria applied in a “blinded” fashion?
- If subgroups with different prognoses were identified, was there adjustment for important prognostic factors?

- If specific prognostic factors were identified, was there validation in an independent “test set” group of patients?

If all five of these criteria are satisfied, the evidence is classified as Class I. If four out of five are satisfied, the evidence is Class II, and if less than 4 are satisfied, it is Class III. Class I level translates to level I recommendations, class II evidence translates to level II recommendations, and class III evidence translates to level III recommendations.

Revision Plans

In accordance with the National Academy of Medicine’s standards for developing clinical practice guidelines, the task force will monitor related publications following the release of this document and will revise the entire document and/or specific sections “if new evidence shows that a recommended intervention causes previously unknown substantial harm; that a new intervention is significantly superior to a previously recommended intervention from an efficacy or harms perspective; or that a recommendation can be applied to new populations.”⁶ In addition, the task force will confirm within five years from the date of publication that the content reflects current clinical practice and the available technologies for the evaluation and treatment for patients with VS.

SUMMARY OF THE PREVIOUS GUIDELINE RECOMMENDATIONS:

FN Monitoring

Question 1: Does intraoperative FN monitoring during VS surgery lead to better long-term FN function?

Target population: This recommendation applies to adult patients undergoing VS surgery regardless of tumor characteristics.

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

Question 2: Can intraoperative FN monitoring be used to accurately predict favorable long-term FN function after VS surgery?

Target population: This recommendation applies to adult patients undergoing VS surgery.

Recommendation: Level 3: Intraoperative FN monitoring can be used to accurately predict favorable long-term FN function after VS surgery. Specifically, the presence of favorable testing reliably portends a good long-term FN outcome. However, the absence of favorable testing in the setting of an anatomically intact FN does not reliably predict poor long-term function and therefore cannot be used to direct decision-making regarding need for early reinnervation procedures.

Question 3: Does an anatomically intact FN with poor electromyogram electrical responses during intraoperative testing reliably predict poor long-term FN function?

Target population: This recommendation applies to adult patients undergoing VS surgery.

Recommendation: *Level 3*: Poor intraoperative electromyogram electrical response of the FN should not be used as a reliable predictor of poor long-term FN function.

Cochlear Nerve Monitoring

Question 4: Should intraoperative eighth CN monitoring be used during VS surgery?

Target population: This recommendation applies to adult patients undergoing VS surgery with measurable preoperative hearing levels and tumors smaller than 1.5 cm.

Recommendation: *Level 3*: Intraoperative eighth CN monitoring should be used during VS surgery when hearing preservation is attempted.

Question 5: Is direct monitoring of the eighth CN superior to the use of far-field auditory brain stem responses?

Target population: This recommendation applies to adult patients undergoing VS surgery with measurable preoperative hearing levels and tumors smaller than 1.5 cm.

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

The above questions and recommendations served as the basis for this guidelines update. There were two primary limitations worth mentioning. First, the questions posed were not in a PICO format and thus were not designed to compare groups, with the exception of question 5. Therefore wording for the questions was updated. Second, this broader guideline statement was intended to answer more fundamental questions, such as whether or not intraoperative FN or eighth nerve monitoring should be used during VS surgery.

Since the publication of this foundational guideline⁵, there have been several technical developments in IONM. This Guidelines Update serves to critically review the literature surrounding these novel monitoring strategies and their predictive power in characterizing VS surgery outcomes.

RESULTS

The literature search yielded 222 abstracts. The authors reviewed all abstracts obtained from the literature search and identified those meeting criteria for full text review and extraction, addressing the clinical questions, in accordance with the literature search strategy. The task force members identified the evidence available to answer the targeted clinical questions.

The task force selected 49 full-text articles for full text review. Of these, 15 were included for evidence tables and subject to systematic review⁷⁻²⁰. This is depicted graphically in the PRISMA diagram (Figure 1).

Question 1: Does the use of intraoperative FN monitoring provide superior long-term FN functional outcomes compared to anatomic dissection alone?

Recommendation: Level III: Intraoperative FN monitoring provides superior long-term FN functional outcomes compared to anatomic dissection alone.

Of the 49 articles that resulted from abstract review, 8 were marked as pertinent to this question. To be included in this section, the study had to fall into one of two categories. The first category was strictly those articles that provided objective FN outcome data (i.e. postoperative HB score) in at least one cohort in which intraoperative FN monitoring was employed and at least one cohort where only anatomical dissection was used without continuous intraoperative monitoring. The second category was more permissive and included articles that examined whether FN outcome was related to the electrophysiologic parameter studied. While the second category does not directly answer the question, the authors felt that a conclusion regarding the value of neuromonitoring for FN outcomes could still be drawn from the data. After final review, 5 studies were included for analysis, all of which were graded as Class III evidence. Data extracted from each article included number of patients, study design, surgical approach, which electrophysiologic parameters were recorded, the time at which FN function was evaluated, and what grading system was used.

Given that intraoperative FN monitoring has become routine clinical practice for lateral skull base surgery, there is a relative paucity of articles comparing FN outcomes between monitored and unmonitored groups. In 2017, Xu et al²⁰ reported the results of a retrospective single institution study of 53 patients who underwent microsurgical resection of large VS (mean tumor size of approximately 40 mm) via retrosigmoid approach. Patients were separated into a monitored group and control group of roughly equal size. The authors found that at short, intermediate, and long-term follow up, the monitored group has statistically significant better FN function. Rates of total or subtotal resection were similar.²⁰ These findings were corroborated in a retrospective review of 62 patients published by Hou et al in 2018¹³. In that study, patients were divided randomly into a monitored group (observation group), and one that had anatomical dissection only (control group). A potential limitation of the study was the relatively low rate of anatomic preservation of the FN in both groups (78.8% and 51.7% in the observation and control groups, respectively), and no specific documentation regarding tumor size. In 2016, Taddei¹⁸ and colleagues published a series of 51 consecutive patients who had microsurgical removal of a VS at a single institution. Two groups were described: group 1 only had a “facial stimulator” but no continuous

monitoring while group 2 had continuous monitoring and the use of a stimulator. The authors reported a higher rate of FN preservation and HB grade 1 or 2 facial function in the continuously monitored group. A potential limitation is that up to 25% of patients in each group had some degree of facial paralysis (HB grade 2 or 3) prior to surgery, which may limit generalizability, given how rare preoperative facial paralysis is in VS patients¹⁸. In spite of the limitations noted, the data from these studies will likely not be reproduced in future publications given the essentially universal implementation of continuous neuromonitoring at high-volume skull base centers.

As an adjunct to the data analyzed above, the authors included two additional articles that provide data to estimate the efficacy of FN monitoring in improving FN outcomes. In 2014, Ashram et al²¹ reported the results of a prospective single institution study of 42 patients who underwent VS resection via retrosigmoid or translabyrinthine approaches. In this report, FN monitoring was conducted using continuous EMG in a 5-channel setup (mentalis, orbicularis oris, nasalis, orbicularis oculi, and frontalis). The results were compared to a hypothetical 2-channel group where the responses from mentalis, nasalis, and frontalis were omitted. The multichannel setup, in particular the inclusion of the mentalis muscle, allowed earlier and more efficient detection of mechanically elicited EMG activity. Notably, increasing EMG activity portended a poorer intermediate- and long-term FN outcome.²¹ A report by Bernardeschi examined the predictive value of a reduction in response to supramaximal stimulation in cases of VS surgery where the FN was considered especially adherent to the tumor. In that study, dissection was interrupted if 50% or more of the response to supramaximal stimulation at the brainstem was lost. While this did guide the decision to terminate dissection, there was no significant difference in FN outcome when comparing patients meeting or not meeting the 50% criterion.⁷

Synthesis: Electrophysiologic monitoring of the FN provides superior FN preservation compared to anatomic dissection alone. While less relevant for smaller tumors where the FN tends not to be splayed or displaced, it is most important for larger VS. Focusing on EMG monitoring only, continuous monitoring where attention is paid to non-reassuring EMG activity during dissection has the potential to improve FN outcomes. It remains unclear whether the response to supramaximal stimulation is predictive of FN outcome. The guideline recommendation is consistent with the prior recommendation for the use of FN monitoring, but specifies that the literature supports its superiority over anatomic dissection alone. Future studies assessing the sensitivity and specificity of various EMG findings in a large prospective cohort of patients undergoing VS surgery would be valuable in determining the predictive value of each strategy. A Level III recommendation is made as all articles constituted class III data.

Question 2: Is data from intraoperative FN monitoring superior to clinical and imaging information in predicting short- and long-term FN functional outcomes?

Recommendation: Level III: Electrophysiologic measures are more predictive of long-term FN functional outcomes than clinical information alone. There is insufficient evidence to determine whether electrophysiologic data is superior to clinical information in predicting short-term FN functional outcomes.

Of the 49 articles that resulted from abstract review, 8 were marked as pertinent to this question. To be included in this section, the study had to report short- and long-term FN outcomes following VS surgery in which the predictive power of electrophysiologic monitoring was compared to that of clinical information such as patient or tumor characteristics. After final review, 4 studies were included for analysis, all of which were graded as Class III evidence. Data extracted from each article included number of patients, study design, surgical approach, what patient or tumor data were recorded and analyzed, which electrophysiologic parameters were recorded, the time at which FN function was evaluated, and what grading system was used.

While it remains unclear whether patient demographics or surgical approach reliably correlate with FN functional outcome, extrameatal tumor size remains to be the most commonly utilized preoperative predictor in patient counseling. This was demonstrated in a study by Bloch et al of 624 patients who underwent surgery for VS, where pre-operative tumor size was the only statistically significant predictor of FN functional outcome.²² However, there remains significant heterogeneity in FN-tumor adherence, tumor consistency, and FN position that result in variable FN outcomes for a given tumor size. As these characteristics often lie on a spectrum and are difficult to categorize, electrophysiologic measures are often the only means of quantifying the surgical trauma to the FN resulting from dissection.

Liu et al in 2015 reported a series of 106 patients who underwent microsurgical removal of large VS via retrosigmoid approach. Monitoring schema included EMG and FMEP and the predictive value of tumor size, train time (a form of non-reassuring EMG activity), FMEP ratio, and maximal response amplitude ratio were analyzed. Both FMEP ratio and tumor size were highly correlated with immediate and late FN functional outcome. Notably, the level of significance was greater for FMEP ratio ($p < 0.001$) compared to tumor size ($p < 0.01$).¹⁵ In 2017, Hong et al performed a univariable analysis of individual predictors (tumor characteristics, patient age, surgical approach characteristics, and whether or not intraoperative electrophysiologic monitoring was used) and found that both tumor diameter and the use of intraoperative monitoring were correlated with FN functional outcome.¹² However, the results of this study are limited given the lack of multivariable analysis. Ling et al in 2018¹⁴ found that FMEP amplitude ratio was more highly correlated with postoperative FN function ($p < 0.0001$) when compared to maximum

tumor diameter ($p=0.025$). Most recently, Ren et al in 2021¹⁶ performed a large retrospective review of 256 patients who underwent surgery for VS that included a broader range of clinical predictors in the statistical analysis. Small tumor size (<1.5 cm) and lower body mass index (BMI) were associated with better immediate postoperative FN outcomes. However, only achieving gross-total resection and > 100 microvolt EMG responses intraoperatively were correlated with better long-term FN function on multivariate analysis. These results suggest that those patients who had complete tumor resection likely harbored tumors with less FN-tumor adherence, perhaps indicated by higher amplitude EMG responses. The predictive value of this EMG criterion should not be used in isolation, however. According to a study by Neff et al in 2005, minimum stimulus intensity in mA and response amplitude in microvolts have the highest predictive value when used in concert than if either is used in isolation, even when using a higher threshold for response amplitude²³.

Synthesis: Electrophysiologic measures, specifically FMEP amplitude ratio and final EMG response amplitude, may be more predictive of long-term FN functional outcome when compared to clinical information alone. While not the focus of this question, tumor size appears to remain the clinical predictor of greatest importance in predicting FN functional outcome. It remains unclear whether electrophysiologic responses are superior to clinical information in predicting immediate postoperative FN functional outcomes. This difference may be related to less severe FN injury (i.e. Sunderland grade 1 or 2 injuries) exacerbated by patient or surgical factors that resolves to some degree over time. A notable limitation is the time at which short-term FN function is assessed. In the study by Ren et al¹⁶, for example, immediate FN function was graded within 24 hours of surgery. In contrast, Liu et al measured immediate FN function at 3-7 days postoperatively. It is well known that patients frequently experience a decline in FN function over the first few days following VS surgery that is thought to be related primarily to neural edema or devascularization. In comparison to the prior guideline on this topic, the updated guideline statements recognize that clinical information can be used to predict FN functional outcomes and addresses the question of whether intraoperative electrophysiologic data is more or less predictive of FN functional outcomes than clinical information alone. Future multi-institutional studies would be valuable in determining reproducibility of the electrophysiologic markers of FN injury given significant heterogeneity in monitoring strategies and timing of FN grading. A Level III recommendation is made as all articles constituted class III data.

Question 3: Is the use of transcranial FN motor evoked potentials or BR testing superior to free-running EMG and direct FN stimulation in predicting short- and/or long-term FN functional outcomes?

Recommendation(s): There is insufficient evidence to determine whether transcranial FMEP or BR is superior to EMG-based monitoring schema in predicting FN functional outcomes.

Of the 49 articles that resulted from full text review, 11 were marked as pertinent to this question. To be included in this section, the study had to report an analysis of FN functional outcome that used FMEP measures and EMG-based measures as outcome predictors. While a direct comparison was not mandatory, at minimum an analysis of which electrophysiologic parameters that were most highly correlated with outcome was required. After final review, 5 studies were included for analysis, all of which were graded as Class III evidence. Data extracted from each article included number of patients, study design, surgical approach, which electrophysiologic parameters were recorded for FMEP and EMG based monitoring schema, the time at which FN function was evaluated, and what grading system was used.

FN motor evoked potentials are responses recorded from facial musculature elicited using transcranial electrical stimulation of the motor cortex. Akin to EMG-based monitoring, there are multiple ways in which FMEP responses can be analyzed and subsequently categorized for surgical guidance. The correlation between FMEP and FN functional outcome has been demonstrated in multiple studies²⁴⁻²⁶. In the study by Liu et al¹⁵ referenced above, an additional analysis comparing FMEP ratio (response at the end of the case to the maximum level at the start of the case), FMEP maximum response amplitude (MRA), and intraoperative A-train time was conducted. The authors concluded that FMEP ratio showed the highest correlation with immediate and late FN function when compared to A-train time and MRA ratio¹⁵. Tawfik et al reported a series of 82 consecutive patients, 20 of whom had FMEP recorded in addition to EMG while 62 had EMG only. There was no significant difference in FN outcome between groups, though FMEP remained highly specific for predicting postoperative FN function¹⁹. The relatively small FMEP cohort and asymmetric cohort size may have limited the ability to resolve differences between groups.

Subsequent work by Frigeni in 2020 analyzed the predictive value of EMG A-train activity, noting a sinusoidal, symmetrical high frequency waveform was considered to be predictive of FN palsy⁹, when compared to preoperative BR testing. On multiple logistic regression analysis, A-train activity, when correctly identified, was more predictive of FN outcome than BR testing, but FMEP was not included in this study⁹. Hendriks et al compared direct nerve stimulation, free running EMG, and FMEP and found that FMEP threshold change of less than 20 mA resulted in a FN outcome better than HB grade 3, but that A-trains were not correlated with FN functional outcome¹¹. Most recently, Greve et al published a retrospective review of 60 consecutive patients who had surgery with FMEP and EMG

monitoring. The authors found that using a specific FMEP-based criterion (see Table 3 for details) was more predictive than A-trains on EMG^{10,27}.

Synthesis: While FMEP-based monitoring can be used to predict FN functional outcome, there is insufficient evidence to determine whether FMEP or BR is superior to EMG-based monitoring strategies. While several groups have reported outcomes with FMEP monitoring, the interpretation of FMEP results remains challenging. Similarly, while EMG A-train activity is considered the most non-reassuring pattern in VS surgery, correctly identifying the specific pattern is not trivial. It is likely that these limitations, in addition to relatively small sample sizes in the reports cited, preclude a determination of superiority of one strategy over the other. As well, little is known about how to employ FMEP findings to inform extent of resection and whether real-time data can be used to guide surgical maneuvers, in the manner that EMG activity is employed. Larger prospective studies at institutions with extensive experience with both monitoring strategies would be vital to compare the two and evaluate ways to incorporate data from both in predicting outcomes. A Level III recommendation is made as all articles constituted class III data.

Question 4: Is intraoperative cochlear nerve monitoring superior to ABR monitoring in predicting short- and long-term hearing preservation outcomes?

Recommendation(s): *There is insufficient data to determine whether CNAP is superior to far-field ABR in monitoring hearing function in hearing preservation surgery for VS.*

Of the 49 articles that resulted from full text review, 21 were marked as pertinent to this question. To be included in this section, the authors must have reported comparison of direct CNAP monitoring and far-field ABR with documented postoperative hearing results. Acceptable hearing testing descriptions included pure tone average/ Word recognition score (WRS) and AAO-HNS hearing class determined from audiometric testing. After final review, only 1 study was included for analysis, and was graded as Class III evidence. Data extracted from the article included number of patients, study design, surgical approach, the method of auditory pathway monitoring, the method of audiometric evaluation and when the audiogram was completed, and what system was used to categorize audiometric results, when applicable.

The article by Sun et al published in 2018¹⁷ included a series of 126 consecutive patients operated at a single institution. All underwent a middle fossa approach for resection of a small VS. The authors concluded that an absent N1 amplitude reached 100% positive predictive value for worsening of hearing class. In contrast, the negative predictive value, suggesting maintenance of preoperative hearing, was 50% NM- Perhaps inserting a statement regarding the inability to use CNAP optimally in cases of large VSs would be useful. when the waveform was intact. Intraoperative ABR had similar positive (86%) and

negative (84%) predictive value for changes in postoperative hearing¹⁷. This suggests that, when used in isolation, CNAP is less likely to resolve deleterious downstream effects due to the anatomical position (i.e. proximal 8th nerve) where the recording electrode is placed.

Synthesis: There remains insufficient data at present to determine whether CNAP is superior to far-field ABR in predicting postoperative hearing function during hearing preservation surgery for VS. Given that ABR offers complimentary information to CNAP, it is likely that the ideal method of monitoring would combine the two strategies. Direct CNAP may also be difficult or impossible in larger tumors due to tumor involvement of the proximal 8th nerve at the root entry zone. The recommendation of the present update is consistent with the previous guideline. There is a significant need for more comparative studies in this area. Considering the variability in surgical approach for hearing preservation (i.e. where some institutions strongly prefer middle fossa to retrosigmoid), a multi-institutional effort would be advisable.

Question 5: Does the monitoring of adjacent CN s (CN s V, IX, X, XI, and XII) provide for better preservation of their function than carrying out surgery without these CN s being monitored?

Recommendation(s): *There is insufficient evidence to determine whether monitoring of other regional CN s affects functional preservation.*

Of the 49 articles that resulted from full text review, 1 was pertinent to this question. To be included in this section, the authors must have showed a comparison of regional CN outcomes when EMG monitoring was used for CN s V, IX, X, XI, and XII and when it was not. Unfortunately, zero articles matched this criterion. The one article that resulted from the literature search, authored by Romagna et al²⁸, summarized their experience with monitoring of the vagus nerve during CPA tumor surgery. The authors concluded that endotracheal tube surface electrodes could be reliably used to indicate CN X palsy. There was no comparison to a group without monitoring, nor were other regional CN s included.

Synthesis: No recommendation can be made as to whether monitoring of regional CN s affects functional preservation in VS surgery. Though these nerves are not directly involved by VS, they are at risk during posterior fossa surgical approaches and CPA tumor dissection. Future studies are needed to determine 1) which regional CN s can be reliably monitored during VS surgery, 2) whether continuous monitoring prevents injury, and 3) what is the additional cost of monitoring “uninvolved” CN s.

DISCUSSION

These guidelines support the routine use of IONM in all VS cases for monitoring the integrity of regional CN s. The growing body of literature on FN monitoring and outcome prediction has increased our

understanding of prognostication and the relative weight of intraoperative monitoring data and preoperative tumor or patient characteristics. The optimal FN monitoring strategy likely includes a combination of free-running EMG (with active monitoring for A-trains and other potentially non-reassuring waveforms) and continuous evoked potential monitoring schema such as FMEP. While chiefly determined by tumor size and position within the internal auditory canal and cerebellopontine angle, predicting hearing preservation using intraoperative measures remains challenging. While ABR can predict preservation of hearing with near complete certainty when the waveform is unchanged or improved throughout the case, waveform averaging adds a time delay that limits its ability to be used as a dissection guide. Real-time CNAP monitoring holds promise but remains technically challenging with no widely available atraumatic electrodes to deliver the stimulus. It is unclear whether lower CN monitoring is required during VS surgery. Since monitoring requires little additional instrumentation, the authors would consider its use during surgery for very large VS or in a reoperation situation where the nerves may not separate easily from the nearby cerebellum or arachnoid, for instance.

KEY ISSUES FOR FUTURE RESEARCH AND CONCLUSIONS

As it is well established that traditional EMG and ABR-based monitoring strategies are “here to stay,” the authors recommend that research efforts focus on novel monitoring strategies. Utilizing a combination of preoperative tests such as BR or ABR and complimentary intraoperative measurements may provide better prognostic information when compared to single intraoperative measures such as EMG response NM-amplitude or stimulus threshold. Multi-institutional collaborations with consistent monitoring protocols across sites would likely sufficient data to power a comparative study. Ideally, a prospective study where patients are examined for FN function or hearing function at set time points by blinded observers would be designed to reduce bias and maximize generalizability. Ultimately, the authors acknowledge that this goal will be challenging to achieve given the complexity of electrode placement, monitoring technologies, and interpretation, in combination with variations in surgical technique or approach. It is encouraging that the body of literature on IONM in VS surgery continues to grow in parallel with the advancement of function preservation skull base surgery.

Conflicts of Interest

All Guideline Task Force members were required to disclose all potential COIs prior to beginning work on the guideline, using the COI disclosure form of the AANS/CNS Joint Guidelines Review Committee. The CNS Guidelines Committee and Guideline Task Force Chair reviewed the disclosures and either approved or disapproved the nomination and participation on the task force. The CNS Guidelines Committee and

Guideline Task Force Chair may approve nominations of task force members with possible conflicts and restrict the writing, reviewing, and/or voting privileges of that person to topics that are unrelated to the possible COIs.

Disclosure of Funding

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

Disclaimer of Liability

This clinical systematic review and evidence-based guideline was developed by a physician volunteer task force as an educational tool that reflects the current state of knowledge at the time of completion. Each chapter is designed to provide an accurate review of the subject matter covered. This guideline is 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.

Acknowledgments:

The guidelines task force would like to acknowledge the CNS Guidelines Committee for their contributions throughout the development of the guideline, the AANS/CNS Joint Guidelines Review Committee, as well as the contributions Trish Rehring, MPH, Director for Evidence-Based Practice Initiatives for the CNS, and Janet Waters, MLS, BSN, RN, for assistance with the literature searches. Throughout the review process, the reviewers and authors were blinded from one another. At this time the guidelines task force would like to acknowledge the following individual peer reviewers for their contributions: Patti Raksin, Tjoumakaris, Andrew Carlson, Neil Majmundar, Jeff Mullin and Koji Ebersole.

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Appendix I: Literature Searches

Search Strategies

OID MEDLINE

- 1 Facial Nerve/ and (monitor* or neuromonitor* or electromyogra* or event related potential* or event-related potential* or evoked potential* or n1 wave* or n2 wave* or n3 wave* or n4 wave* or p2 wave* or p50 wave* or NERVE STIMULAT*).mp. 1796
- 2 exp Cranial Nerves/ and (monitor* or neuromonitor* or electromyogra* or event related potential* or event-related potential* or evoked potential* or n1 wave* or n2 wave* or n3 wave* or n4 wave* or p2 wave* or p50 wave* or NERVE STIMULAT*).mp.15138

- 3 ((cranial nerve* or facial nerve* or marginal mandibular branch or marginal mandibular nerve* or nerve vii or nerve viis or nerve of wrisberg or nervus faciali or nervus facialis or nervus intermedius or nervus intermedius of wrisberg or wrisberg nerve or wrisberg nervus intermedius) and (MONITOR* or neuromonitor* or electromyogra* or event related potential* or event-related potential* or evoked potential* or n1 wave* or n2 wave* or n3 wave* or n4 wave* or p2 wave* or p50 wave* or NERVE STIMULAT*)).mp. 4569
- 4 (facial nerve/ or cranial nerves/) and exp evoked potentials/ 514
- 5 Cochlear Nerve/ and (MONITOR* or NEUROMONITOR*).mp. 191
- 6 ((acoustic nerve* or auditory nerve* or cochlear nerve*) and (MONITOR* or NEUROMONITOR*)).mp. 430
- 7 Evoked Potentials, Auditory, Brain Stem/ 9163
- 8 (acoustic evoked brain stem potential* or acoustic evoked brainstem potential* or auditory brain stem evoked response* or auditory brain stem response* or auditory brainstem evoked response* or auditory brainstem response* or brain stem auditory evoked potential* or brainstem auditory evoked potential*).ti,ab,kw. 9621
- 9 exp Trigeminal Nerve/ and (MONITOR* or NEUROMONITOR*).mp. 362
- 10 ((nerve v or nerve vs or nervus trigeminus or trigeminal nerve*) and (MONITOR* or NEUROMONITOR*)).mp. 329
- 11 Glossopharyngeal Nerve/ and (monitor* or neuromonitor*).mp. 40
- 12 (glossopharyngeal nerve* and (monitor* or neuromonitor*)).mp. 64
- 13 Vagus Nerve/ and (monitor* or neuromonitor*).mp. 855
- 14 ((nerve x or nerve xs or nervus vagus or pneumogastric nerve or pneumogastric nerves or vagus nerve*) and (monitor* or neuromonitor*)).mp. 1252
- 15 Accessory Nerve/ and (monitor* or neuromonitor*).mp. 24
- 16 ((accessory nerve* or cranial nerve xi or eleventh cranial nerve* or nerve xi or nerve xis or nervus accessorius or spinal accessory nerve*) and (monitor* or neuromonitor*)).mp. 60
- 17 Hypoglossal Nerve/ and (monitor* or neuromonitor*).mp. 81
- 18 ((cranial nerve xii or cranial nerve xiis or hypoglossal nerve* or nerve xii or nerve xiis or nervus hypoglossus or twelfth cranial nerve*) and (monitor* or neuromonitor*)).mp. 128
- 19 (SURGER* or SURGICAL* or OPERATION* or RESECTION* or MICROSURG* or MICRO-SURG* or NEUROSURG* or NEURO-SURG* or INTRAOPERATIV* or INTRA-OPERATIV* or OPERATIV* or PERIOPERATIV* or PERI-OPERATIV*).mp. 3851086
- 20 or/1-18 29702
- 21 19 and 20 6555
- 22 exp Neuroma, Acoustic/8763

- 23 ((vestib* or acoustic) adj3 (neuroma* or neurilemmoma* or neurilemoma* or neurinoma* or tumor* or tumour* or schwannoma*)).mp. 11046
- 24 (acoustic nerve cancer* or acoustic neurofibroma* or acusticus neurinoma* or auditory nerve neurinoma* or ear schwannoma* or angle tumor* or angle tumour* or cerebellopontine angle tumor* or neurinoma of the acoustic nerve or neurosensory deafness* or sensoryneural deafness* or sensory neural deafness*).ti,ab,kw. 1211
- 25 22 or 23 or 24 12489
- 26 limit 25 to english language 10469
- 27 Animals/ not Humans/ 4974929
- 28 26 not 27 10374
- 29 comment/ or editorial/ or letter/ or review/ or systematic review/ 5102112
- 30 28 not 29 8685
- 31 exp adolescent/ or exp child/ or exp infant/ 3849849
- 32 exp Adult/ 7797507
- 33 31 not 32 2052582
- 34 30 not 33 8366
- 35 limit 34 to dt=20150101-20220522 2297
- 36 in vitro techniques/ 387712
- 37 Culture Techniques/ 47809
- 38 Drug Evaluation, Preclinical/ 54481
- 39 Disease Models, Animal/ 383220
- 40 Xenograft Model Antitumor Assays/ 44247
- 41 35 not (36 or 37 or 38 or 39 or 40) 2275
- 42 21 and 41 153

EMBASE.COM

((('facial nerve'/exp OR 'cranial nerve'/exp) AND (monitor*:ti,ab,kw,de OR 'neuro-monitoring':ti,ab,kw,de OR neuromonitor*:ti,ab,kw,de OR electromyogra*:ti,ab,kw,de OR 'event related potential':ti,ab,kw,de OR 'evoked potential':ti,ab,kw,de OR 'n1 wave':ti,ab,kw,de OR 'n2 wave':ti,ab,kw,de OR 'n3 wave':ti,ab,kw,de OR 'n4 wave':ti,ab,kw,de OR 'p2 wave':ti,ab,kw,de OR 'p50 wave':ti,ab,kw,de OR 'nerve stimulation':ti,ab,kw,de) OR (('cranial nerve' OR 'facial nerve' OR 'marginal mandibular branch' OR 'marginal mandibular nerve' OR 'nerve vii' OR 'nerve viis' OR 'nerve of wrisberg' OR 'nervus facialis' OR 'nervus facialis' OR 'nervus intermedius' OR 'nervus intermedius of wrisberg' OR 'wrisberg nerve' OR 'wrisberg nervus intermedius') AND (monitor* OR neuromonitor* OR electromyogra* OR 'event related potential' OR 'event-related potential' OR 'evoked potential' OR 'n1 wave' OR 'n2 wave' OR 'n3 wave' OR 'n4 wave' OR 'p2 wave' OR 'p50 wave' OR 'nerve stimulation')) OR (('evoked response'/exp OR 'evoked response':ti,ab,kw) AND ('facial nerve'/exp OR 'cranial nerve'/exp)) OR (('cochlear nerve'/exp OR 'acoustic nerve' OR 'auditory nerve' OR 'cochlea nerve' OR 'nervus acusticus' OR 'nervus cochlearis' OR 'pars acusticus nervi vestibulocochlearis' OR 'vestibulocochlear nerve acoustic part' OR 'vestibulocochlear nerve cochlear part') AND (monitor* OR neuromonitor* OR 'neuro-monitoring')) OR 'auditory evoked potential'/exp OR 'auditory evoked

potential':ti,ab,kw OR 'acoustic evoked brain stem potential' OR 'acoustic evoked brainstem potential' OR 'auditory brain stem evoked response' OR 'auditory brain stem response' OR 'auditory brainstem evoked response' OR 'auditory brainstem response' OR 'brain stem auditory evoked potential' OR 'brainstem auditory evoked potential' OR ('trigeminal nerve'/exp AND (monitor* OR neuromonitor* OR 'neuro-monitoring')) OR (('nerve v' OR 'nerve vs' OR 'nervus trigeminus' OR 'trigeminal nerve') AND (monitor* OR neuromonitor* OR 'neuro-monitoring')) OR ('glossopharyngeal nerve'/exp AND (monitor* OR neuromonitor* OR 'neuro-monitoring')) OR ('glossopharyngeal nerve' AND (monitor* OR neuromonitor* OR 'neuro-monitoring')) OR ('vagus nerve'/exp AND (monitor* OR neuromonitor* OR 'neuro-monitoring')) OR (('nerve x' OR 'nerve xs' OR 'nervus vagus' OR 'pneumogastric nerve' OR 'pneumogastric nerves' OR 'vagus nerve') AND (monitor* OR neuromonitor* OR 'neuro-monitoring')) OR ('accessory nerve'/exp AND (monitor* OR neuromonitor* OR 'neuro-monitoring')) OR (('accessory nerve' OR 'nerve xi' OR 'nerve xis' OR 'nervus accessorius' OR 'spinal accessory nerve') AND (monitor* OR neuromonitor* OR 'neuro-monitoring')) OR ('hypoglossal nerve'/exp AND (monitor* OR neuromonitor* OR 'neuro-monitoring')) OR (('hypoglossal nerve' OR 'nerve xii' OR 'nerve xiis' OR 'nervus hypoglossus') AND (monitor* OR neuromonitor* OR 'neuro-monitoring')) AND (surger*:ti,ab,kw,de OR surgical:ti,ab,kw,de OR operation*:ti,ab,kw,de OR resection*:ti,ab,kw,de OR microsurg*:ti,ab,kw,de OR 'micro-surgical':ti,ab,kw,de OR 'micro-surgery':ti,ab,kw,de OR neurosurg*:ti,ab,kw,de OR 'neuro-surgery':ti,ab,kw,de OR intraoperativ*:ti,ab,kw,de OR 'intra-operative':ti,ab,kw,de) AND ('acoustic nerve cancer':ti,ab,kw OR 'acoustic nerve neurinoma':ti,ab,kw OR 'acoustic nerve tumor':ti,ab,kw OR 'acoustic nerve tumour':ti,ab,kw OR 'acoustic neurofibroma':ti,ab,kw OR 'acusticus neurinoma':ti,ab,kw OR 'auditory nerve neurinoma':ti,ab,kw OR 'ear schwannoma':ti,ab,kw OR 'angle tumor':ti,ab,kw OR 'angle tumour':ti,ab,kw OR 'neurinoma of the acoustic nerve':ti,ab,kw OR 'neurosensory deafness':ti,ab,kw OR 'sensoryneural deafness':ti,ab,kw OR 'sensory neural deafness':ti,ab,kw OR ((vestib* OR acoustic) NEAR/3 (neuroma* OR neurilemmoma* OR neurilemoma* OR neurinoma* OR tumor* OR tumour* OR schwannoma*)) AND [english]/lim NOT ('animal'/exp NOT 'human'/exp) NOT ('juvenile'/exp NOT 'adult'/exp) NOT ('letter'/exp OR 'editorial'/exp OR 'conference paper'/exp OR 'review'/exp) NOT ('case report'/exp NOT 'case control study'/exp) NOT (('acoustic nerve cancer':ti,ab,kw OR 'acoustic nerve neurinoma':ti,ab,kw OR 'acoustic nerve tumor':ti,ab,kw OR 'acoustic nerve tumour':ti,ab,kw OR 'acoustic neurofibroma':ti,ab,kw OR 'acusticus neurinoma':ti,ab,kw OR 'auditory nerve neurinoma':ti,ab,kw OR 'ear schwannoma':ti,ab,kw OR 'angle tumor':ti,ab,kw OR 'angle tumour':ti,ab,kw OR 'neurinoma of the acoustic nerve':ti,ab,kw OR 'neurosensory deafness':ti,ab,kw OR 'sensoryneural deafness':ti,ab,kw OR 'sensory neural deafness':ti,ab,kw OR ((vestib* OR acoustic) NEAR/3 (neuroma* OR neurilemmoma* OR neurilemoma* OR neurinoma* OR tumor* OR tumour* OR schwannoma*)) AND [english]/lim NOT ('animal'/exp NOT 'human'/exp) NOT ('juvenile'/exp NOT 'adult'/exp) NOT ('letter'/exp OR 'editorial'/exp OR 'conference paper'/exp OR 'review'/exp) NOT ('case report'/exp NOT 'case control study'/exp) AND 'conference abstract'/it) AND [01-01-2015]/sd NOT ('preclinical study'/exp OR 'animal experiment'/de OR 'in vitro study'/exp)

Appendix II: Rating Evidence Quality

Classification of Evidence on Therapeutic Effectiveness and Levels of Recommendation

Class I Evidence Level I (or A) Recommendation	Evidence from one or more well-designed, randomized controlled clinical trial, including overviews of such trials.
Class II Evidence Level II (or B) Recommendation	Evidence from one or more well-designed comparative clinical studies, such as non-randomized cohort studies, case-control studies, and other comparable studies, including less well-designed randomized controlled trials.
Class III Evidence Level III (or C) Recommendation	Evidence from case series, comparative studies with historical controls, case reports, and expert opinion, as well as significantly flawed randomized controlled trials.

Classification of Evidence on Prognosis and Levels of Recommendation

Class I Evidence Level I (or A) Recommendation	All 5 technical criteria above are satisfied.
Class II Evidence Level II (or B) Recommendation	Four of five technical criteria are satisfied.

Class III Evidence Level III (or C) Recommendation	Everything else.
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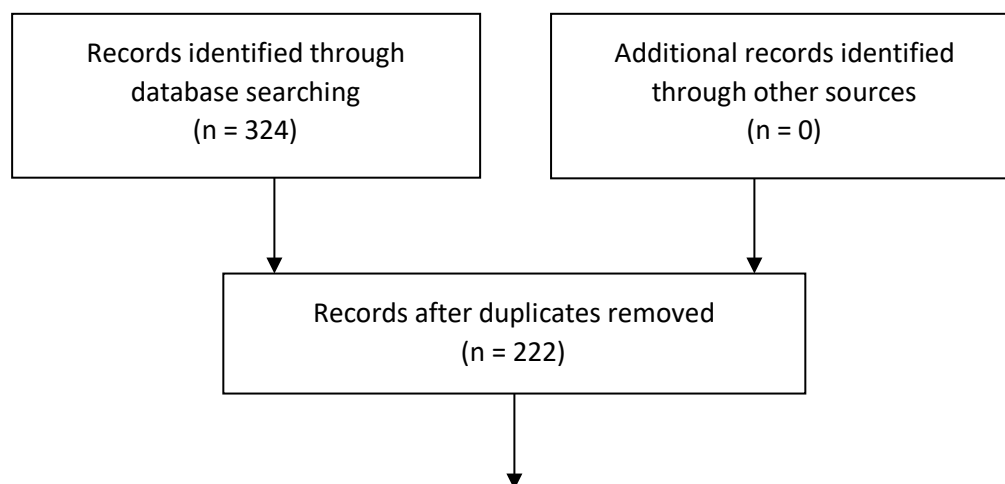
Classification of Evidence on Diagnosis and Levels of Recommendation

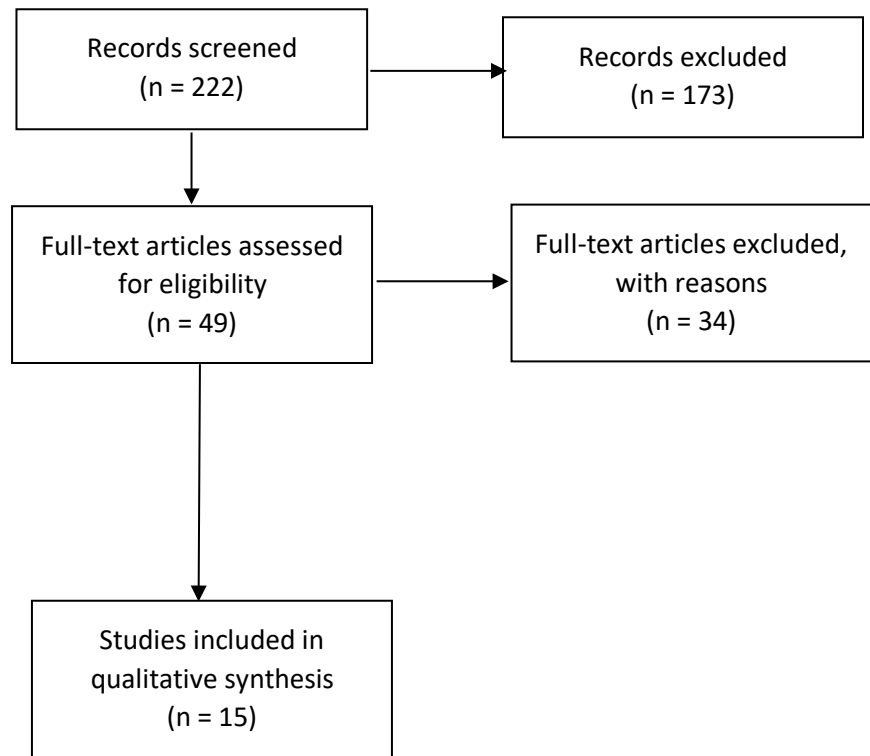
Class I Evidence Level I (or A) Recommendation	Evidence provided by one or more well-designed clinical studies of a <i>diverse</i> population using a “gold standard” reference test in a blinded evaluation appropriate for the diagnostic applications and enabling the assessment of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios.
Class II Evidence Level II (or B) Recommendation	Evidence provided by one or more well-designed clinical studies of a <i>restricted</i> population using a “gold standard” reference test in a blinded evaluation appropriate for the diagnostic applications and enabling the assessment of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios.
Class III Evidence Level III (or C) Recommendation	Evidence provided by expert opinion or studies that do not meet the criteria for the delineation of sensitivity, specificity, positive and negative predictive values, and, where applicable, likelihood ratios.

Classification of Evidence on Clinical Assessment and Levels of Recommendation

Class I Evidence Level I (or A) Recommendation	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic > 0.60.
Class II Evidence Level II (or B) Recommendation	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic > 0.40.
Class III Evidence Level III (or C) Recommendation	Evidence provided by one or more well-designed clinical studies in which interobserver and/or intraobserver reliability is represented by a Kappa statistic < 0.40.

Appendix III: PRISMA Flowchart





From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

Appendix IV. Evidence Tables

Table 1: Comparing FN outcomes with neuromonitoring versus anatomical dissection alone

Author/year	Study Description	Data Class	Conclusion
Chen, 2021 ⁸	Retrospective, cross-sectional review, n=436. All patients underwent retrosigmoid approach and meatal drilling for VS removal at a single	Class III	Statistically significant difference in extent of tumor resection by type of monitoring strategy (E vs. E+I vs. E+N) but no difference in FN or hearing functional outcome.

	institution from 2008 to 2017. FN EMG, BAEP, ipsilateral trigeminal EMG, and motor and somatosensory evoked potentials were recorded. Patients had electrophysiological monitoring only (E), electrophysiological monitoring plus intraoperative imaging (CT or MRI) (E+I), or electrophysiological monitoring plus neuronavigation (E+N). FN function was evaluated at 3 months postoperatively. HB grading system and AAO-HNS hearing classification systems used.		Authors Conclusions: Tumor size affects FN localization. Intraoperative neuronavigation and electrophysiologic monitoring may be helpful to improve the extent of resection. Comments and Conclusions: Short follow up time with some patients only followed for 3 months. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.
Bernardeschi, 2018 ⁷	Retrospective review of prospectively maintained database, n=25. All patients underwent surgical removal of a large (mean CPA diameter 28 mm) VS via translabyrinthine or retrosigmoid approach	Class III	Low volume of residual tumor (< 0.5 cc) when tumor removal was terminated based on 50% or greater drop in supramaximal stimulation amplitude. However, no significant difference in FN functional outcome was noted when comparing patients

	during a 12 month period (2014). Electrophysiological monitoring of FN was employed in all cases. Dissection was interrupted if response to supramaximal stimulation (2 mA) of the FN comparing brainstem to stylomastoid foramen was reduced by approximately 50%. Immediate and 1-year postoperative FN outcomes were assessed. HB grading system was used. Excluded patients with NF2 or those with preoperative FN palsy.		meeting and not meeting the 50% criterion. Author Conclusions: Electrophysiology can help guide the decision to terminate dissection with particularly adherent tumors. Conclusions and Comments: Only included patients with incomplete resection and reduced FN responses by supramaximal stimulation. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.
Taddei, 2016 ¹⁸	Retrospective review, n=51 consecutive patients. All patients underwent surgical removal of a VS at a single institution from 2005-2011.	Class III	Statistically significant difference between monitored and non-monitored groups. Specifically, higher rates of excellent (HB grade 1 or 2) and intermediate (HB grade 3 or 4) were noted in the continuously monitored group. Author Conclusions: Bipolar nerve stimulation

	Individuals with NF2 or recurrent tumors were excluded from study. Group 1 did not have continuous FN monitoring (only a facial stimulator). Group 2 had continuous FN monitoring and use of a stimulator. HB grading system was used.		and continuous EMG provided a high rate of FN preservation: Conclusions and Comments: Authors reported HB grade 2 or 3 FN function preoperatively in up to 25% of patients in each group, which raises the question of generalizability, as it is very rare to have preoperative facial weakness. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.
Hou, 2017 ¹³	Retrospective review, n=62 patients. All patients underwent surgical removal of a VS at a single institution via retrosigmoid approach. Patients were divided randomly into two groups, 33 of whom had intraoperative neurophysiologic monitoring (observation group) and 29 who did not (control group).	Class III	Patients who had continuous EMG monitoring of the FN had higher rates of anatomical preservation, and a higher proportion of better FN function. In addition, outcomes were statistically significantly better across all patient reported outcomes domains. There was no difference in the rate of total resection. Author Conclusions: Intraoperative FN monitoring offered higher anatomical and functional preservation rate and

	Rates of complete resection, FN outcome, and patient-reported outcomes measures (physiological, social, emotional, functional, and correlated symptoms) were compared. While use of the HB grading system was not explicit in the manuscript, the grades of function reported were similar.		improved quality of life outcomes. Conclusions and Comments: There was a low rate of anatomic preservation of the FN in both groups and no documentation regarding tumor size. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.
Xu, 2017 ²⁰	Retrospective review, n=53 patients. All patients underwent microsurgical resection using a retrosigmoid approach for resection of large VS (mean tumor size of approximately 40 mm) Intraoperative EMG and FN motor evoked potentials via transcranial stimulating electrodes were used for FN monitoring. Patients were separated into a monitored group (n=29) and a control group (n=24).	Class III	At 2 weeks, 3 months, and 6 months after surgery, the monitored group had statistically significant better FN function. Rates of total or subtotal resection were similar between the groups. Author Conclusions: Intraoperative monitoring showed no significant difference in resection rate but did contribute to FN anatomic and functional preservation. Conclusions and Comments: Generalizable study given comparable rates of FN preservation with other published series. Classification of evidence on prognosis class III.

	HB grading system was used.		Did not blind outcome measure. No validation in an independent “test set” of patients.
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Abbreviations: VS, vestibular schwannoma; FN, facial nerve; EMG, electromyography; BAEP, brainstem auditory evoked potentials; CT, computed tomography; MRI, magnetic resonance imaging; HB, House-Brackmann, AAO-HNS, American Academy of Otolaryngology – Head and Neck Surgery

Table 2: Predictive value of intraoperative monitoring compared to clinical information

Author/year	Study Description	Data Class	Conclusion
Ren, 2021 ¹⁶	Retrospective review, n=256. All patients underwent microsurgery for VS using translabyrinthine, retrosigmoid, or middle fossa approaches. Potential clinical predictors included age, sex, BMI, tumor size, prior treatment, surgical approach, symptoms, preoperative HB score, extent of resection, and EMG response. HB grading system was used.	Class III	On multivariate analysis, FN EMG response over 100 uV to a low amplitude stimulus (0.05 mA) was the most predictive of HB I or II facial function. Extent of resection (gross-total resection) was correlated with better facial function as well (p=0.003). Tumor size and surgical approach were not statistically significantly correlated. While BMI was correlated with worse facial function immediately postoperatively, it was not at latest follow up and therefore not part of multivariate analysis. Author Conclusions:

			While small size (≤ 1.5 cm) and lower BMI were associated with good immediate postoperative FN outcomes, only GTR and >100 microvolt intraoperative EMG FN amplitude were significant prognostic indicators of good long term FN function on multivariate analysis. Comments and Conclusions: Only study with all three surgical approaches represented in the data. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.
Ling, 2018 ¹⁴	Prospective study, n=106. All patients underwent microsurgical excision of VS via retrosigmoid approach. Predictors of FN outcome analyzed included age, gender, side, maximum extrameatal tumor diameter, preoperative HB grade, and FMEP	Class III	Final to start FMEP amplitude ratio was the most statistically significant predictor of FN functional outcome at hospital discharge and last follow-up. Other statistically significant predictors at last follow-up included: maximum extrameatal diameter, preoperative HB grade, starting FMEP amplitude, FMEP latency, and extent of resection.

	amplitudes (at start and end), latency, stimulation intensity, FMEP ratio, and extent of resection. HB grading system was used. A “satisfactory” outcome was deemed HB grade I or II.		Author Conclusions: FMEP amplitude ratio of >57% could predict HB I or II long-term postoperative function. Comments and Conclusions: Somewhat limited as all patients had large tumors. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.
Hong, 2017 ¹²	Retrospective review, n=105. All patients underwent retrosigmoid approach for microsurgical resection. Potential clinical predictors included age, tumor size, intraoperative electrophysiologic monitoring, whether the IAC was drilled, whether the tumor recurred, the presence of cystic degeneration,	Class III	Both tumor diameter and the use of intraoperative electrophysiologic monitoring were correlated with FN functional outcome. Tumor diameter over 5 cm was shown to have markedly poorer FN functional outcomes. Author Conclusions: Long term (≥ 1 year) FN function was related to immediate postoperative FN function, tumor size, and whether FN

	hydrocephalus, surgical approach. Statistical analysis was performed on individual predictors; multivariable analysis was not conducted. HB grading system was used.		monitoring was used. Age, surgical approach, whether the IAC was drilled, the presence of cystic degeneration, eventual recurrence, duration of symptoms, or hydrocephalus were not correlated with FN outcome. Comments and Conclusions: Lack of multivariable analysis is a significant weakness to this study. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.
Liu, 2015 ¹⁵	Retrospective study, n=106 patients. All patients underwent large VS (≥ 30 mm) resection via retrosigmoid approach at a single institution. EMG and FMEP monitoring were used for the FN. BAEP monitoring was used if hearing was present. The predictive value of tumor size, train time,	Class III	Tumor size ($p < 0.01$) and FMEP ratio ($p < 0.001$) were both highly correlated with immediate and late postoperative FN function. Author Conclusions: Indicative factors of both immediate and long-term postoperative FN function in large VSs include tumor size, intraoperative train time, start to final FMEP ratios and proximal to distal MRA ratios.

	FMEP ratio, and maximal response amplitude ratio were compared using Spearman correlation analysis. FN function was assessed preoperatively, at 3-7 days postoperatively, 3 months postoperatively, and 2 years postoperatively. HB grading system was used.		Comments and Conclusions: 26.4% of patients had HB II or III FN function preoperatively, which may affect generalizability. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.
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Abbreviations: VS, vestibular schwannoma; HB, House-Brackmann; BMI, body mass index; EMG, electromyography; IAC, internal auditory canal; FMEP, facial motor evoked potential; AAO-HNS, American Academy of Otolaryngology – Head and Neck Surgery

Table 3: Benefit of novel FN monitoring methods

Author/year	Study Description	Data Class	Conclusion
Greve, 2021 ¹⁰	Retrospective review, n=60 consecutive patients with VS. All patients underwent resection via retrosigmoid approach at a single center. FMEP was elicited by TES and was compared to spontaneous EMG activity. Surgeon was alerted when FMEP amplitude decreased or if EMG showed A-train	Class III	Using the bilateral motor threshold criterion (difference in stimulation threshold level from dural opening to end of tumor resection) of over 20% in combination with an optimistic approach (warning issues only if all facial muscles deteriorated on the affected side) was superior to intraoperative warnings such as A-trains. Prior work (Greve 2020), the 20% cutoff showed the

	activity (monomorphic high-frequency EMG activity patterns). The bilateral motor threshold criterion was defined as the ratio of the final to baseline ipsilateral motor threshold minus the contralateral final to baseline ratio. A cutoff value of $\geq 20\%$ was set to assess sensitivity and specificity. HB grading system was used.		highest sensitivity (76%) to predict HB deterioration ≥ 2 compared to other predictive criteria, such as using only the ipsilateral motor threshold or an amplitude ratio. Author Conclusions: The optimistic approach combined with the above defined FMEP criteria may guide safer VS surgery by reducing false positive and false negative warnings. Comments and Conclusions: Optimistic and traditional warning approaches only applied to 75% of patients as the remaining fraction did not have FMEP responses in all facial muscles. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.
Hendriks, 2020 ¹¹	Retrospective review, n=43 patients.	Class III	FMEP threshold change of less than 20 mA had a good (HB < 3) FN outcome.

	All patients underwent resection via retrosigmoid approach at a single center. Direct nerve stimulation, free-running EMG, and FMEP were monitored, in addition to BAEP when hearing was present. FN function was assessed at 6 weeks, 6 months, and 1 year after surgery. HB grading system was used.		Author Conclusions: The correlation between FMEP and FN outcome was statistically significant at all time points, while A-train time was not. Comments and Conclusions: Correlation between threshold increase and HB score was present at 6 weeks, 6 months, and 1 year after surgery. Data set comprised of large tumors only which may limit generalizability. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.
Frigeni, 2020 ⁹	Retrospective review, n=62 patients included for analysis. All patients underwent translabyrinthine approach for resection of VS. Patients underwent preoperative BR, ENoG, and EMG preoperatively and	Class III	BR testing was the only preoperative indicator of poor FN outcome. Multiple logistic regression revealed that the odds ratio for A-train activity was 9.81-11.72 compared to 5.54-8.20 for BR testing, suggesting that correctly identified A-train activity is more

	intraoperative direct nerve stimulation, FN mean action potential (first finding of FN, brainstem, and at IAC meatus), and free-running EMG. FN function was assessed on the day of discharge, 7 days postoperatively, and 1 year postoperatively. HB grading system was used.		predictive of FN outcome. Author Conclusions: Preoperative pathologic BR testing and A-train activity were correlated with poor long term (1 year) FN outcomes. Comments and Conclusions: FMEP was not used. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.
Tawfik, 2019 ¹⁹	Retrospective review, n=82 consecutive patients. All patients underwent surgical resection of VS via translabyrinthine, retrosigmoid, middle fossa, or combined approaches. FMEP was recorded in addition to facial EMG in 20 patients (the post-FMEP group), while 62 underwent EMG monitoring only (the pre-FMEP group).	Class III	No significant difference in FN outcome was noted between pre- and post-FMEP groups. Author Conclusions: Intraoperative FMEP is highly specific and moderately sensitive in predicting postoperative FN function, but its use may not improve outcomes overall. Comments and Conclusions:

	FN function was assessed at the time of hospital discharge and at > 9 months postoperatively. HB grading system was used.		Asymmetric cohort size for pre- and post-FMEP implementation groups. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.
Liu, 2015 ¹⁵	Retrospective study, n=106 patients. All patients underwent large VS (≥ 30 mm) resection via retrosigmoid approach at a single institution. EMG and FMEP monitoring were used for the FN. BAEP monitoring was used if hearing was present. The predictive value of tumor size, train time, FMEP ratio (end of case to maximum level at start of case), and maximal response amplitude (MRA) ratio were compared using Spearman correlation analysis. FN function was assessed preoperatively, at 3-7 days postoperatively, 3 months postoperatively,	Class III	FMEP ratio showed the highest correlation with immediate and late postoperative facial function when compared to train time and MRA ratio. Author Conclusions: Tumor size, intraoperative A-train time, start to final FMEP ratios, and proximal to distal MRA ratios were correlated with immediate and long-term FN function. Comments and Conclusions: Only large tumors included which may limit generalizability. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.

	and 2 years postoperatively.		
	HB grading system was used.		

Abbreviations: VS, vestibular schwannoma; FMEP, facial motor evoked potential; TES, transcranial electrical stimulation; BAEP, brainstem auditory evoked potential; HB, House-Brackmann; EMG, electromyography; BR, blink reflex; ENoG, electroneuronography

Table 4: Predictive value of CNAP monitoring compared to ABR.

Author/year	Study Description	Data Class	Conclusion
Sun, 2018 ¹⁷	Retrospective review, n=126 consecutive patients. All patients underwent middle fossa approach for resection of VS. Audiologic monitoring was performed using far-field ABR and near-field CNAP. Audiometric testing was performed preoperatively and approximately 1 month postoperatively. 54.8% of patients had one subsequent postoperative audiogram that occurred at a mean 22 months after surgery. ABR and CNAP results were evaluated	Class III	Positive predictive value of absent N1 amplitude (suggesting worsening of postoperative hearing class) reached 100% for CNAP, while negative predictive value of intact waveform (suggesting maintenance of postoperative hearing class) was 50%. In contrast, positive predictive value of absent ABR waveform for worse postoperative WRS class was 86% while negative predictive value was 84%. Classification of evidence on prognosis class III. Did not blind outcome measure. No validation in an independent “test set” of patients.

	independently and in combination to estimate sensitivity and specificity. Hearing outcome was categorized using AAO-HNS Committee on Hearing and Equilibrium reporting guidelines and WRS class.		
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Abbreviations: VS, vestibular schwannoma; ABR, auditory brainstem response; CNAP, cochlear nerve action potential; AAO-HNS, American Academy of Otolaryngology – Head and Neck Surgery; WRS, word recognition score

Appendix V. Conflicts of Interest

Task Force Member	Disclosure
<i>Julie Honaker PhD, AuD</i>	Nothing to Disclose
<i>Ben Allen Strickland, MD</i>	Nothing to Disclose
<i>Eric J. Lehrer, MD</i>	Servier Pharmaceuticals, Novocure Inc.
<i>Sheryl Green, MBBCh</i>	Nothing to Disclose
<i>John P. Marinelli MD</i>	Medtronic
<i>Christopher S. Graffeo MD, MS</i>	Nothing to Disclose
<i>Isabelle M. Germano, MD, MBA</i>	Brianlab
<i>Mateo Ziu, MD</i>	Omniscient Neurotechnology America Ltd; GT Medical Technologies, Inc
<i>Walavan Sivakumar, MD</i>	Stryker Corporation
<i>Sherwin Tavakol, MD</i>	IRRAS USA, Inc.; Globus Medical, Inc.
<i>Lucas Paul Carlstrom, MD, PhD</i>	Kuros Biosciences USA, Inc
<i>Jamie J. Van Gompel, MD</i>	Medtronic, Cadence

<i>Ian Dunn, MD</i>	Nothing to Disclose
<i>Jeffrey J. Olson, MD</i>	Verastem, Inc., Research Grant American Cancer Society, Editorial Consultant; Azurity Pharmaceuticals, Inc.
<i>Ghazal S. Daher MD</i>	Nothing to Disclose
<i>Matthew L. Carlson, MD</i>	Cochlear Americas, Advanced Bionics, Stryker Corporation; IotaMotion, Inc.; Stryker Corporation
<i>Neil S. Patel, MD</i>	Cochlear Americas, Zeiss, Viridian Therapeutics, IotaMotion, Inc.
<i>Michael Sughrue, MD</i>	Omniscient Neurotechnology America Ltd
<i>Constantinos G. Hadjipanayis, MD, PhD</i>	Stryker Corporation; Integra LifeSciences Corporation; Omniscient Neurotechnology America Ltd
<i>Jeffrey Jacob, MD</i>	Stryker Corporation; KLS; Synthes