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Review

EAONO Position Statement on Vestibular Schwannoma: Imaging Assessment. What are the Indications for Performing a Screening MRI Scan for a Potential Vestibular Schwannoma?

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Currently, cerebellopontine angle tumor and, more specifically, vestibular schwannoma is diagnosed using magnetic resonance imaging (MRI). The main reason to perform an MRI scan is to determine asymmetrical sensorineural hearing loss. The extent of asymmetry differs in the presentation of vestibular schwannoma, making it difficult to determine when to perform imaging diagnostics. Several studies have determined the probability of the presence of a cerebellopontine angle lesion using different audiological protocols. Further, there is also a cost aspect: what are the accepted sensitivity and specificity of these protocols? In this study, we reviewed the existing protocols.

KEYWORDS: Vestibular schwannoma, MRI, asymmetrical hearing loss

INTRODUCTION

The incidence of vestibular schwannomas is estimated to be 13–20 per million [1, 2]. The diagnostic work-up to determine or exclude vestibular schwannoma (or cerebellopontine angle lesion in general) has evolved over the years. Several studies have been conducted on this. Before the invention of magnetic resonance imaging (MRI), auditory brainstem responses (ABRs) and computed tomography (whether or not with contrast enhancement) were the gold standard. Studies conducted in 1990s and early 2000s were focused on establishing the role of MRI, which is to perform an MRI scan rather than an ABR test [3-5]. Once the superiority of MRI was proven, the widespread availability and ever improving image quality of MRI in the Western world has led to a remarkable shift in the diagnostic model of performing imaging when a cerebellopontine angle process is actually expected toward the more defensive attitude of "excluding a cerebellopontine angle lesion," gradually increasing the sensitivity (a sensitivity of 100% indicates that all lesions are found upon imaging) of a used algorithm (if any) to perform an MRI scan. A recent estimation is that, currently, only 1.09–5.23% (specificity) of all MRI scans performed for asymmetric hearing loss leads to the detection of vestibular schwannoma [6-8].

Traditionally, mostly (the degree of) asymmetric hearing loss has been subject to the discussion of when to perform an MRI scan, and this is what mainly will be discussed here. Several audiometric criteria (or "protocols") have been proposed to standardize the indications to perform an MRI scan, varying from very selective and strict to broad criteria. Moreover, the tendency to perform imaging depends on the hospital setting, local traditions, associated symptoms, patients' age, and comorbidity and is also subject to the perseverance of the patient and gut feeling of the physician.

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Apart from asymmetric hearing loss, tinnitus, unilateral peripheral vestibulopathy not explained otherwise (rather function loss than paroxysmal vertigo), co-existing trigeminal neuropathy, or a combination of these symptoms can be reasons to perform an MRI scan. Because these are more dichotomous outcome measures (or probably because hearing can be measured more accurately), there has been no discussion regarding these symptoms in previous studies.

EVIDENCE

There is no prospective research available on this topic. However, there are studies regarding the specificity and sensitivity of different proposed audiometric algorithms. Different studies describing audiological protocols that are used to allocate to screening using MRI were all reviewed and are mentioned in the evidence table. Cheng et al. [8] reviewed and compared the specificity and sensitivity of available algorithms by retrospectively applying them on a large cohort (n=1751) of patients [3, 9-20]. It was a high-quality study facilitating the discussion on choosing the ideal audiological protocol, which is used as the basis of the evidence table. An important disadvantage of that study is the lack of translation into terms of cost-effectiveness. It is useful to know about the most sensitive protocol, for example, for use in a tertiary referral center, and the more specific protocols in countries without ample financial resources, but a reasonable compromise between good sensitivity on the one hand and screening on the other hand is what would be the most useful in the daily practice of most physicians dealing with this problem. Gimsing et al. [21] proposed a protocol that provides these criteria. They noted that "in clinical work, it is important to consider another aspect of specificity, namely the proportion of patients that each protocol will allocate to screening". The proposed protocol was (1) ≥20 dB asymmetry at two neighboring frequencies or unilateral tinnitus or (2) ≥15 dB asymmetry at two frequencies between 2 and 8 kHz. In the present study, eight different study protocols were retrospectively tested on 424 patients [9, 10, 14, 15, 17-20], with the diagnosis established (tumor/no tumor). Depending on the criteria used, the amount of "false-negative" patients (tumor, but no MRI performed) and "false-positive" patients (no tumor, but MRI performed) differs. Each protocol has a certain sensitivity and specificity. The higher the sensitivity, the more schwannomas are diagnosed. The higher the specificity, the less schwannomas would be missed. Moreover, there is a (related) screening rate, i.e., the fraction of audiograms that allocate to perform an MRI scan, varying from 18% to 35% (prospectively analyzed for a cohort of 210 patients by Gimsing et al. [21]). This is directly related to the costs of screening. An American study has estimated the average cost of diagnosing one patient with vestibular schwannoma as US$61,650 (retrospective chart review, no specific audiological protocol used) [22]. If the abovementioned fraction of 1%–5% is used (the percentage of MRI scans that lead to the diagnosis of vestibular schwannoma), this would lead to an average cost of €10,000–€40,000 per diagnosed schwannoma (price of an MRI scan set at €400) [6-8].

A recent diagnostic review and meta-analysis was performed to specifically investigate the diagnostic accuracy (defined as the optimal combination of sensitivity and specificity) of these screening protocols [23]. It concluded that most studies were of poor-to-moderate quality. Results of five pure-tone audiometry protocols, which have been frequently proposed in literature, were pooled [13, 20, 21]. The highest diagnostic accuracy was achieved by the protocol established by the AAO-HNS, which prescribes an MRI scan for patients with an average asymmetry of ≥15 dB on 0.5-3 kHz frequencies. Its sensitivity and specificity reached 90.9% and 57.5%, respectively. However, 3 kHz (used n this protocol) is generally not included in standard audiometry. The protocol described by Seattle et al. prescribes an MRI scan for patients with an average asymmetry of ≥15 dB on frequencies 1-8 kHz (excluding the 3 kHz frequency) and reaches a slightly lower sensitivity and specificity of 89.2% and 43.8%, respectively. None of the described screening protocols could diagnose all patients with vestibular schwannoma.

Other audiological findings are worse predictors than audiograms. Absent stapedial reflexes occur more or less equally in patients with vestibular schwannoma and those without any tumor. The loss of speech discrimination more frequently occurs in patients with vestibular schwannoma; however, several patients have a loss of <10% [21]. Vestibular schwannoma occurs in 4% of patients with sudden sensorineural hearing loss [24]. Furthermore, Gimsing et al. [21] evaluated the shape of the audiogram and found no strong association of the shape of the audiogram with the presence of vestibular schwannoma; however, there might be a minimal predilection for a flat-shaped audiogram.

An interesting and promising study described the possibility of a computerized technique in predicting and, therefore, allocating for MRI screening using audiological and MRI data on a group of patients without vestibular schwannoma [9]. A so-called Gaussian process ordinal regression classifier was used to determine and predict the presence of vestibular schwannoma. With 129 patients, the program achieved a sensitivity and specificity of 95% and 56%, respectively (30% better than audiological protocols with a similar sensitivity). Patient age, the presence of vertigo, and unilateral tinnitus were also taken into account.

CONCLUSION

No prospective studies answering this research question are available; however, there is a series of useful retrospective studies. Eventually, the position of the clinician or, in this case, the EAONO is based on the balance between minimal sensitivity on the one hand and maximal cost on the other hand. The optimal protocol still depends on the setting of the clinician and the availability of resources.

Remarks

This text comprises a summary of available retrospective studies in this field of research. Please realize that there is no single prospective study whatsoever that covers this research question. However, the pragmatic answer can be found by testing different audiological protocols on cohorts of patients with available audiological and MRI data retrospectively. Therefore, the systematic reviewing of literature becomes less interesting. Therefore, the text format might be less GRADE-compatible than initially intended.

Moreover, one important thing not been taken into account, i.e., the likelihood to act on a positive finding on an MRI scan. Ever since the increasing availability of MRI scans, the size of vestibular schwannomas at the time of diagnosis has dramatically decreased. Simul-

Table 1. Literature review – Evidence Table

Author	Year	Study characteristics	Sensitivity */***	Specificity **/***	Summary of findings	Screening rate	GRADE Quality of evidence	GRADE Strength of recommendation
Cheng	2012	3-year cross-sectional analysis: comparison of all available audiometric protocols screening for vestibular schwannomas			No optimal value is chosen with respect to specificity and sensitivity of different protocols, however well designed study		+++	strong
****		Single-frequency comparison protocols						
UK Department of Health		≥20 dB at a single frequency between 0.5 and 4 kHz	83.2%	62.6%				
Welling	1990	≥15 dB at a single frequency between 0.5 and 4 kHz	87.9%	52.1%		36%		
Margolis	2008	≥15 dB at a single frequency	87.9%	44.7%				
Saliba	2009	≥15-dB asymmetry at 3 kHz (RULE 3000)	87.9%	57.3%				
Schlauch	1995	≥20-dB asymmetry at 4 kHz (RULE 4000)	82.1%	62.6%		17%		
		Two adjacent frequency comparison protocols						
Dawes	2001	≥20 dB at any 2 neighboring frequencies	82.6%	61.1%		24%		
Margolis	2008	≥10 dB at any 2 neighboring frequencies	93.2%	31.6%				
Cueva	2004	≥15 dB at any ≥2 neighboring frequencies	85.8%	48.7%				
		Comparison of averaged multiple frequency protocols						
AAO-HNS		≥15 dB between ears averaging 0.5–3 kHz	87.4%	65.4%	Highest specificity (sensitivity, 87.37%); specificity, 65.38% (other abnormality or normal) and 66.04% (radiologically normal)		++	strong
Sheppard	1996	≥15 dB between ears averaging 0.5–8 kHz	86.8%	60.1%				
Hunter	1999	≥15 dB between ears averaging 1–8 kHz	86.3%	60.0%				
Mangham	1991	≥10 dB between ears averaging 1 to 8 kHz	91.6%	44.2%	Highest sensitivity (sensitivity 91.58%); specificity 44.23% (other abnormality or normal) and 44.91% (radiologically normal)	35%	++	strong
Schlauch	1995	≥20 dB between ears averaging 1 to 8 kHz	81.1%	66.3%		17%		
Sheppard	1996	≥15 dB between ears averaging 0.25 to 8 kHz	86.8%	61.1%		18%		
Obholzer	2004	≥15dB if better ear is ≤30 dB HL (0.25–8 kHz) or ≥20 dB if better ear is >30 dB HL (0.25–8 kHz)	83.7%	66.4%		24%		
Gimsing	2009	(1) 20 dB asymmetry at 2 neighboring frequencies between 2 and 8 kHz or unilateral tinnitus, or (2) 15 dB asymmetry at two frequencies	92%	50%	Lowest costs with high sensitivity and reasonable specificity	23%	+++	strong
		Protocols included for different reasons						
Lee	2012	VS in patients with SSHL	N/A	N/A	12/295 = 4% of patients with SSNHL have VS		++	strong
Nouraei	2007	Screening patients with sensorineural hearing loss for VS using a Bayesian classifier	95%	56%	Goal: to evaluate whether machine-learning technology can improve the sensitivity and specificity of identifying patients at risk of VS based on clinical and audiological data		+	weak

* Sensitivity of 100%: no vestibular schwannoma would be missed
** Specificity of 100%: no false-positive diagnosis based on the diagnosis (or no MRI without vestibular schwannoma would be performed)
*** Sensitivity and specificity rates differ slightly in original articles because these are pooled data from the article by Cheng
**** Discarded because of poor outcome

taneously, there is widespread evidence that conservative policy for small- and medium-sized tumors is often the most favorable, particularly in the elderly. €40,000 for a diagnosis that most probably will remain untreated (not to mention the follow-up scans) is quite a burden on health expenses. Whether this advocates more strict rules to perform an MRI scan in the first place remains to be investigated. The unwanted side effect of a more strict protocol would perhaps be to miss different pathologies in the cerebellopontine angle. Assuming that different (possibly malignant) etiologies would generally be associated with a faster deterioration of hearing, would there be a place for repeated audiometry again, just like in earlier days?

Position of EAONO

The best audiological protocol to allocate for MRI screening for vestibular schwannoma is subject to the setting in which it is used, and the discussion is ongoing regarding its sensitivity and specificity and the related costs. The EAONO advises to follow the following algorithm:

The proposed protocol:

(1) ≥20 dB asymmetry at two neighboring frequencies or unilateral tinnitus

(2) ≥15 dB asymmetry at two frequencies between 2 and 8 kHz

More sensitive protocols are optional but will obviously lead to higher costs. In a tertiary referral center, a protocol with a very high sensitivity is justified.

Apart from audiological protocols, the EAONO encourages the idea of a computerized "self-learning" algorithm that uses audiological and other (dichotomous) data to predict the presence of vestibular schwannoma. A large-scale prospective multicenter study with this program would be highly valuable and, perhaps, the key to cost-effectiveness while keeping sensitivity rates acceptable. In contrast, the probability of the treatment of (elderly) patients with positive MRI findings should be taken into account.

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Editor's Note:

The EAONO Project on guidelines of Otology and Neurotology was initiated by Franco Trabalzini and the Working Groups began working in 2011. Since then a considerable work has been issued to produce the first Consensus Documents.

The working Group on Vestibular Schwannoma have esteemed members from dedicated centers all over Europe. I wish to express my thanks to the working group leaders Miguel Aristegui and Jacques Magnan for their great effort as well as to all the other active members of the group.

Miguel Aristegui, Shakeel Saeed, Simon Lloyd, Per-Caye Thomasen and Jacques Magnan's comments for this "Consensus Document" have been very much appreciated.

This study is very much respected by the Editorial of the Journal in this regard.

Prof. Dr. O. Nuri Ozgirgin
Editor in Chief

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