RESEARCH ARTICLE

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Using Non-Contrast Magnetic Resonance Imaging for Detection of Vestibular Schwannoma Assessment: A Systematic Review and Diagnostic Accuracy Meta-Analysis

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ABSTRACT

Background and Aim: Non-contrast magnetic resonance imaging (MRI) offers high spatial resolution without the need for contrast agents and has been recognized as a useful imaging technique since the early 1990s. The study aimed to evaluate the effectiveness of T2wi compared to gadolinium-enhanced T1-weighted imaging in diagnosing VS.

Methods: We performed a systematic search of literature in PubMed, Web of Science, and Scopus with relevant keywords. Studies that did not perform MRI or had insufficient data were excluded. Data extraction was performed based on a standardized sheet. Meta analysis was performed with STATA, R, and RStudio.

Results: The initial search retrieved 6,088 articles from which 1,872 duplicates were removed. Finally, 10 studies were included based on our eligibility criteria. The pooled sensitivity of MRI in detection of vestibular schwannoma on patient level was 97% (95% CI: 82% - 100%, p-value < 0.01) and its specificity was 98% (95% CI: 89% - 100%, p-value < 0.01). The pooled sensitivity of MRI in detection of vestibular schwannoma on ear level was 98% (95% CI: 87% - 100%, p-value < 0.01) and its specificity on ear level was 99% (95% CI: 96% - 99%, p-value < 0.01). The pooled mean dice score was 87.42 (95%CI: 82-92).

Conclusion: Non-contrast MR imaging offers precise evaluations of vestibular schwannoma in comparison to enhanced T1-weighted imaging. T2wi shows outstanding diagnostic precision for vestibular schwannomas and presents strong reliability in diagnostic evaluations.

Keywords: Vestibular schwannoma, Neoplasm, Lesion, Diagnostic accuracy, Magnetic resonance imaging, MRI, Sensitivity, Specificity, Acoustic neuroma

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INTRODUCTION

Acoustic neuromas, also known as vestibular schwannomas, vestibular neuromas, or acoustic neurofibromas, originate from Schwann cells and can be intracranial or extra-axial tumors. Typically located near the cochlear or vestibular nerve, they often occupy the cerebellopontine angle. Approximately 20% of tumors affecting the internal carotid artery are meningiomas, which may occur elsewhere in the brain[1-3]. Bilateral acoustic neuromas are predominantly seen in individuals with type 2 neurofibromatosis. Comprising 6–10% of all brain tumors, acoustic schwannomas are histopathologically benign and commonly arise from the sheath of cranial nerve VIII. As they grow, they exert pressure on cranial nerves VII, VIII, and V, as well as the brainstem, leading to symptoms such as tinnitus, hearing loss, dizziness, vertigo, and gait instability. Treatment options for acoustic schwannomas include observation, microsurgery, and radiation therapy. The choice of treatment depends on factors such as the tumor's size and location, the patient's hearing level, and their age[4-6].

As the prevalence of incidental and asymptomatic tumors increases, more patients and healthcare providers opt for serial MRI monitoring. Typically, follow-up MRI scans are conducted initially every 6 months, and later at intervals of 12 to 24 months. Currently, gadolinium-enhanced T1-weighted imaging (GdT1wi) is widely regarded as the standard method for detecting Vestibular Schwannomas (VS)[7-11]. Regardless of the chosen treatment approach (surgery, stereotactic radiosurgery, or conservative management), patients with VS typically undergo multiple GdT1wi scans during sequential follow-up to assess tumor growth[12-14].

The use of contrast agents in MRI scans, such as gadolinium-based agents, is associated with various drawbacks, including time consumption, costliness, and potential side effects like allergic reactions and nephrogenic systemic fibrosis. Moreover, recent radiology studies have indicated that gadolinium-based contrast agents can accumulate in the brain parenchyma. As an alternative to gadolinium-enhanced T1-weighted imaging (GdT1wi), some research suggests utilizing high-resolution T2-weighted magnetic resonance imaging (T2wi) for monitoring Vestibular Schwannomas (VS)[15-17]. T2wi offers high spatial resolution without the need for intravenous contrast agents and has been recognized as a useful imaging technique since the early 1990s. This study aimed to assess whether T2wi could serve as an effective monitoring tool compared to GdT1wi in patients with VS. The objective was to determine whether T2wi could accurately diagnose VS.

MATERIALS & METHODS

This systematic review and meta-analysis study was conducted based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guideline 2020[18].

Search strategy: Two authors performed a systematic search of literature in the following electronic databases: PubMed, Web of Science, and Scopus. No time limitation was defined and all English studies from the beginning until April, 2024 were included. The relevant medical subject heading (MeSH) terms and related keywords were used in combination to build the search strategy; ("magnetic resonance imaging" OR "MRI") AND ("vestibular schwannoma" OR "acoustic schwannoma" OR "vestibular neuroma").

Eligibility criteria: Our eligibility criteria were defined based on the PICO framework: (P) Population: patients suspected for VS. (I) Not Applicable. (C) MRI findings. (O) detection of VS lesions. Those studies that did not perform MRI or did not perform any diagnostic accuracy measures were excluded. Studies that performed other imaging modalities, lacked individual data, or were not in English, were also excluded.

Data extraction and outcome measures: A standardized Excel sheet was prepared for data extraction. Two independent authors performed the data extraction based on the aforementioned data extraction sheet. Disagreement between these two authors, regarding inclusion, exclusion or data extraction, was discussed and resolved by a third author. The data extraction sheet included the following study characteristics: first author's name, year of publication, study design, country, true positive, true negative, false positive, false negative, total number of cases, mean age, and reference of comparison.

Data synthesis and Statistical Analysis: We used R (R Foundation for Statistical Computing, Vienna, Austria), RStudio (RStudio, Inc., Boston, MA), and STATA 17.0 for the statistical analysis and creating the figures. The pooled sensitivity and specificity were calculated based on metadta package in STATA and mada package in R. The sensitivity and specificity were pooled using the hierarchical logistic regression. The Diagnostic Odds Ratio (DOR), Negative Likelihood Ratio (NEGLR), and Positive Likelihood Ratio (POSLR) were calculated and graphed using mada package in R. The 95% confidence interval was also estimated using the binomial distribution. The forest plots and Receiver Operating Characteristic (SROC) plots were also created[19-21].

RESULTS

Our initial search retrieved 6,088 articles from PubMed, Scopus, and Web of Science, from which 1,872 duplicates were removed. After screening the title and abstract of 4,216 records, 63 full texts were retrieved, among which 10 studies (**Figure 1**) were included based on our eligibility criteria[6, 8, 9, 13, 17, 22-26]. Among the 10 included studies, 9[6, 8, 9, 13, 17, 22-25] were included in the meta-analysis and 1 study did not enter this process[26]. More detail regarding the study characteristics of the included studies is summarised in (**Table 1**).

The pooled sensitivity of MRI in detection of vestibular schwannoma on patient level was 97% (95% CI: 82% - 100%, p-value < 0.01). The pooled specificity MRI in

Table 1: The pooled sensitivity, specificity and heterogeneity of the included studies.

Pooled Statistics for Patient Level Outcomes							
Study	**Year**	**SEN**	**95%CI**	**p**	**SPC**	**95%CI**	**p**
Overall	-	97	82-100	<0.01	98	89-100	<0.01
Hentschel et al. (22)	2018	87	60-98	-	99	98-100	-
Karol et al. (23)	2018	78	58-91	-	73	54-87	-
Marx et al. (6)	1999	100	69-100	-	100	78-100	-
Neve et al. (24)	2022	100	97-100	-	98	91-100	-
Soulie et al. (9)	1998	100	86-100	-	93	85-97	-
Valesano et al. (13)	2018	91	76-98	-	100	89-100	-
Heterogeneity	Tau2				I2		
Generalized	7.06				32.45%		
Sensitivity	2.93				30.05%		
Specificity	2.66				37.26%		
Pooled Statistics for Ear Level Outcomes							
Study	**Year**	**SEN**	**95%CI**	**p**	**SPC**	**95%CI**	**p**
Overall	-	98	87-100	<0.01	99	96-99	<0.01
Hentschel et al. (22)	2018	90	73-98	-	100	99-100	-
Karol et al. (23)	2018	92	88-95	-	98	97-99	-
Marx et al. (6)	1999	100	72-100	-	100	91-100	-
Neve et al. (24)	2022	100	98-100	-	98	94-100	-
Soulie et al. (9)	1998	100	93-100	-	93	88-96	-
Valesano et al. (13)	2018	91	76-98	-	100	96-100	-
Heterogeneity	Tau2				I2		
Generalized	1.38				25.72%		
Sensitivity	3.83				23.96%		
Specificity	0.87				47.88%		
Pooled Statistics for Dice Score							
Study	**Year**	**Mean**	**95%CI**	**I2**	**Tau2**	**p-value**	**n**
Overall	-	87.42	82.82-92.02	100%	21.25	<0.01	672
Neve et al. (24)	2022	82	-	-	-	-	112
Neves et al. (25)	2023	89	-	-	-	-	122
Shapey et al. (8)	2019	93	-	-	-	-	243
Yao et al. (17)	2022	85	-	-	-	-	195

*SEN=sensitivity; SPC=specificity; CI=confidence interval

detection of vestibular schwannoma on patient level was 98% (95% CI: 89% - 100%, p-value < 0.01). Further detail is available in (**Figures 2 & 3**).

The pooled sensitivity of MRI in detection of vestibular schwannoma on ear level was 98% (95% CI: 87% - 100%, p-value < 0.01). The pooled specificity MRI in detection of vestibular schwannoma on ear level was 99% (95% CI: 96% - 99%, p-value < 0.01). Further detail is available in (**Figures 4 & 5**).

The pooled mean dice score was 87.42 (95%CI: 82-92). Although the patient level and ear level studies did not show any significant heterogeneity, the Dice score showed significant heterogeneity with I2 of 100% and p-value of less than 0.01. Further information regarding forest of Dice score is summarized in (**Figure 6**). The Diagnostic Odds Ratio (DOR) and negative and positive likelihood ratios are summarized in Appendix 1-6.

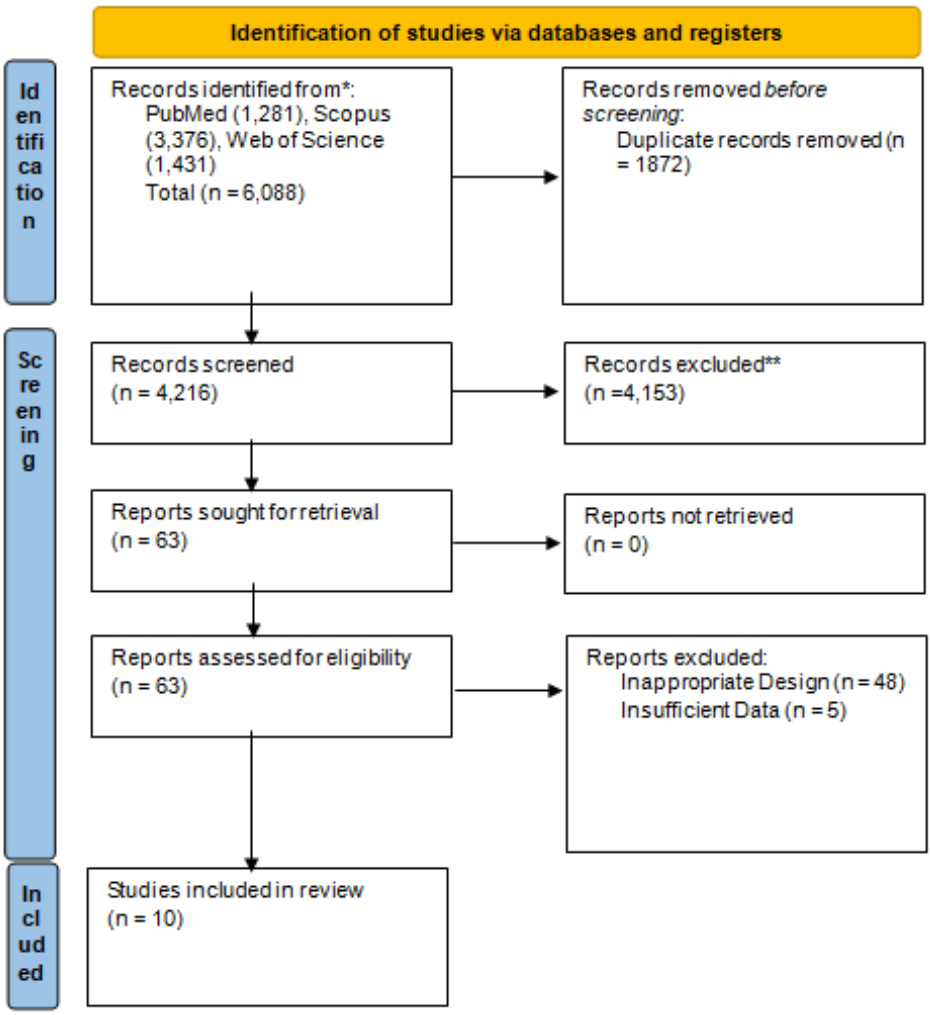

Figure 1: PRISMA flowchart of the included studies.

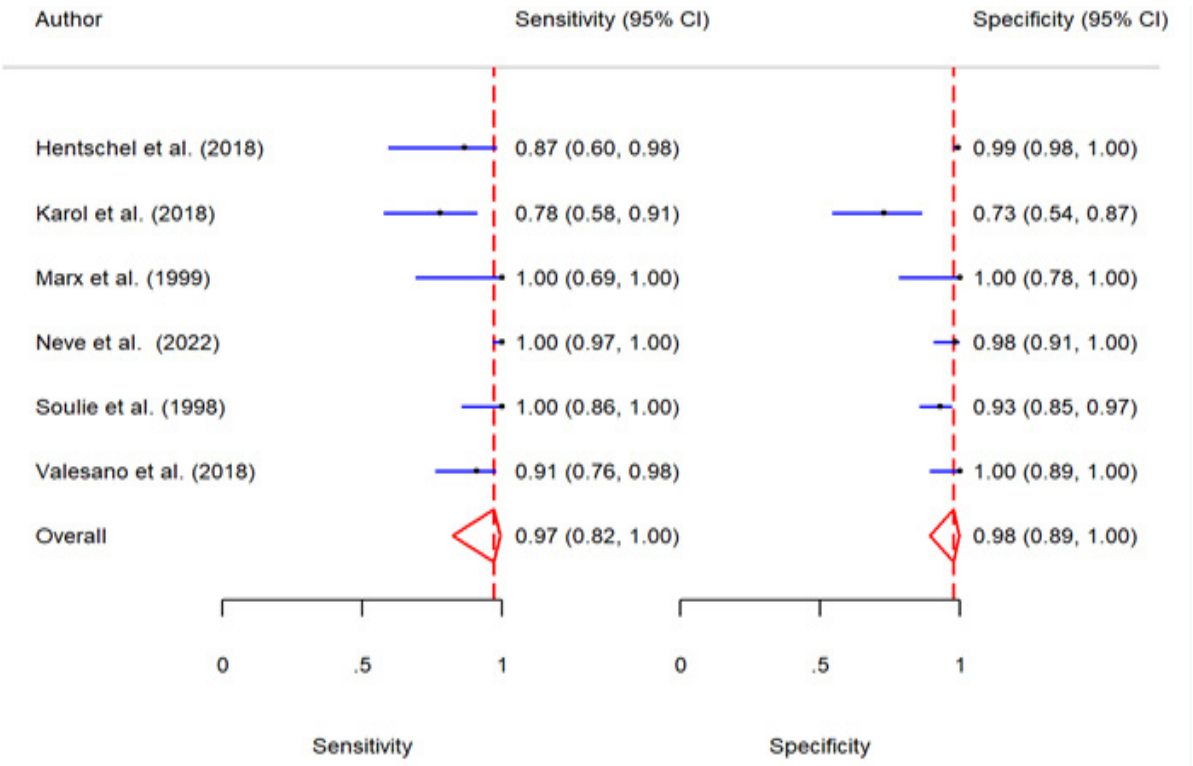

Figure 2: Patient level pooled sensitivity and specificity of MRI.

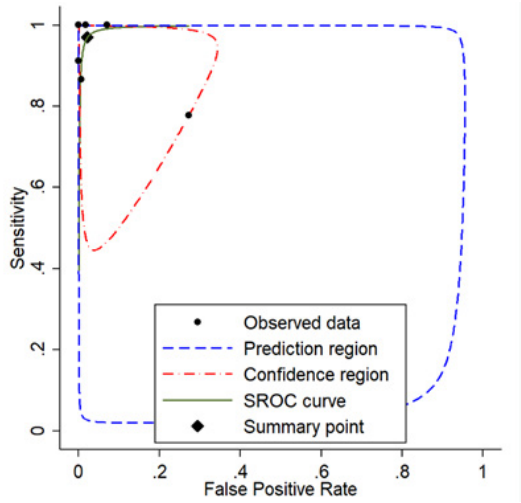

Figure 3: The Receiver Operating Characteristic (ROC) plot of MRI on patient level.

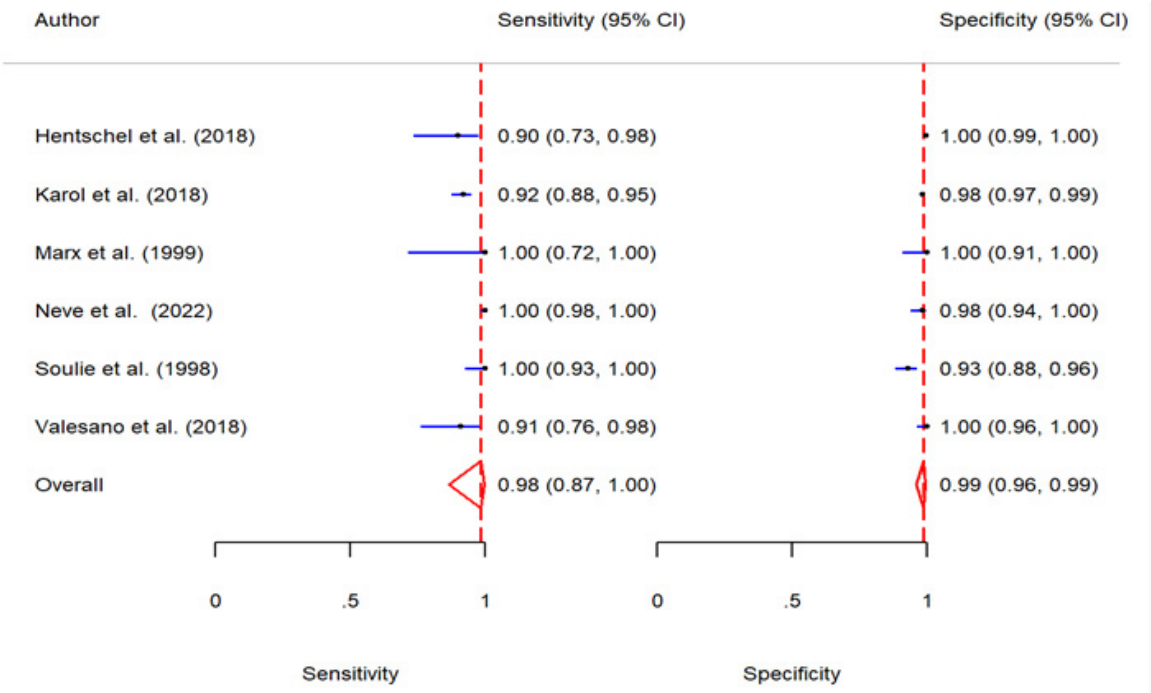

Figure 4: Ear level pooled sensitivity and specificity of MRI.

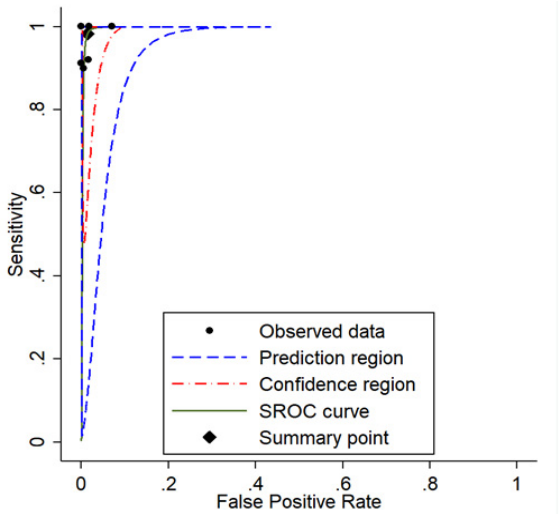

Figure 3: The Receiver Operating Characteristic (ROC) plot of MRI on patient level.

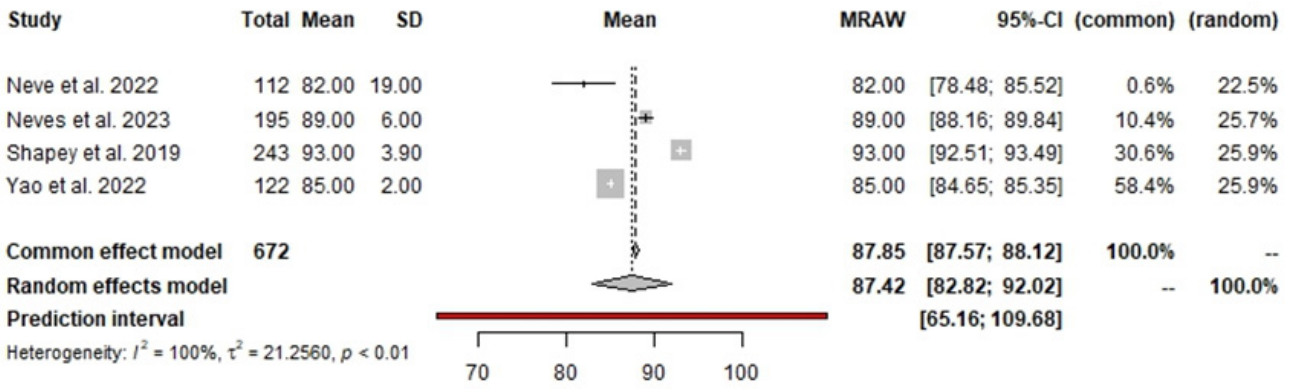

Figure 6: Pooled mean dice score among the included studies.

DISCUSSION

Based on the findings of our systematic review and meta-analysis study, MRI had high sensitivity and specificity for detecting vestibular schwannomas. The pooled sensitivity and specificity of MRI in detection of vestibular schwannoma on patient and ear level was 97%, 98%, 98%, and 99%, respectively. The pooled mean dice score was also 87.42%. Overall, the studies have shown low heterogeneity for sensitivity and specificity, however, the dice score showed high levels of heterogeneity.

Two systematic reviews have conducted comparative analyses of high-resolution T2-weighted imaging (T2w) and gadolinium-enhanced T1-weighted imaging (GdT1w) in the assessment of vestibular schwannoma. Both reviews concluded that GdT1w, considered the gold standard, exhibited high sensitivity and specificity[1, 27, 28]. Interestingly, there were no observed differences in measured tumor diameter between T2w and GdT1w sequences. Moreover, the specific T2w protocol utilized did not influence the reported sensitivity or specificity. Kim et al. noted that despite variations in protocols, the T2 dephasing remained similar, with differences primarily attributed to the characteristics of the MRI machines. This allowed for the grouping of protocols for comparison purposes[29-31].

The advancement in MRI sequencing has facilitated the accurate identification of vestibular schwannoma without the need for contrast agents. Hentschel et al. conducted a study highlighting that specialized training in radiological interpretation was not essential. In their research, they demonstrated this by having a medical doctor, who had received only a brief tutorial and had no prior experience in neuroradiology, serve as the second examiner[32-35]. Despite the absence of formal training, there was strong agreement between raters, indicating that accurate interpretation of noncontrast T2-weighted images can be achieved even without specific expertise in neuroradiology[22, 36-38].

The findings of this study suggest that a noncontrast MRI protocol, such as T2-weighted imaging (T2wi), is comparable to conventional MRI protocols, like gadolinium-enhanced T1-weighted imaging (GdT1wi), in assessing the size of vestibular schwannomas (VS). Additionally, our analysis indicates that T2wi is as effective as GdT1wi in detecting VS[5, 39, 40]. Furthermore, the study demonstrates the excellent reliability of T2wi, with high agreement observed among both inter- and intraobserver evaluations. These results support the use of noncontrast T2wi for the detection and monitoring of patients with VS[10, 40-42].

The utilization of a paramagnetic contrast agent enhances the delineation of tumor boundaries, enabling radiologists to distinguish acoustic neuromas from other Cerebellopontine Angle (CPA) tumors, including meningiomas, with exceptional precision[15, 16, 43]. However, this enhancement comes with notable drawbacks, including increased financial expenses compared to non-contrast MRI, and nearly doubling the duration of the procedure. Moreover, there is a risk of complications such as nephrogenic systemic fibrosis associated with the use of contrast agents[16, 17, 44].

Previous research has explored the feasibility of utilizing non-contrast T2-weighted imaging (T2wi) for the accurate diagnosis of Vestibular Schwannoma (VS). A comprehensive review of the literature, including univariate meta-analyses of sensitivity and specificity, indicated that non-contrast MRI demonstrated high sensitivity and cost-effectiveness in diagnosing acoustic neuromas. High-resolution T2wi was deemed to be of adequate quality for reliably diagnosing VS of any size and could potentially replace routine contrast-enhanced T1-weighted imaging (T1wi)[7, 45, 46]. However, it is worth noting that pooling sensitivity and specificity data may lead to overestimation due to the negative correlation often observed within studies. Hence, more sophisticated statistical approaches are warranted in meta-analyses of diagnostic test accuracy[12, 14, 26, 47].

The SROC (Summary Receiver Operating Characteristic) approach has emerged as the preferred method for meta-analyzing studies that provide both sensitivity and specificity data. This approach transforms each sensitivity-specificity pair into a single measure of accuracy known as the Diagnostic Odds Ratio (DOR). One advantage of the DOR approach is its ability to address the inherent correlation between sensitivity and specificity values[2, 4, 48, 49].

Additionally, it accommodates the heterogeneity across studies arising from variations in the thresholds chosen by researchers. Considering this negative curvilinear correlation is crucial when pooling data for meta-analyses. The DORs can be effectively utilized in meta-analyses of diagnostic studies. Therefore, we conducted a bivariate meta-analysis using DORs instead of pooling sensitivity and specificity data. Furthermore, we assessed the inter- and intra-observer agreement to evaluate the reliability of high-resolution T2-weighted imaging[3, 50, 51].

CONCLUSION

The findings of this meta-analysis suggest that T2-weighted imaging (T2wi) provides accurate measurements of vestibular schwannoma when compared to gadolinium-enhanced T1-weighted imaging (GdT1wi). T2wi exhibits excellent diagnostic accuracy for vestibular schwannomas (VS) and demonstrates high reliability in diagnostic assessments. Nevertheless, additional studies are necessary to validate the outcomes of our investigation.

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