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The Role Of Non-Echoplanar Diffusion-Weighted Magnetic Resonance Imaging & Apparent Diffusion Coefficient In Diagnosis Of Primary Cholesteatoma And Cholesteatoma Recidivism

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ABSTRACT

Cholesteatoma, a challenging otolaryngological condition, necessitates accurate diagnosis to prevent severe complications. This study evaluates the diagnostic performance of non-echoplanar diffusion-weighted magnetic resonance imaging (DW-MRI) in primary cholesteatoma and recurrent cases following mastoidectomy. For primary cholesteatoma, DW-MRI exhibited a sensitivity of 86.3%, specificity of 100%, with a p-value <0.001. In recurrent cases, DW-MRI achieved 100% sensitivity and 100% specificity (p-value <0.001). These compelling results suggest the potential of DW-MRI to reduce unnecessary surgeries and enhance patient care. Nevertheless, standardization and further research are crucial to optimize its clinical utility. Non-echoplanar DW-MRI emerges as a promising diagnostic tool for cholesteatoma, with the potential to minimize the need for second-look surgeries.

Keywords

Cholesteatoma, Diffusion-weighted MRI, Non-echoplanar MRI, Otolaryngology

INTRODUCTION

Cholesteatoma, a keratin-producing squamous epithelial mass within the middle ear, remains a challenging and critical concern in the field of otolaryngology worldwide [1]. This pathological condition originates from the tympanic membrane and steadily progresses, invading the middle ear and posing a significant threat to auditory health [1]. Left untreated, cholesteatoma can lead to severe complications, including hearing loss, vertigo, facial nerve paralysis, and, in extreme cases, meningitis. Surgical intervention is the primary mode of treatment, and it can be classified into two main techniques: canal wall up (CWU) and canal wall down (CWD) mastoidectomy, based on whether the posterior canal wall is preserved or removed, respectively. The canal wall down technique results in an open mastoid cavity, facilitating post-operative inspection for potential recurrence, although it demands regular maintenance to remove accumulated wax and secretions [2]. On the other hand, the canal wall up technique preserves the mastoid cavity, which is advantageous for future hearing aid fitting and reduces the risk of swimming-associated otorrhea. However, this closed cavity is associated with a higher risk of residual (36%) and recurrent (18%) diseases compared to canal wall down mastoidectomy, necessitating routine second-look surgeries after the primary procedure [2] [3].

In this context, diffusion weighted imaging (DWI), a magnetic resonance (MR) technique, plays a pivotal role by harnessing the movement of water molecules within tissues to create contrast in MR images. DWI is sensitive to changes in tissue cellularity, cell membrane integrity, and fluid viscosity, with more restricted water movement generating higher signal intensity on DWI [4]. The apparent diffusion coefficient (ADC), a quantitative measure of water diffusion, has become an integral part of assessment due to its ability to provide a true quantitative display of water diffusivity, free from the T2 shine-through effect. However, the accuracy of ADC maps is influenced by the choice of b-values and the risk of prolonged exam duration with increased patient movement [5]. Cholesteatoma is known for its characteristic restricted diffusion on DWI, attributed to its keratin content, which results in high signal intensity, even at low b-values (0 s/mm2), in contrast to brain tissue. Yet, this high signal intensity on low b-values reverses to low signal values on the ADC map due to restricted diffusion. In contrast, non-cholesteatoma lesions, such as granulation tissue, inflammation, and fluid, exhibit a different pattern of signal intensity, emphasizing the diagnostic utility of DWI in distinguishing these conditions[6].

The choice of DWI sequence is crucial for ear and skull base imaging. Echoplanar DWI, with its shorter acquisition time, is affected by air/bone susceptibility artifacts and distortion, limiting its diagnostic potential in skull base and temporal bone examinations. In contrast, non-echoplanar techniques, offering larger image matrices and thinner slice thickness, enhance image quality and enable the detection of smaller lesions, making them an essential component of modern MR imaging devices[7]. This paper aims to assess the diagnostic performance of ADC and DWI in detecting primary cholesteatomas and Recurrent or persistent cholesteatoma following mastectomy in order to assess the possible substitute value of diffusion weighted MRI and ADC for the scheduled second look surgery after surgery.

Patients and Methods

Study Design: Observational prospective study.

Setting: The research was conducted in the radiology department of Fayoum University Hospital, and it involved patients referred from the Otorhinolaryngology department as well as those from the outpatient clinic. This study was conducted after obtaining approval from the research and ethical committee.

Population of Study and Sample Size: The study included a total of fifty-three patients who met the following criteria:

Inclusion Criteria:

- Age Group: Patients of any age were eligible for inclusion.
- Both Sexes: Both males and females were included in the study.
- Primary Cholesteatoma: Patients presenting with suspected primary cholesteatoma either clinically or through CT examination.
- Known Cholesteatoma Patients: Patients with a known history of cholesteatoma and suspected post-operative recurrence, who were scheduled for a second look surgery.
- Canal Wall Up Mastoidectomy: Patients who had undergone primary canal wall up mastoidectomy and were scheduled for a second look surgery.
- Consent: Patients who provided informed consent.

Exclusion Criteria:

- Patients with absolute contraindications to MRI examination.
- Patients who declined to provide consent.
- Patients with a history of severe claustrophobia or anxiety disorders that might significantly impede their ability to undergo an MRI examination.

Study Duration: The study was conducted from December 2018 to November 2021.

Imaging Equipment: MR imaging was performed using a Toshiba Vantage Titan 1.5T machine equipped with a phased array coil.

Imaging protocol:

Sequence: DWI (b =0 & 1000) on axial plane, TR = 5000 ms, TE = 66 ms. FOV = 220 x 220 mm, slice thickness = 8 mm, gap = 1 mm.

Additionally, a coronal T2-weighted and an axial T1-weighted image were performed for precise anatomic localization and to rule out cholesterol granuloma. No intravenous contrast media was applied. ADC maps were generated using a built-in software package from b = 0 and b = 1000 s/mm^2 images. For each patient, a circular region of interest (ROI) with an area of 55 mm^2 was created on central slices containing the largest portion of the lesion. The ROI was positioned on solid areas of the lesion while excluding any cystic and/or necrotic regions. ADC values were calculated automatically, and each ROI was measured three times, with the mean value recorded.

Statistical Analysis:

Data collected was coded for ease of manipulation and double-entered into Microsoft Access. Data analysis was performed using Statistical Package for Social Science (SPSS) software version 22 on Windows 7 (SPSS Inc., Chicago, IL, USA). Descriptive analysis was conducted, presenting qualitative data in numbers and percentages, and quantitative parametric data was described using arithmetic means and standard deviations. The Chi-square test was used to compare between two or more than two qualitative groups. Sensitivity and specificity tests were employed, including the use of the Receiver Operating Characteristic (ROC) curve for evaluating a new test. A significance level of $P < 0.05$ was considered statistically significant.

Ethical Considerations:

Approval for this research was granted by the Faculty of Medicine Research Ethical Committee with issue number: D194, dated 17/02/2019, guaranteeing adherence to ethical standards and laws.

Informed consent from all patients.

Results

The study included fifty-three patients with age ranged between 7 and 69 years old and mean age of study group (29.8± 18.1); it involved 25 male patients (47.2% of cases) and 28 female patients (52.8% of cases).

Table (1): Frequency of patient's status among study groups.

Variables	Number	%
Primary	41	77.4%
Post CWD	11	20.8%
Post CWU	1	1.9%

Table (2): Comparisons of cholesteatoma diagnosis by MRI in different patient's status compared to operative/ pathological findings.

	MRI		Operative Findings		P-value	Sig.
Primary	**Number**	**Ratio**	**Number**	**Ratio**		
Cholesteatoma	19	46.35%	22	53.65%	**0.12**	**NS**
No Cholesteatoma	22	53.65%	19	46.35%		
Post CWD						
Cholesteatoma	4	36.36%	4	36.36%	**0.99**	**NS**
No Cholesteatoma	7	63.64%	7	63.64%		
Post CWU						
Cholesteatoma	0	0%	0	0%	----	---
No Cholesteatoma	1	100	1	100%		

Table (3): Sensitivity and specificity of non-echoplanar diffusion weighted MRI In diagnosis of cholesteatoma.

Status	Sensitivity	Specificity	PPV	NPV	AUC
Primary cholesteatoma	90%	100%	100%	85.7%	94.2%
Post-CWD	100%	100%	100%	100%	100%
Overall	88.5%	100%	100%	90%	97.1%

77.4% of cases were suspected to have primary cholesteatoma lesions, 20.8% had previous radical surgeries with suspected residual/ recurrent cholesteatoma lesions, and 1.9% had previous conservative surgery **(table 1 showing patients status frequency in the study)**

Twenty-two cases were proven to have primary cholesteatoma (53.65%) via operative and pathology reports while nineteen didn't have cholesteatoma (46.35%). Among these cases nineteen cases were correctly diagnosed by MRI showing typical diffusion restriction diagnostic of cholesteatoma, while three cases didn't show appreciable diffusion restriction and were not properly diagnosed **(figures 1: axial MR DWI & ADC images showing right sided mass of restricted diffusion denoting primary cholesteatoma)**.

Among patients who had previous canal wall down mastoidectomy four cases were pathologically proven to have residual/ recurrent cholesteatoma masses on second look surgeries (36.36%) while seven cases were free of cholesteatoma (63.64%). MRI could successfully diagnose all four cases to have residual/ recurrent cholesteatoma masses showing typical diffusion restriction. MRI was also able to show that the rest of cases to be free of residual/ recurrent disease **(figures 2: axial MR DWI & ADC images showing right sided small mass of restricted diffusion denoting recurrent cholesteatoma)**.

Single case had previous canal wall up mastoidectomy (conservative surgery) with no evidence of residual/ recurrent cholesteatoma on second look surgery and diffusion weighted MRI **(figures 3: axial MR DWI & ADC images showing no sizeable masses of diffusion restriction denoting no residual/ recurrent cholesteatoma).**

(Table 2 Comparisons of cholesteatoma diagnosis by MRI in different patient's status compared to operative/ pathological findings), (figure 1: Comparisons of cholesteatoma diagnosis by different methods of diagnosis among study group).

Overall sensitivity and specificity tests for MRI illustrated sensitivity of (88.5%) and a specificity of (100%) with (100%) positive predicted value and (90%) negative predicted value with p-value <0.001. **(Table 3: Sensitivity and specificity of non-echoplanar diffusion weighted MRI In diagnosis of cholesteatoma) (Figure 2: ROC curve for MRI in diagnosis of cholesteatoma)**

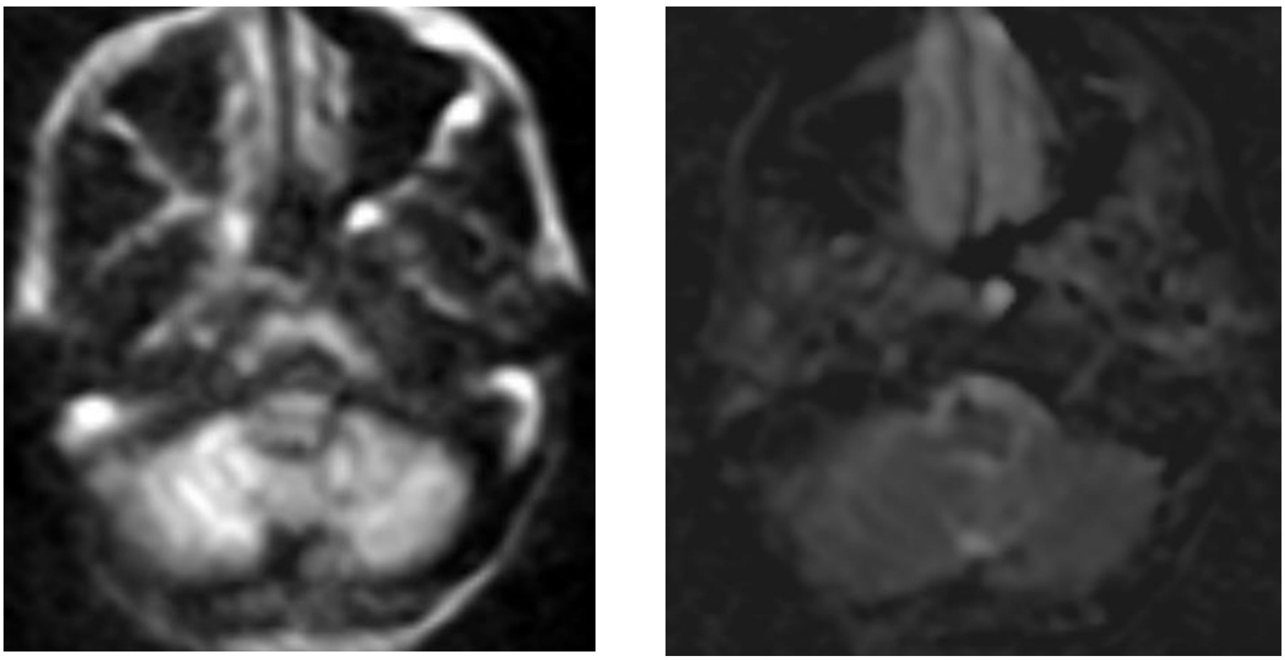

Figure (1): MRI axial image: non-echoplanar diffusion weighted sequence (right) showing right attic mass of restricted diffusion appearing of bright signal intensity and returning hypointense signal intensity on ADC (left image) denoting cholesteatoma.

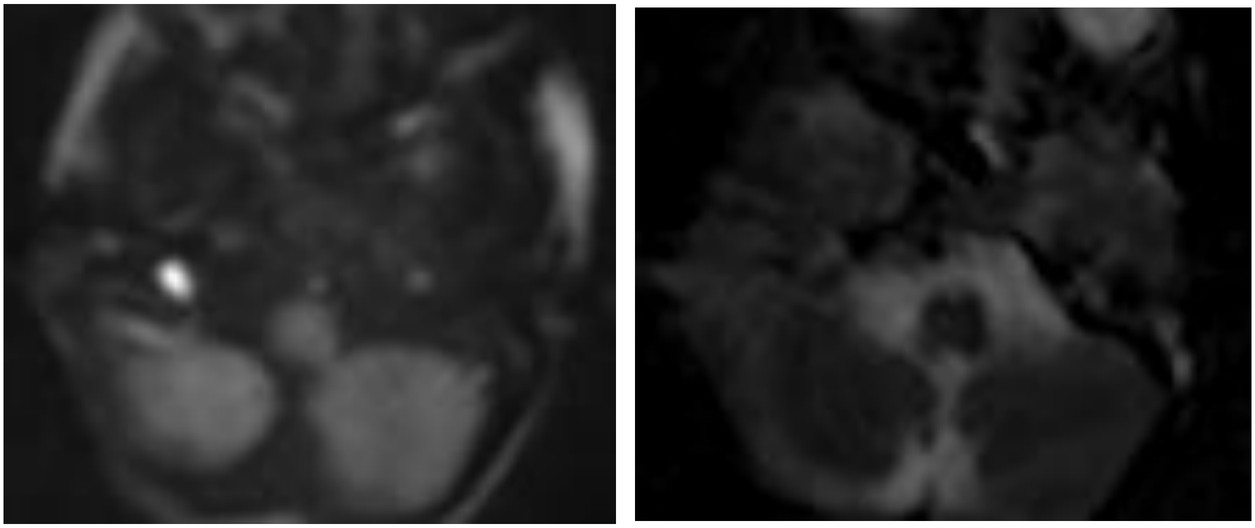

Fig. (2): axial diffusion weighted MRI (right) and axial ADC map (left) showing diffusion restricted mass displaying bright signal on DWI and hypointense signal on ADC map denoting recurrent cholesteatoma.

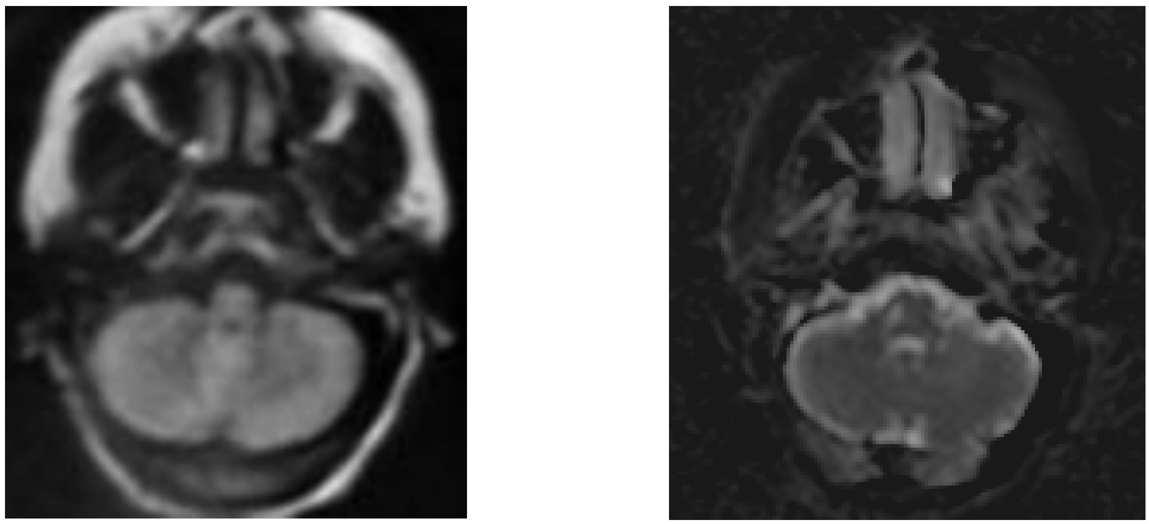

Figure (3): (Right) Axial non echoplanar diffusion weighted MRI and (left) Axial ADC map showing no sizeable masses of diffusion restriction denoting no residual/ recurrent cholesteatoma.

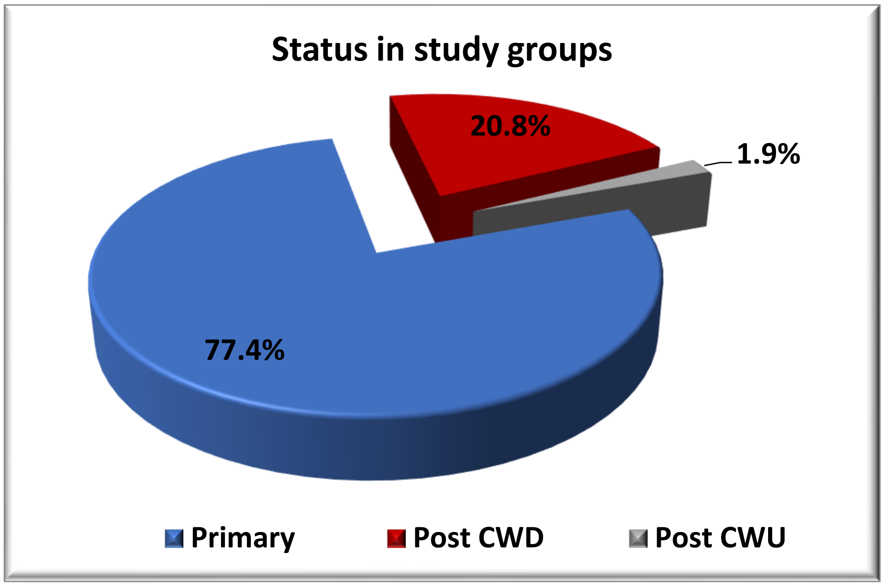

Figure (4): Patient's status in study groups

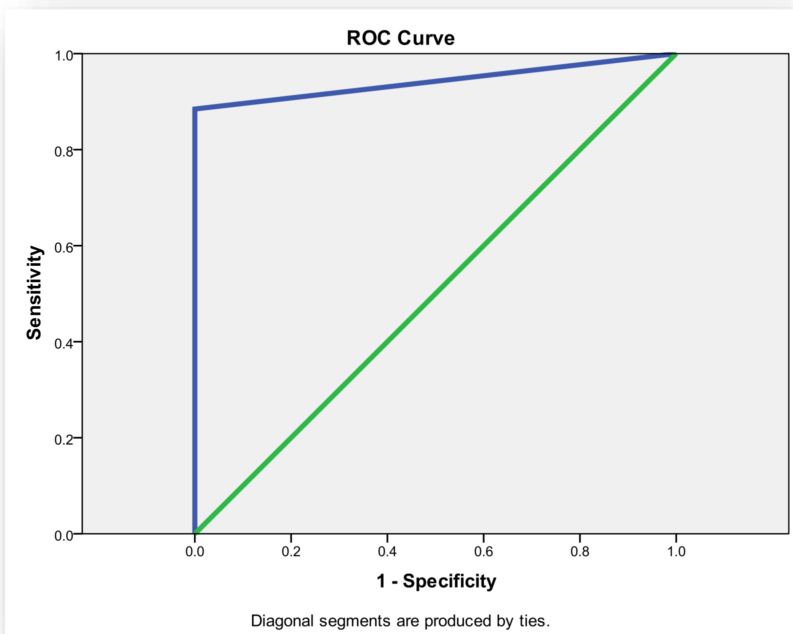

Figure (5): ROC curve for MRI in diagnosis of cholesteatoma.

Discussion

Cholesteatoma is a significant otolaryngologic pathology with potentially serious complications, including hearing loss, vertigo, facial nerve paralysis, and even meningitis if left untreated [8]. Cholesteatoma is primarily diagnosed through clinical examination, but surgical revision is necessary for a definitive diagnosis and to differentiate it from chronic suppurative otitis media (CSOM) with or without cholesteatoma[9][10]. A non-invasive diagnostic technique that can accurately detect cholesteatoma, particularly in its early stages, is highly valuable. It improves the prognosis for primary cholesteatoma and aids in identifying post-operative residual or recurrent cases [11]. The diagnosis and management of cholesteatoma are critical to prevent these complications and improve patient outcomes. The current standard for diagnosis primarily relies on clinical examination and high-resolution computed tomography (HRCT) [12]. However, HRCT has limitations, particularly in detecting small lesions and distinguishing between cholesteatoma and other middle ear pathologies [13]. In recent years, non-echoplanar diffusion-weighted magnetic resonance imaging (DW-MRI) has emerged as a promising alternative for the detection of cholesteatoma [14]. The results of this study demonstrate that non-echoplanar DW-MRI offers high sensitivity and specificity in diagnosing both primary and residual/recurrent cholesteatoma.

For primary cholesteatoma, our study found that non-echoplanar DW-MRI had an impressive sensitivity of 86.3% in detecting cholesteatoma, with a high specificity of 100%. This indicates that DW-MRI can be a valuable tool for the initial diagnosis of cholesteatoma, potentially reducing the need for exploratory surgery in patients with suspected primary cholesteatoma. These findings align closely with previous studies that have reported similar sensitivity and specificity values for non-echoplanar DW-MRI in cholesteatoma detection [15][16]. This is consistent with **De Foer et al.** [17] who reported a high detection rate for postoperative residual cholesteatoma using non-echoplanar diffusion-weighted MRI, with a sensitivity of 90%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 96%. In their study, non-echoplanar diffusion sequences successfully identified 9 out of 10 residual cholesteatomas, with the only missed lesion being a 2-mm cholesteatoma due to motion artifacts in a child's examination.

Furthermore, our study demonstrates that non-echoplanar DW-MRI is particularly effective in identifying residual or recurrent cholesteatoma in patients who have undergone previous mastoidectomy procedures. The sensitivity, specificity, and positive predictive value for detecting residual/recurrent cholesteatoma post-mastoidectomy were all 100%. This suggests that DW-MRI can reliably differentiate between patients who require further surgical intervention and those who do not, improving the management of post-mastoidectomy cases. These results are consistent with previous studies that have reported the high diagnostic accuracy of DW-MRI in this context [18].

While our study and several others have reported high sensitivity and specificity for non-echoplanar DW-MRI in cholesteatoma detection, it is important to acknowledge that there have been variations in reported results across different studies. A meta-analysis by [19] **(Peter M, Eleni L, et al, 2012)** found that the sensitivity of non-echoplanar DW-MRI in detecting cholesteatoma was 94%, but it also noted limitations in reliably detecting cholesteatomas under 3 mm in size. This suggests that the diagnostic accuracy of DW-MRI may be influenced by the size of the lesion. In another study conducted by [7], [20], the sensitivity of non-echoplanar DW-MRI was reported to be approximately 71.82%, with specificity at 89.36%. These results, while indicating promise for DW-MRI, suggest that the technique may have variability in its diagnostic performance based on the specific protocol and equipment used. In summary, the findings of our study support the growing body of evidence that non-echoplanar DW-MRI is a valuable tool in the diagnosis of cholesteatoma. Its high sensitivity and specificity, both for primary and postoperative cases, make it a compelling option for clinicians in the assessment and management of cholesteatoma.

Strengths and Limitations

In this study, the diagnostic strengths and limitations of non-echoplanar diffusion-weighted MRI (DW-MRI) in the assessment of cholesteatoma were rigorously evaluated, presenting findings with both clinical relevance and ethical consideration. The research encompassed a diverse patient population, including primary cholesteatoma and postoperative cases, providing a comprehensive examination of the technique’s diagnostic performance in real-world scenarios within an otolaryngological context. The study adhered to stringent ethical principles, ensuring the rights and welfare of participants, and reflected a commitment to responsible research conduct. A notable strength was the high specificity and positive predictive value demonstrated by non-echoplanar DW-MRI, particularly in postoperative cases, highlighting its potential to reduce unnecessary surgical interventions and enhance patient care. However, the study also had limitations, including a relatively small sample size, the single-center setting, and the retrospective nature of data analysis. Variability in DW-MRI protocols and a lack of exploration into the influence of lesion size on diagnostic accuracy further underscore the need for larger, multicenter, and standardized studies to refine the clinical applicability of this promising imaging technique.

Conclusion

Non-echoplanar diffusion weighted MRI once again proves its exquisite diagnostic performance regarding both detection and exclusion of primary cholesteatoma and cholesteatoma recidivism and with few technical and clinical considerations it could successfully reduce the number of or entirely replace needed second look surgeries.

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Data availability:

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