Detection of Cholesteatoma using Diffusion Magnetic Resonance Imaging

Original Article

[1]Mohamed Modather Abdel Naeem, [2]Shimaa Farghaly Gad, [3]Ahmed Abd El Aleem Abd El Wahab, [4]Amer Ragab Ahmed

Department of [1,3,4]Otorhinolaryngology, [2]Radio-Diagnosis, Assiut University Hospital, Assiut, Egypt.

ABSTRACT

Introduction: Cholesteatoma is a retraction pocket or cyst lined by squamous epithelium containing keratin debris occurring in the pneumatized portions of temporal bone, have a propensity for growth, bone destruction and is considered "unsafe" ear requires surgical treatment. High resolution CT is the method of choice for imaging cholesteatoma, but it cannot differentiate cholesteatoma from other soft tissues or mucoid secretions, especially in patients who have previous surgery, thus diffusion weighted MRI (DW-MRI) is recently used for differentiating cholesteatoma from other pathologies.
Objectives: We aimed to evaluate the role of DW-MRI in diagnosis of de novo and recurrent cholesteatoma.
Patients and Methods: We enrolled forty patients with suspected cholesteatoma either de novo or recurrent. All patients were subjected to complete history taking, otoscopic examination, HRCT scan and DW- MRI scanning with calculation of the apparent diffusion co-efficient (ADC). Then, surgical exploration of the middle ear was done, and we correlated between the operative and DW-MRI results.
Results: We found ADC values ranged between 0.1-1.7 with median ADC value was 0.8 mm^2/s. ADC cut-off point for detecting cholesteatoma was 0.8. P values for ADC, were significant for both denovo and recurrent cases, 0.044 and 0.039 respectively. Also, we found that DW-MRI had a sensitivity of (83%), specificity (75%), PPV (88%), NPV (67%) for detection of cholesteatoma in de novo cases, and a sensitivity of (80%), specificity (75%), PPV (89%) and NPV (60%) for recurrent cases.
Conclusion: DW-MRI could be a sensitive non-invasive tool for detecting cholesteatoma.

Key Words: ADC, cholesteatoma, DW-MRI.

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Corresponding Author: Amer Ragab Ahmed, MSc, Department of Otorhinolaryngology, Assiut University Hospital, Assiut University, Assiut, Egypt, **Tel.:** 01002990923, **E-mail**: amerragab2020@yahoo.com

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INTRODUCTION

Cholesteatoma is a sac lined with keratinized epithelium enveloped in a connective tissue matrix develop in the air cells of the temporal bone and it may be congenital or acquired[1]. Cholesteatoma is usually diagnosed clinically, but the use of imaging techniques could increase the accuracy of diagnosis. HRCT is considered the method of choice but, HRCT has a low specificity in detection of cholesteatoma because its unable to differentiate cholesteatoma from other soft tissue growths such as granulation tissues, especially in residual or recurrent cases[2].

DW-MRI is a new tool in diagnosis of cholesteatoma; it measures the diffusion of water molecules in the tissues, and this can be detected by calculating the apparent diffusion co-efficient (ADC). The diffusion may be restricted or facilitated, restricted diffusion gives a low ADC values while facilitated diffusion gives a high ADC values. cholesteatoma causes a restricted diffusion and usually a hyper intense signal on DW-MRI sequences[3].

Several studies have shown that non-echo planar DW- MRI (non-EP DWI), is more sensitive than the echo planar DW- MRI (EP DWI) and this is possibly due to the low susceptibility of non-EP DWI for artifacts, thin slice thickness and the higher resolution of images[4].

Non-E-PDWI techniques have been considered more reliable for detection of cholesteatomas with a small size which may be as smaller as 2 mm; even in the presence of inflammation, as it delineates only the keratin debris within the cholesteatoma[5].

Although the DW-MRI adds a more coast, many second look surgeries could be avoided if the results of DW-MRI were negative. One of the major disadvantages of DW-MRI is the unclear anatomical landmarks of the temporal bone, so proper imaging of cholesteatoma could be obtained by fusion of HRCT images with DW- MRI images[6].

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PATIENTS AND METHODS:

We enrolled 40 patients clinically suspected of having cholesteatoma; either denovo (26 patients), or recurrent (14 patients). The study included 28 females and 12 males, their age ranged from 6-56 years old, and the mean age was 27 years. All patients had preoperative HRCT, conventional non contrast MRI and DW-MRI scan of the petrous temporal bone. Patients were prepared to have an accurate MRI examination by giving them instructions to keep calm without movement or swallowing to avoid artifacts and psychological preparation regarding the scanner environment. MRI examination was performed using 1.5 tesla super conducting MR imager (Achieva, Philips medical systems, Netherlands B.V), the examination was done using surface coils with small field of view and thin sections. Patients were positioned in supine position, and a circularly polarized surface coil was placed over the head. A fast scan in sagittal, axial, and coronal planes was performed without injection of contrast material. Sagittal spin echo images were obtained initially to prescribe the location of axial images. Thin (2-4 mm) axial T1 and T2-weighted images with a repetition time (TR) of 500-600ms and 3000ms respectively, and echo time (TE) of 8-9ms and 100ms respectively were obtained with intersection gap of 1mm. Field of view (FOV) was 220 to 250 mm with matrix of 256 x 256 for axial images. Axial T1 & T2 images were extended from the arcuate eminence to the mastoid tip. In addition, DW-MRI and ADC maps were obtained using a multi-section single shot spin echo planar imaging (EPI) sequence (TR/TE/NEX: 3395/100ms) with diffusion sensitivities of b-values = 0,50,400, 800 and 1000. The diffusion gradients were applied sequentially in the three orthogonal directions. Sections of 2,5 mm thickness, inter-slice gap of 1,2 mm, a 230-255 mm FOV and, a 256 x 256 matrix were used with average scan time of 35s. ADC maps were automatically calculated by MRI machine software and included in the sequence. On ADC map, multiple regions of interest (ROIs) over the lesion were measured. ADC values was calculated at b values (0, 50, 400, 800 and 1000). ADC values were expressed in a square millimeter per second. All diffusion weighted images were analyzed by a blinded radiologist. Standard T2 weighted images were evaluated for a moderate hyper intense signal in comparison to the brain tissue.

Exploration of the suspected ear was done within 2 weeks after radiology, and evaluation of the middle ear and mastoid for the presence of cholesteatoma or other pathology was done. Surgical findings considered to be positive for cholesteatoma if there was a keratin debris or a closed sac filled with keratin, then comparison between the surgical and DW- MRI results was done.

Statistical analysis:

SPSS (statistical package for social science) version 23 have used. Qualitative data were expressed as percentages and numbers while quantitative data were presented as mean, median, standard deviation and range.

P value ≤ 0.05 was thought to be significant and, P *value > 0.0001* was highly significant. We have used the receiver operative characteristic (ROC) curve to calculate sensitivity, specificity; PPV, NPV and accuracy of DM-MRI in detecting cholesteatoma and also for calculation of the cut-off point of ADC was done.

RESULTS:

In our study, 40 patients were included; out of them 18 patients had left CSOM, 16 patients had right CSOM, while 6 patients had bilateral CSOM. Also, 16 patients presented by persistent otorrhea, 12 patients presented by aural polyp, and the remaining 12 patients presented by attic granulations or perforation, as shown in (Table 1).

Table 1: Patients' characteristics:

Variable	Category	N = 40
Laterality	Bilateral	6 (15%)
	Left	16 (40%)
	Right	18 (45%)
Clinical Findings	Attic Granulation and Perforation	12 (30%)
	persistent otorrhea	16 (40%)
	Aural Polyp	12 (30%)

Regarding diffusion weighted MRI results, we found that 28 patients (70%) had shown restricted diffusion; out of them 18 patients were de novo and 10 patients had recurrent disease, while the remaining 12 patients (30%) had shown facilitated diffusion; out of them 8 patients were de novo cases and 4 patients had recurrent disease [qualitative method]. Then, we calculated the ADC values [quantitative method], and we found a range of (0.1-1.7) with median value about (0.8 mm2/s) as shown in (Table 2).

Table 2: MRI results.

Variable	Result		N = 40
Diffusion MRI findings	Restricted diffusion		28 (70%)
	Facilitated diffusion	12 (30%)	
ADC value	Mean ± SD		0.9 ± 0.4
	Median (Range)	0.8 (0.1-1.7)	
		Diffusion result	
	Restricted	Facilitated	Total
De Novo	18 (64.3%)	8 (66.7%)	26 (65%)
Recurrent	10 (35.7%)	4 (33.3%)	14 (35%)
Total	28 (70%)	12 (30%)	40 (100%)

When we correlated between DW-MRI results and surgical findings in denovo cases, we found 15 patients (83.3%) were truly positive (an example is shown in Fig.1A), and 3 patients (16.7%) were falsely positive for cholesteatoma (an example is shown in Fig.1B) out of 18 patients with restricted diffusion.

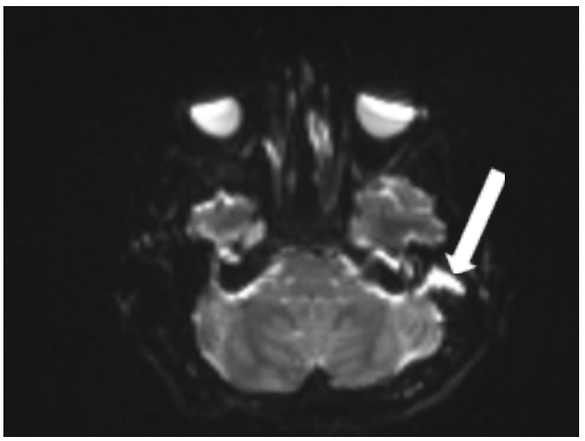
On the other hand, we found 6 patients (75%) were truly negative, and 2 patients (25%) were falsely negative for cholesteatoma out of 8 patients with facilitated diffusion as shown in (Table 3).

Table 3: Accuracy of diffusion MRI among denovo cases

	Diffusion result		
	Restricted (N=18)	Facilitated (N=8)	Total (N=26)
Cholesteatoma	15 (83.3%)	2 (25%)	17 (65%)
No	3 (16.7%)	6 (75%)	9 (35%)
Total	18 (69.3%)	8 (30.7%)	26 (100%)

Fig.1 (A&B) ….

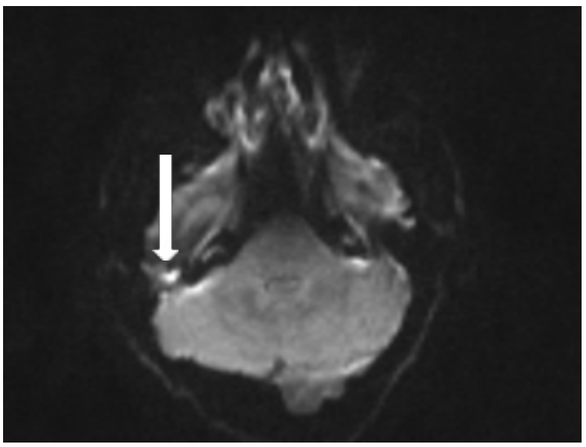
A



DW-MRI showing a focus with restricted diffusion (lt side) suggesting cholesteatoma (white arrow).

Operative result: confirms the presence of cholesteatoma (true positive).

B



DW-MRI showing a small focus of restricted diffusion , (Rt side) suggesting cholesteatoma (white arrow).

Operative result: No cholesteatoma found but a large tympanosclerotic patch was found (false positive).

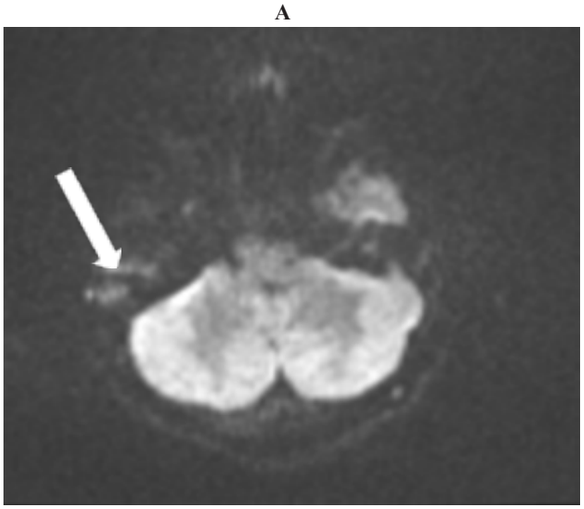
While in recurrent cases, we found 8 patients (80%) were truly positive, and 2 patients (20%) were falsely positive for cholesteatoma out of 10 patients with restricted diffusion. On the other hand, we found 3 patients (75%) were truly negative (an example is shown in Fig.2A), and 1 patient (25%) was falsely negative for cholesteatoma (an example is shown in Fig.2B) out of 4 patients with facilitated diffusion as shown in (Table 4).

Table 4: Accuracy of diffusion MRI among recurrent cases

	Diffusion result		
	Restricted (N=10)	Facilitated (N=4)	Total (N=14)
Cholesteatoma	8 (80%)	1 (25%)	9 (64.2%)
No	2 (20%)	3 (75%)	5 (35.8%)
Total	10 (71.4%)	4 (28.6%)	14 (100%)

Fig.2 (A&B) ….

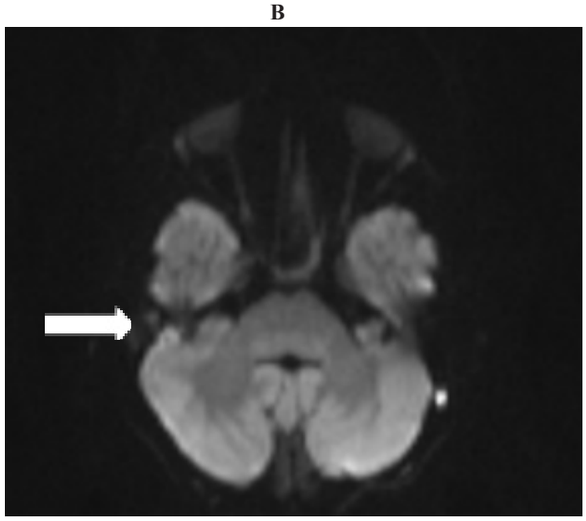
A



DW-MRI showing Facilitated diffusion with no restriction (Rt side ,white arrow) suggesting no cholesteatoma

Operative results: shows tough polypoidal mucosa filling the antrum and middle ear, with no cholesteatoma found (true negative) .

B



DW-MRI showing Facilitated diffusion withno restriction(Rt side ,white arrow) suggesting no cholesteatoma

Operative results: shows granulation tissues filling the antrum and middle ear, but a localized Small attic cholesteatoma was found about (3mm), which couldn't be detected by MRI (false negative).

According to our study, diffusion MRI has a qualitative predictive value in cholesteatoma with an accuracy (81%, 78.5%), sensitivity (83%, 80%), specificity (75%, 75%), PPV (88%, 89%), NPV (67%, 66%) for denovo and recurrent cases respectively, as shown in (Table 5).

Table 5: Qualitative value of diffusion MRI in Prediction of cholesteatoma.

Parameter	Denovo	Recurrent
Accuracy	81%	78.5%
Sensitivity	83%	80%
Specificity	75%	75%
Positive predictive value	88%	89%
Negative predictive value	67%	60%

While apparent diffusion coefficient (ADC) has a quantitative predictive value in cholesteatoma with an accuracy (76%, 83.5%), sensitivity (75%, 88%), specificity (78%, 67%), PPV (77%, 75%), NPV (76%, 89%) for denovo and recurrent cases respectively, with significant *p-value* as shown in (Table 6).

Table 6: Quantitative value of ADC in prediction of cholesteatoma

Parameter	De Novo	Recurrent
Accuracy	76.5%	83.5%
Sensitivity	75%	88%
Specificity	78%	67%
Positive predictive value	77%	75%
Negative predictive value	76%	89%
P-value	0.044	0.039

DISCUSSION

Diagnosis of primary or recurrent cholesteatoma is still a challenge, and the second look surgery remains the most reliable method to diagnose cholesteatoma in cases of recurrent disease, which may result in unnecessary surgery. Also a delayed diagnosis of patients may occur to avoid any additional surgery, as a result, the need for new imaging techniques has been raised to detect residual or recurrent cholesteatoma[6].

The usage of DW-MRI in diagnosis of cholesteatoma either primary or recurrent is growing rapidly in practice , and two DWI techniques have been used; echo planer and non-echo planer DW- MRI[7].

DW-MRI has a high sensitivity and specificity for detecting cholesteatoma; which is related to to the specific composition of cholesteatoma, where its high keratin content gives a hyper intense signal. It is known that cholesteatoma usually gives a moderately hyper intense signal on T2-weighted images and an isointense signal on T1-weighted images[5].

As regards to denovo cases, we found that DW-MRI had an accuracy of 81%, sensitivity 83%, specificity 75%, PPV 88%, and NPV 67%, which were nearly matched with de foer *et al*., in their study of 57 denovo cases, which had a sensitivity about 82.6%, specificity 87.2%, NPV 96%, and PPV 56.5%[5].

While, in recurrent cases, we found that DW-MRI had an accuracy of 78.5%, sensitivity 80%, specificity 75%, PPV 89%, and NPV 60% for detection of cholesteatoma. Aikele *et al*., in a study of 22 recurrent cases found that DW-MRI had a sensitivity of 77 %, specificity 100%, PPV 75%, and NPV 100%[8]. But, our results were not matched with Stasolla *et al*., in their study of 18 cases, where DW-MRI had a sensitivity of 86%, specificity 100%, NPV 100%, and PPV 92%[9].

Regarding to false +ve results in denovo cases, although there was a restriction in preoperative DW-MRI, we found a large tympanoscleroric patch in the middle ear with no cholesteatoma in one case. Also, in another case, the patient was presented with mastoid abscess, and we found pus and granulations in the middle ear with absence of cholesteatoma. While, in false -ve cases, we found small foci of cholesteatoma intra operatively although there was no restriction in preoperative DW-MRI (almost in all cases cholesteatoma was found to be less than 4-5 mm).

Regarding to false +ve results in recurrent cases, although there was a restriction in preoperative DW-MRI, in one case we found a large cartilage graft from the previous surgery with absence of cholesteatoma, and in another case which also presented with mastoid abscess, we found pus and granulations with absence of cholesteatoma, while, in false -ve cases, we found also some small foci of cholesteatoma intraoperatively in absence of restricted diffusion preoperatively.

There are some known conditions which may lead to a false-positive results with the DW-MRI such as presence of pus (as in mastoid abscess), mucous, surgically inserted materials and the bone marrow of a non-pneumatized temporal bone[10]. While the smaller sized cholesteatoma is the major cause for the false negative results as in a study done by dubrulle *et al*., who found that the size limit for detecting cholesteatoma by the DW-MRI was about 5 mm despite the absence of artifacts and the higher resolution of the sequences[11].

There is an evidence that cholesteatoma has lower ADC values than nonspecific tissues which is attributed to the presence of large amount of granulations and/or fibrosis in non cholesteatomatous diseases[12].

In our study, calculation of ADC value revealed a range of 0.1-1.7 with a median value about 0.8 mm^2/s.

In some cases, it was difficult to calculate ADC value due to the small size of cholesteatoma (less than 5 mm).

Our study nearly matched with Russo *et al*., in a study of 100 patients underwent preoperative DW-MRI 15 days before first- or second-look surgery, average ADC value for cholesteatoma was 0.85 mm^2/s[13]. Also, Cavaliere *et al*., in their study which aimed to detect the different ADC values of a cholesteatoma and a granulation tissue groups, and they found that there were a different ADC values for both groups with Statistically strong differences in ADC values between cholesteatoma (median 0.84 mm^2/s) and granulation tissues (median 2.21 mm^2/s) with a cut-off value of about 0.86[14].

As regards to validity of ADC in prediction of cholesteatoma, we found a cut-off point of about 0.8, with sensitivity of (80%), specificity (94%), PPV (93%) and NPV (82%) for the ADC.

Study limitations:

1. DW-MRI in the head and neck is still limited by some technical problems especially the susceptibility to artifacts and the low spatial resolution. Technical developments of DWI sequences with advanced coils in the field of > 3tesla MRI could overcome these disadvantages.

2. Artifact from air in the head may cause difficulty to measure ADC in small lesion.

3. Poor anatomical delineation of ADC map.

4. Qualitative method depends on the experience of the radiologist.

CONCLUSION

From our study and regarding to our results, we conclude that DW-MRI has an important role in diagnosis of either primary or recurrent cholesteatoma of the middle ear and some conditions such as the presence of surgically implanted material or pus may lead to a false positive results. Also, the small sized cholesteatomas may not be detected and ADC may not be calculated in these cases.

CONFLICT OF INTEREST

There are no conflicts of interest.

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