ORIGINAL ARTICLE

Diagnostic Capacity of Non-echo Planar Diffusion-weighted MRI in the Detection of Primary and Recurrent Cholesteatoma

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KEYWORDS
Cholesteatoma; Magnetic resonance imaging; Non-echo-planar diffusion-weight

Abstract

Introduction and aims: the aim of this study was to determine the certainty of non-echo-planar imaging diffusion-weighted magnetic resonance imaging (non-EPI DW MRI) in the diagnosis of primary and recurrent cholesteatoma in patients with clinical suspicion of cholesteatoma, assessing the sensitivity and specificity of the test in both groups.

Methods: Seventy-five patients with clinical suspicion of cholesteatoma were included in our study. Forty-eight cases had primary suspicion of cholesteatoma and 27 cases had recurrent suspicion of cholesteatoma. All patients received non-EPI DW MRI tests before surgery, and radiological and surgical findings were compared.

Results: Sensitivity, specificity and the positive and negative predictive value for primary diagnosis of cholesteatoma group were 91.2%, 50%, 81.6% and 70%, respectively. For the recurrent cholesteatoma group these results were 100%, 66.7%, 90.9% and 100%, respectively.

Conclusion: Non-echo-planar imaging diffusion-weighted magnetic resonance imaging is a high sensitivity imaging test for detecting cholesteatoma, for both primary diagnosis and for recurrent cases.

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Capacidad diagnóstica de la resonancia magnética con técnica de difusión no eco-planar en la detección de colesteatomas primarios y recurrentes

Resumen

Introducción y objetivos: El objetivo de este estudio es determinar la fiabilidad de la resonancia magnética con técnica de difusión no eco-planar en el diagnóstico de pacientes con sospecha clínica de colesteatoma primario y recurrente, evaluando la sensibilidad y especificidad de la prueba en ambos grupos.

Métodos: 75 pacientes con sospecha clínica de colesteatoma fueron incluidos en el estudio. 48 pacientes presentaban sospecha clínica de colesteatoma primario y 27 pacientes presentaban sospecha clínica de colesteatoma recurrente. En todos los pacientes se realizó una resonancia magnética con técnica de difusión no eco-planar previa a la cirugía, y se compararon los resultados radiológicos con los resultados quirúrgicos obtenidos.

Resultados: La sensibilidad, especificidad, valor predictivo positivo y negativo en el grupo de colesteatoma primario fue del 91,2%, 50%, 81,6% y 70% respectivamente y en el grupo de colesteatoma recurrente fue del 100%, 66,7%, 90,9% y 100%, respectivamente.

Conclusion: La RM con técnica de difusión no eco-planar es una prueba altamente sensible en el diagnóstico del colesteatoma tanto en pacientes con colesteatoma primario como en recurrencias.

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Introduction

Cholesteatoma is a destructive and expanding benign tumor that can produce bony erosion in middle ear, mastoid, petrous apex or external ear canal with subsequent appearance of complications. The diagnosis of cholesteatoma is based primarily on clinical examination. According to Pizzini et al. high-resolution computed tomography (CT) remains the radiologic method of choice to evaluate cholesteatoma. CT is an excellent image test to show anatomy but cannot differentiate between soft tissue middle ear pathologies and cholesteatoma. Non-echo-planar imaging (non-EPI) diffusion-weighted (DW) magnetic resonance imaging (MRI) shows a hyperintense lesion that is suspicious of cholesteatoma.

MRI has dramatically improved in the last two decades in the field of otolaryngology, acquiring high-definition images of the head and neck and particularly in the detection of cholesteatoma. There are different DW MRI techniques, which include echo-planar imaging (EPI) DW MRI and non-EPI DW MR, which are useful in the evaluation of primary or recurrent cholesteatoma. EPI DW MRI shows poor diagnostic value, because it is not able to demonstrate cholesteatoma when it is smaller than 5 mm due to artifacts and lower imaging matrix. On the other hand, non-EPI DW MRI improves the image quality. Actually, non-EPI DW MRI is the most sensitive and specific of all imaging techniques available for the diagnosis of cholesteatoma helping to develop criteria in surgical planning in some cases.

The purpose of this study is to compare the non-EPI DW MRI findings to the pathology after surgery, which, evidently, either confirms or excludes the diagnosis.

Materials and Methods

Patients

We performed a prospective study in a cohort of 75 consecutive patients who met criteria for clinical cholesteatoma. Patients were selected on an otology outpatient clinic and were divided into two groups according to the suspect of primary cholesteatoma or recurrent cholesteatoma. 48 patients (64%) were included in primary cholesteatoma group and 27 patients (36%) were included in recurrent cholesteatoma group.

We performed a non-EPI DW MRI in all of them. Every patient included in our study was operated on and pathologic study was performed in all of the cases. An experienced neurotologist surgeon performed all the surgical procedures included in the study. This study was approved by the clinical investigation ethics board of our hospital and it is adherent to the tenets of the Declaration of Helsinki of the World Medical Association on ethical principles for medical research involving human beings.

Inclusion criteria were clinical suspicion of primary cholesteatoma (on clinical examination by an ENT specialist) or suspicion of recurrent or residual cholesteatoma during follow-up after previous surgery.

Patient age, previous otology history, otoscopy, otology signs, hearing loss in audiogram, CT scan results, MRI DW results, surgery technique performed and histological findings after surgery were the recorded data.

Imaging Protocol

MRI was performed with a Philips Achieva 1.5T (Philips Medical Systems, Eindhoven, The Netherlands) and 8 channel
head coil. We obtained coronal diffusion DWI multishot turbo spin echo (b value=800, slice thickness 3 mm, TR=3000 ms, TE=82 ms, flip angle=90°, ECG-gating), coronal turbo spin echo T2 (5 mm slices, TR=3000 ms, TE=82 ms and a flip angle=90°); Axial T2 weight DRIVE_HR.SENSE focused in posterior fossa (0.6 mm slices, TR=1500 ms, TE=151 ms with flip angle=90°); Coronal Turbo spin echo T1 (3 mm slices, TR=550 ms, TE=15 ms, flip angle=90°) and Coronal Turbo spin echo T2 (3 mm slices, TR=4440 ms, TE=110 ms, flip angle=90°) focused in middle ear. No postgadolinium T1 weight images were used in our protocol.

**Imaging Interpretation**

Consultants from the Head and Neck Radiology Department interpreted non-EPI DW MRI. The criteria for the diagnosis of cholesteatoma at non-EPI DW MRI was based on the evidence of a hyperintense middle ear and/or mastoid lesion, compared with the signal intensity of the brain, on b=0/s/mm² images that persists or increases on high b value (800 s/mm²) images.

**Statistical Analysis**

Statistical analysis was performed by Statistic R Program version 3.0.1 for Windows. Parameters calculated of the performance of a diagnostic method were sensitivity (SS), specificity (SP) and positive and negative predictive values (PPV, NPV), including 95% confidence interval (CIs) for each value. A 2×2 contingency table was conducted for each comparison of test results (MRI) and diagnosis (pathologic findings). Final diagnosis was established with surgical findings in all cases.

**Results**

Non-EPI DW MRI was performed in 75 cases operated with confirmatory pathologic study. Non-EPI DW MRI was interpreted as negative in 14 cases and as positive in 61 cases. Pathologic findings showed the absence of cholesteatoma in 20 cases and confirmed cholesteatoma in 55 cases. 11 cases were true negative cases and 52 cases were true positive cases (Fig. 1). Therefore, 3 false negatives and 9 false positives were found. Total SS, SP, PPV and NPV were 0.945 (95% CI, 0.849, 0.989), 0.55 (95% CI, 0.315, 0.769), 0.852 (95% CI, 0.738, 0.930) and 0.786 (95% CI, 0.492, 0.953) respectively. Results are summarized in Table 1.

**Discussion**

Cholesteatoma is a disease with a high recurrence rate. Therefore an accurate diagnostic method would be valuable for a correct confirmation before surgical revision. CT is incapable to determine the presence of cholesteatoma and differentiate it from other inflammatory disorders with a poor sensitivity and specificity (42% and 48% respectively).\(^1\) EPI sequence and post-gadolinium MRI were previously helpful in cases where there was a doubt, but they had important technical difficulties as poor spatial resolution and the presence of artifacts at the skull base air–bone interface.\(^1\) Non-EPI DW MRI has overcome these technical difficulties and it is now a highly sensitive and specific way to detect cholesteatoma (Table 2). However, the capacity of non-EPI DW MRI to detect cholesteatoma could be different in patients with primary cholesteatoma\(^3,13,14\) and with recurrent cholesteatoma.\(^3,14,15\) Non-EPI DW MRI has proved useful to avoid second look surgery or after previous cholesteatoma surgery when traditional imaging methods cannot be able to detected cholesteatoma recurrence,\(^7\) but in primary cholesteatoma some clinical protocols are selecting CT as the method of choice,\(^1\) leaving non-EPI DW MRI as further imaging test in certain cases. Pizzini et al. demonstrated

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Test Results for DW MRI.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DW MRI</td>
</tr>
<tr>
<td></td>
<td>Total</td>
</tr>
<tr>
<td>PA</td>
<td>+</td>
</tr>
<tr>
<td>–</td>
<td>11</td>
</tr>
<tr>
<td>+</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
</tr>
</tbody>
</table>

PA: pathology; –: negative; +: positive.
a SS, SP, PPV and NPP of 100% in 17 patients with primary and 13 patients with relapsing cholesteatoma. Profant et al. reported 33 patients, 16 of them diagnosed with primary cholesteatoma and 17 patients with recurrent cholesteatoma and suggested that it is preferable to use non-EPI DW MRI in revision surgery, because both false positive (two cases) and false negative (one case), occurred in the primary cholesteatoma diagnostic group. We found non-EPI DW MRI useful with a high sensitivity in both situations, primary and recurrent cholesteatoma (91.2% and 100% respectively).

We reported a lower SP in primary and recurrent cholesteatoma group (50% and 66.7% respectively) when comparing with others studies (Table 2). Low specificity is due to the high number of false positives that we describe in our study. We described 9 false positive due bone dust in one case as Dubrulle published in 2006, an abscess in one case as Kasbekar published in his study and six patients without the presence of cholesteatoma in surgery. One false positive case was a 57-year-old patient with clinical suspicion of cholesteatoma in which MRI was interpreted as an enhanced lesion in right ear. Cholesteatoma was not found during surgery and diagnosis on squamous cell carcinoma of auditory ear canal was confirmed by pathological analysis. Also 3 false negative were obtained in our study because of 2 questionable lesions with doubtful hyperintensity in non-EPI DW MRI and 1 false negative case with small pearl of cholesteatoma that non-EPI DW MRI could not detect before surgery.

Some authors have reviewed the diagnostic capacity of non-EPI DW MRI. There is a systematic review from Jindal et al. with non-EPI DW MRI studies that includes a total of 207 patients from various studies and also, a meta-analysis from Li et al. that includes a total of 342 patients from 10 studies. Jindal reported a SS of 91%, SP of 96%, PPV of 97% and NPV of 85% and Li reported a SS of 0.94 (95% confidence interval, 0.80–0.98) and SP of 0.94 (95% confidence interval, 0.85–0.98). These articles present a high number of cases, but both have the same limitation of gathering different studies, each of them

<table>
<thead>
<tr>
<th>Authors</th>
<th>No.</th>
<th>DW MRI</th>
<th>SS</th>
<th>SP</th>
<th>PPV</th>
<th>NPV</th>
<th>Size limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dubrulle et al. (2006)</td>
<td>24</td>
<td>Non-EPI</td>
<td>100</td>
<td>91</td>
<td>93</td>
<td>100</td>
<td>5</td>
</tr>
<tr>
<td>De Foer et al. (2010)</td>
<td>63</td>
<td>Non-EPI</td>
<td>83</td>
<td>87</td>
<td>96</td>
<td>57</td>
<td>NA</td>
</tr>
<tr>
<td>Dhepnorrarat et al. (2009)</td>
<td>22</td>
<td>Non-EPI</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>3</td>
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<tr>
<td>Huins et al. (2010)</td>
<td>18</td>
<td>Non-EPI</td>
<td>86</td>
<td>100</td>
<td>100</td>
<td>67</td>
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<tr>
<td>Pizzini et al. (2010)</td>
<td>11</td>
<td>Non-EPI</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>2</td>
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<tr>
<td>Rajan et al. (2010)</td>
<td>15</td>
<td>Non-EPI</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>3</td>
</tr>
<tr>
<td>Plouin-Gaudon et al. (2010)</td>
<td>17</td>
<td>Non-EPI</td>
<td>62</td>
<td>88</td>
<td>89</td>
<td>58</td>
<td>4</td>
</tr>
<tr>
<td>Lehman et al. (2009)</td>
<td>10</td>
<td>Non-EPI</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>3</td>
</tr>
<tr>
<td>Khemani et al. (2011)</td>
<td>36</td>
<td>Non-EPI</td>
<td>82</td>
<td>90</td>
<td>96</td>
<td>64</td>
<td>3</td>
</tr>
<tr>
<td>Profant et al. (2012)</td>
<td>33</td>
<td>Non-EPI</td>
<td>96.15</td>
<td>71.43</td>
<td>92.59</td>
<td>83.33</td>
<td>3</td>
</tr>
<tr>
<td>Lingam et al. (2013)</td>
<td>72 episodes (56 patients)</td>
<td>Non-EPI</td>
<td>91</td>
<td>88</td>
<td>-</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>Kasbekar et al. (2011)</td>
<td>19</td>
<td>Non-EPI</td>
<td>43−71</td>
<td>92−58</td>
<td>75−50</td>
<td>73−78</td>
<td>4</td>
</tr>
</tbody>
</table>

Non-EPI: non-echo-planar imaging; DW MRI: diffusion-weight magnetic resonance; SS: sensibility; SP: specificity; PPV: positive predictive value; NPV: negative predictive value; non-EPI: non-echo-planar imaging; NA: not available; size limit: mm.
with small numbers, in which not every patient had surgical confirmation. Also, each study had its own technical settings for MRI studies. In our opinion these compromises the validity of the results of the meta-analysis. We present a comparison between primary cholesteatoma and recurrent cholesteatoma group with a uniform protocol, and pathologic confirmation in all cases, which could make our data more reliable.

Comparison between primary and recurrent cholesteatoma group concluded that differences were not statisically significant in our study, maybe because groups have no similar number of cases (primary cholesteatoma group have more than double number of patients than recurrent cholesteatoma group). Thus, more studies with a greater number of patients could provide more information in the future.

Other limitations of our study was not to determinate the size of the cholesteatoma in non-EPI DW MRI as De Foer.9 We did not use ADC value on our non-EPI DW MRI sequence. Lingam et al. described that the use of apparent diffusion coefficient value (ADC) improves the already high specificity, allowing for the correct identification of two out of three false positive cases.23 We did not estimate the location of cholesteatoma, as performed by Khemani et al.24 Also, the use of a 1.5 T MRI scanner, that is not the most commonly used scanner in clinical practice, is a limitation to consider in the study.

Conclusion

This study was aimed to compare the non-EPI DW MRI diagnostic capacity to the pathologic findings obtained in surgery. We found non-EPI DW MRI to be a highly sensitive test to detect cholesteatoma, both for primary diagnosis and for recurrent cases. Therefore we suggest that non-EPI DW MRI be used as a screening tool in patients with suspect of primary and recurrent cholesteatoma to help to obtain a certain diagnosis and avoid unnecessary surgery when possible.

Conflicts of Interest

The authors declare that they have no conflict of interest.

References

7. De Foer B. Non echo planar, diffusion-weighted magnetic resonance imaging (periodically rotated overlapping parallel lines with enhanced reconstruction sequence) compared with echo planar imaging for the detection of middle-ear cholesteatoma. J Laryngol Otol. 2011;125:877–8, author reply 8.

