Original article

Contribution of magnetic resonance imaging to the diagnosis of middle ear cholesteatoma: Analysis of a series of 97 cases

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\begin{abstract}
Objectives: To evaluate the reliability of magnetic resonance imaging (MRI) for the diagnosis of middle ear cholesteatoma and to determine the contribution of each MRI sequence.

Patients and methods: A series of 97 cases was reviewed, corresponding to 89 patients (43 women, 46 men). Each patient was assessed by the following MRI protocol: T1-weighted, T2-weighted, early contrast-enhanced T1-weighted, delayed contrast-enhanced T1-weighted, and diffusion-weighted sequences. All patients were operated, for the first time in 16 cases and for second-look surgery in 81 cases.

Radiological findings were compared to surgical and histological findings. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated for each sequence.

Results: Seventy-four cholesteatomas were diagnosed at surgery. These lesions had a mean diameter of 8.29 ± 5.46 mm. The smallest cholesteatoma in this series was 2 mm in diameter. Diffusion-weighted and delayed contrast-enhanced T1-weighted sequences had a sensitivity of 84.9% and 90.4%, a specificity of 87.5% and 75%, a positive predictive value of 95.4% and 91.7%, and a negative predictive value of 65.6% and 72%, respectively. T1-weighted, T2-weighted, and early contrast-enhanced T1-weighted sequences had a low specificity.

Conclusions: MRI is a reliable imaging modality for the diagnosis of middle ear cholesteatoma. Diffusion-weighted and delayed contrast-enhanced T1-weighted sequences were discriminant. In the context of postoperative follow-up of cholesteatoma, these sequences allow better selection of cases requiring second-look surgery.

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\end{abstract}

1. Introduction

Middle ear cholesteatoma is defined as the presence of keratinized squamous epithelium in the middle ear cavities. In the vast majority of cases, the positive diagnosis of cholesteatoma is based exclusively on clinical examination, especially otoscopic findings. Computed tomography (CT) is recommended in the context of preoperative assessment of cholesteatoma [1] in order to exclude osteitis complications, to try to specify extensions of the cholesteatoma and to evaluate the anatomical conformation of the tympanomastoid cavity. In some cases, when the diagnosis cannot be confirmed by clinical examination alone, CT scan can provide arguments in favour of cholesteatoma by showing opacity with rounded contours associated with adjacent osteolysis [2].

The treatment of cholesteatoma is surgical, based on two techniques, called canal wall up (CWU) and canal wall down (CWD) tympanoplasty. CWU tympanoplasty ensures a more comfortable postoperative course for the patient, but is associated with a higher residual cholesteatoma rate [3]. Tympanic membrane grafting also prevents satisfactory otoscopic surveillance. For these reasons, systematic second-look surgery was performed 12 to 18 months after a first CWU tympanoplasty to detect and treat any residual lesions.

Computed tomography, as well as conventional morphological magnetic resonance imaging (MRI) T1-weighted, T2-weighted, and early contrast-enhanced T1-weighted sequences have been shown to present a number of limitations for the surveillance of patients operated for middle ear cholesteatoma [4].

Over the last decade, a number of studies have tended to demonstrate the capacity of new MRI sequences to distinguish cholesteatoma from other types of postoperative opacities,
questioning the need for systematic second-look surgery: delayed contrast-enhanced T1-weighted sequences 45 to 60 minutes after gadolinium injection [5,6] and diffusion-weighted imaging (DWI) [7].

In this study, we tried to evaluate the contribution of each MRI sequence and combinations of the various sequences to the diagnosis of middle ear cholesteatoma based on systematic surgical confirmation of imaging findings.

2. Patients and methods

A single-centre, prospective, longitudinal study was conducted from June 2004 to January 2011 in a series of 89 patients (43 women and 46 men, M/F sex ratio: 1.07), with a mean age of 41 ± 21 years at the time of MRI. All patients presented an indication for middle ear surgery in the context of management of cholesteatoma (first surgery or second-look surgery). All patients were assessed by preoperative temporal bone MRI in the same neuroradiology department on a Siemens Avanto 1.5 Tesla machine (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany) or a Siemens Sonata 1.5 Tesla machine (Magnetom Sonata, Siemens Medical Solutions, Erlangen, Germany). The following protocol was systematically applied: axial and/or coronal unenhanced T1-weighted spin echo sequences, axial and/or coronal T2-weighted spin echo sequences, coronal and axial early contrast-enhanced T1-weighted fat-saturated spin echo sequences, coronal and axial early contrast-enhanced T1-weighted fat-saturated spin echo sequences 30 to 60 minutes after gadolinium injection, coronal or axial diffusion-weighted imaging, with axial echo planar imaging (EPI) sequences (sonata machine) or coronal non-echo planar imaging half Fourier single-shot turbo spin echo (EPI HASTE) sequences (Avanto machine), with a b value of 1000 mm²/s, without measuring the apparent diffusion coefficient. MRI images were interpreted before surgery by the senior radiologist in charge of the examination. Each examination was interpreted by a single radiologist. A total of five different radiologists, all experienced in the interpretation of temporal bone imaging, were involved in the study. The various MRI sequences were not interpreted separately and, when necessary, were overlayed with lesion marking by software provided by the manufacturer. The size of the lesions was determined on DWI.

All patients were operated by the same surgical team. The mean interval between MRI and surgery was 4 months. All data concerning the surgical procedure were retrieved from the operation report. The presence or absence of cholesteatoma was recorded and constituted the “gold standard” for the detection of cholesteatoma in this study, and was used as the basis for all statistical analyses. Cases of hyperkeratosis and retraction pockets filled with squames (precholesteatomatous state) were classified with true cholesteatomas. The presence of other abnormalities such as fibrosis, inflammation, cholesterol granuloma, meningoecele, or abscess was also noted. Histological examination was performed to confirm the diagnosis. Two separate operations on the same ear were performed in eight patients and MRI was performed before each of these operations, resulting in a total cohort of 97 cases. Sixteen cases (16.49%) were operated for the first time and the ear had been previously operated in 81 cases (83.51%). The mean interval between the date of previous surgery and MRI for these 81 cases was 31 months.

Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) values for each MRI sequence were calculated (together with their 95% confidence intervals) on the basis of operative findings. The results of the “EPI DWI” and “Non-EPI DWI” groups were analysed separately and the areas under the ROC curve ([(Se + Sp)]/2) were compared between the two groups. A similar analysis was also performed between “first surgery” and “previously operated ear” groups.

The normal distribution of quantitative variables was verified by the Shapiro-Wilk test; quantitative data were compared between groups by Student’s test or Mann-Whitney test when the condition of Student’s test were not met. Qualitative parameters were compared by Fisher’s exact test or Chi-square test.

All analyses were performed with a type 1 error of 5% using STATA v.10 software (Stata Corp).

3. Results

Seventy-four cases of cholesteatomatous lesions were diagnosed during surgery, i.e. in 76.29% of cases. These cases included 63 cholesteatomas (Fig. 1), five cases of hyperkeratosis, two cholesteatomas associated with cholesterol granuloma, and four retraction pockets filled with squames. Another 23 cases (23.71%) presented inflammatory lesions in eight cases, fibrotic lesions in 11 cases, a simple retraction pocket in one case, one mastoid abscess, one meningoecele, and total absence of lesions in one case. Histological examination was performed in 88 of the 97 cases and confirmed the surgical findings in every case. All MRI characteristics of middle ear cholesteatoma and its differential diagnoses are summarized in Table 1.

The lesions detected had a mean diameter of 8.29 ± 5.46 mm. The smallest cholesteatoma measured 2 mm in diameter (Fig. 2) and the largest cholesteatoma measured 25 mm in diameter. T1-weighted, T2-weighted, and early contrast-enhanced T1-weighted sequences presented a sensitivity of 98.6, 91.8 and 95.9%, and a specificity of 4.2, 20.8 and 29.2%, respectively. DWI and delayed contrast-enhanced T1-weighted sequences had a sensitivity of 84.9% and 90.4%, a specificity of 87.5% and 75%, a positive predictive value of 95.4% and 91.7%, and a negative predictive value of 65.6% and 72%, respectively. Se, Sp, PPV, and NPV values for each sequence are presented in Table 2 together with their 95% confidence intervals.

Enhancement of a peripheral rim on delayed contrast-enhanced T1-weighted sequences of cholesteatoma was present in only 30 (40.5%) of the 74 cases.

Diffusion-weighted imaging (DWI) sequences were acquired by EPI in 10.3% of cases and non-EPI HASTE in 89.7% of cases. In the “EPI DWI” group, DWI had a sensitivity of 57.1% [18.4–90.1], a specificity of 100% [29.2–100], a positive predictive value of 100% [39.8–100], a negative predictive value of 50% [11.8–88.2], and an area under the ROC curve of 0.79 [0.59–0.98]. In the “Non-EPI DWI” group, DWI had a sensitivity of 87.9% [77.5–94.6], a specificity of 85.7% [63.7–97], a positive predictive value of 95.1% [86.3–99], a negative predictive value of 69.2% [48.2–85.7], and an area under the ROC curve of 0.87 [0.78–0.95]. Comparison of areas under the ROC curve revealed a significant difference between the two groups (P < 0.05).

No significant difference was observed between the “first surgery” and “previously operated ear” groups.

The two cases of cholesterol granuloma were associated with cholesteatoma, with a false-negative result in one case: radiological diagnosis of isolated granuloma, while the associated cholesteatoma was not detected. Two false-negatives were observed among the five cases of hyperkeratosis (6.75% of all cholesteatomatous lesions) and one false-negative was observed among the four cases of retraction pockets filled with squames. The case of mastoid abscess corresponded to a false-positive, in the context of a lesion measuring 28 mm in diameter. One case of isolated meningoecele was correctly diagnosed on the frontal T1-weighted sequence. Discordant results between DWI (absence of high-intensity signal) and the delayed contrast-enhanced T1-weighted sequences (absence of enhancement) were observed in four cases, in which the intraoperative diagnosis was cholesteatoma.
Fig. 1. MRI of the left temporal bone, coronal section: isointense signal of the left lateral attic on unenhanced T1-weighted sequence (A), hyperintense signal on the T2-weighted sequence (B), with no gadolinium enhancement, even at the late phase (C), and hyperintense signal on DWI (D). Typical appearance of residual cholesteatoma.

<table>
<thead>
<tr>
<th>Disease</th>
<th>T1 signal</th>
<th>T2 signal</th>
<th>Early contrast-enhanced</th>
<th>Delayed contrast-enhanced</th>
<th>DWI signal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesteatoma</td>
<td>Iso/Hypo</td>
<td>Hyper</td>
<td>No</td>
<td>No</td>
<td>Hyper</td>
</tr>
<tr>
<td>Abscess</td>
<td>Hypo</td>
<td>Hyper</td>
<td>No</td>
<td>No</td>
<td>Hyper</td>
</tr>
<tr>
<td>Cholesterol granuloma</td>
<td>Hyper</td>
<td>Hyper</td>
<td>No</td>
<td>No</td>
<td>Hypo</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>Iso/Hypo</td>
<td>Hyper</td>
<td>No</td>
<td>Yes</td>
<td>Hypo</td>
</tr>
<tr>
<td>Inflammation</td>
<td>Iso/Hypo</td>
<td>Hyper</td>
<td>Yes</td>
<td>Yes</td>
<td>Hypo</td>
</tr>
</tbody>
</table>

4. Discussion

Studies on the role of conventional T1-weighted, T2-weighted, and early contrast-enhanced T1-weighted MRI sequences in the surveillance of operated cholesteatoma have demonstrated that inflammatory tissue and cholesterol granuloma can be easily diagnosed on these sequences [8] (Table 1), but that cholesteatoma and fibrosis are more difficult to diagnose. In 1999, based on a

Table 1
Signals observed on MRI after middle ear surgery according to the various tissues.

<table>
<thead>
<tr>
<th>Disease</th>
<th>T1 signal</th>
<th>T2 signal</th>
<th>Early contrast-enhanced</th>
<th>Delayed contrast-enhanced</th>
<th>DWI signal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesteatoma</td>
<td>Iso/Hypo</td>
<td>Hyper</td>
<td>No</td>
<td>No</td>
<td>Hyper</td>
</tr>
<tr>
<td>Abscess</td>
<td>Hypo</td>
<td>Hyper</td>
<td>No</td>
<td>No</td>
<td>Hyper</td>
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<tr>
<td>Cholesterol granuloma</td>
<td>Hyper</td>
<td>Hyper</td>
<td>No</td>
<td>No</td>
<td>Hypo</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>Iso/Hypo</td>
<td>Hyper</td>
<td>No</td>
<td>Yes</td>
<td>Hypo</td>
</tr>
<tr>
<td>Inflammation</td>
<td>Iso/Hypo</td>
<td>Hyper</td>
<td>Yes</td>
<td>Yes</td>
<td>Hypo</td>
</tr>
</tbody>
</table>

Table 2
Sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV) of each MRI sequence expressed as percentage and 95% confidence interval.

<table>
<thead>
<tr>
<th></th>
<th>T1 (%)</th>
<th>T2 (%)</th>
<th>Early contrast-enhanced T1 (%)</th>
<th>Delayed contrast-enhanced T1 (%)</th>
<th>DWI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Se</td>
<td>98.6 [92.6–100]</td>
<td>91.8 [83–96.9]</td>
<td>95.9 [88.5–99.1]</td>
<td>90.4 [81.2–96.1]</td>
<td>84.9 [74.6–92.2]</td>
</tr>
<tr>
<td>Sp</td>
<td>4.2 [0.1–21.1]</td>
<td>20.8 [7.1–42.2]</td>
<td>29.2 [12.6–51.1]</td>
<td>75.0 [53.3–90.2]</td>
<td>87.5 [67.6–97.3]</td>
</tr>
<tr>
<td>PPV</td>
<td>75.8 [65.9–84]</td>
<td>77.9 [67.7–86.1]</td>
<td>80.5 [70.6–88.2]</td>
<td>91.7 [82.7–96.9]</td>
<td>95.4 [87.1–99.0]</td>
</tr>
<tr>
<td>NPV</td>
<td>50 [13–98.7]</td>
<td>45.5 [16.7–76.6]</td>
<td>70 [34.8–93.3]</td>
<td>72.0 [50.6–87.9]</td>
<td>65.6 [46.8–81.4]</td>
</tr>
</tbody>
</table>
series of 18 patients, Van den Abeele et al. [9] reported a sensitivity of 14.23%, while Williams et al. [5] reported a specificity of 33% for early contrast-enhanced T1-weighted sequences for the detection of residual cholesteatoma. Delayed contrast-enhanced T1-weighted sequences and DWI were not used in these two studies. In the present series, the main limitation of T1-weighted, T2-weighted, and early contrast-enhanced T1-weighted sequences concerned their low specificity (Table 2), in line with the data of the literature. The main value of the unenhanced T1-weighted sequence is for detection of cholesterol granuloma, while the T2-weighted sequence constitutes a morphological sequence for localization of the cholesteatoma in combination with DWI.

Two main studies [5,6] have demonstrated an improvement of the specificity and NPV for the detection of residual cholesteatoma following CWU tympanoplasty by the use of delayed contrast-enhanced T1-weighted sequences. For example, Ayache et al. [6], reported the following values: Se: 90%, Sp: 100%, PPV: 100% and NPV: 92%. Our results are concordant with these data. However, a number of lesions, although presenting radiological criteria for cholesteatoma, would not have been detected without DWI, essentially for reasons of size. Williams [5] and Ayache [6] already concluded in their respective publications that the limit of the technique was related to the size of the lesion, while emphasizing the fact that missing a lesion smaller than 3 mm would be associated with a very low risk in view of the slow growth rate of cholesteatoma [10], which would eventually be detected by subsequent MRI follow-up. Venail et al. [11] estimated the mean growth rate of residual cholesteatoma to be 2.74 mm per year.

The first reported use of diffusion-weighted imaging for the diagnosis of residual cholesteatoma was published in 2002 [12]. Stasolla et al. [13], who compared EPI DWI with conventional MRI sequences, reported the following values: Se 92% versus 92%, Sp 100% versus 25%, PPV 100% versus 55%, NPV 92% versus 75%. Venail et al. [11] reported the following values: 60%, Sp 72.73%, PPV 80%, NPV 50%, with a significant increase of these values when the analysis was confined to lesions larger than 5 mm. Highly discordant results have been published in the literature; in 2009, Doshi et al. [14] highlighted the difficulty of comparing the various studies using EPI DWI due to the variability of the imaging parameters and technique used. Another explanation for these discordant results, according to Venail et al. [11], is the marked variability of the size of cholesteatomatous recurrences studied. Our data are in line with those of the most recent literature [1,15], with values tending to demonstrate that DWI is a reliable examination for the surveillance of operated cholesteatoma.

Published studies have mainly concerned the surveillance of previously operated cholesteatomas, as the initial diagnosis of middle ear cholesteatoma is essentially based on clinical examination.

Fig. 2. MRI of the left temporal bone, coronal section: isointense signal of the left lateral attic on unenhanced T1-weighted sequence (A), hyperintense signal on the T2-weighted sequence (B), with no gadolinium enhancement, even at the late phase (C), and hyperintense signal on DWI (D). Left attic cholesteatoma 2 mm in diameter.
systematically completed by preoperative CT assessment. Fitzek et al. [16], in 2002, analysed the results of DWI for the detection of primary cholesteatoma and concluded that EPI DWI was useful in this indication, but that it could not replace other imaging modalities, especially CT. No significant difference was observed in our series between nonoperated and previously operated patients. We can therefore conclude that DWI is a reliable technique in both settings. DWI should not be systematically performed prior to first surgery[1], but can constitute a valuable aid to diagnosis in doubtful cases.

Comparing EPI and non-EPI DWI, De Foer et al. [17] reported that non-EPI turbo spin echo sequences were more reliable than EPI sequences. In a review of the literature published in 2011, Jindal et al. [18] compared the results of eight studies on EPI DWI versus eight studies on non-EPI DWI, by pooling the sensitivity, specificity, negative predictive and positive predictive values for each group of studies and demonstrated the superiority of non-EPI DWI over EPI DWI, in line with the results of our study.

In 2003, Aikele et al. [19] defined the limit of detection of EPI DWI to be lesions with a diameter of 5 mm. In 2005, Ayache et al. reported a limit of detection of 3 mm only on delayed contrast-enhanced T1-weighted sequences. In 2007, De Foer et al. [20] proposed a limit of 2 mm with non-EPI DWI and, in our study, the smallest lesion detected by DWI was 2 mm in diameter and was also visible on the delayed contrast-enhanced T1-weighted sequence. However, this limit of detection must be interpreted cautiously, as DWI is not a morphological sequence and is therefore not appropriate for precise measurements.

Venail et al. [11] reported an improvement of the sensitivity of MRI for small lesions by combining delayed contrast-enhanced T1-weighted and DWI sequences (55.56% versus 33.33% and 44.44% separately). They also considered that image analysis of contrast-enhanced sequences required more experience than image analysis of DWI images. Several publications have reported this combination of sequences to be the most efficient [11,21], with a risk of diagnostic error in the case of isolated analysis of DWI [15]. Moreover, DWI was incriminated in the four cases of discordant results between the two sequences observed in our study. Systematic acquisition of the two sequences in our series achieved a satisfactory level of reliability, as the diagnosis, essentially based on DWI data, was confirmed by the delayed contrast-enhanced T1-weighted sequence, while the approximate site visualized on DWI was more clearly defined by the delayed contrast-enhanced T1-weighted and T2-weighted sequences.

Other authors have proposed abandoning the use of gadolinium-enhanced sequences. In a study published in 2010, Rajan et al. [22] reported a paediatric series of 15 patients examined by HASTE DWI (non-EPI) before second-look surgery. Se, Sp, PPV, NPV values were all 100%. These authors concluded that HASTE DWI is a technique of choice in paediatric populations, especially as it is a rapid examination, without the need for injection and not requiring general anaesthetic. In 2010, De Foer et al. [23] conducted a retrospective study of the value of non-EPI DWI, delayed contrast-enhanced T1-weighted sequence, and a combination of the two sequences for the detection of cholesteatoma in a group of never-operated patients (57 cases) and a group of patients requiring second-look surgery (63 cases). Blinded image review was performed by four radiologists, who did not find any significant improvement of Se, Sp, PPV, and NPV when the two sequences were combined compared to DWI alone. The authors consequently recommended abandoning the use of gadolinium–enhanced sequences in this indication, confining the examination to T1-weighted, T2-weighted, and DWI sequences.

Recent data of the literature tend to prove that MRI, especially DWI, allows more reliable selection of patients requiring second-look surgery [3,23] and the results of the present study are in agreement with the literature. Clark et al. [24] also emphasized the fact that all patients with reassuring MRI, who were therefore not operated, must continue to be followed to exclude a possible lesion smaller than the limits of detection. This strategy does not question our conclusions, in view of the low invasive potential of a lesion measuring less than 2 mm. No consensus has been reached concerning the duration of surveillance; the Société française d’ORL et chirurgie cervico faciale report [25] recommends first follow-up imaging 18 months after surgery. In the absence of any residual lesion, and when the patient remains asymptomatic, imaging should be repeated 12 to 24 months later to exclude the hypothesis of a false-negative first MRI.

5. Conclusion

This study demonstrates the good reliability of MRI for the diagnosis of middle ear cholesteatoma. The key sequence is non-EPI DWI, which has a limit of detection of 2 mm, but a poor lesion localizing capacity, requiring the combined use of a more morphological sequence. The reliability of MRI is equivalent in the setting of nonoperated or previously operated cholesteatoma. The delayed contrast-enhanced T1-weighted sequence is the second discriminant sequence for the detection of cholesteatoma. It is the sequence of choice to confirm the diagnosis when no obvious signal is detected on DWI and it also has a good localizing capacity. T1-weighted, T2-weighted, and T1 early contrast-enhanced T1-weighted sequences have a low specificity.

MRI has a limited place in the initial assessment of nonoperated cholesteatoma: confirmation of the diagnosis in the rare doubtful cases, suspicion of neurotympanic or labyrinthine complications. In the context of follow-up of operated cholesteatoma, MRI allows better selection of patients requiring second-look surgery.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


