The Role of Diffusion-Weighted Magnetic Resonance Imaging in Cholesteatoma Diagnosis and Follow-up: Study With the Diffusion PROPELLER Technique

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KEYWORDS
Cholesteatoma; Diffusion magnetic resonance imaging; Tympanoplasty

Abstract

Introduction and objectives: The diagnosis of cholesteatoma is based on clinical evaluation and computed tomography. New non-echo-planar diffusion-weighted magnetic resonance imaging (MRI) techniques, without intravenous contrast, are capable of differentiating cholesteatoma from inflammatory tissue, cholesterol granuloma and granulation tissues. The technique is very helpful in differential diagnosis of cholesteatoma, mainly after canal wall-up tympanoplasty surgery, to avoid routine second-look surgery in these patients. Congenital cholesteatoma and difficult cases can be detected and correctly diagnosed as well. The aim of this study was to evaluate sensitivity, specificity, positive predictive value and negative predictive value of the diffusion-weighted PROPELLER MRI in cholesteatoma diagnosis.

Methods: A prospective study was performed on 52 patients. Clinical and surgical findings were correlated with diffusion-weighted PROPELLER MRI results.

Results: Sensitivity, specificity and positive and negative predictive values were 92.85%, 92.30%, 92.85% and 92.30%, respectively.

Conclusions: Diffusion-weighted PROPELLER imaging is an effective technique in cholesteatoma diagnosis. It is capable of detecting lesions larger than 2 mm.

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PALABRAS CLAVE
Colesteatoma; Resonancia magnética de difusión; Timpanoplastia

Papel de la resonancia magnética de difusión en el diagnóstico y seguimiento del colesteatoma. Estudio con la técnica PROPELLER difusión

Resumen
Introducción y objetivos: El diagnóstico del colesteatoma se basa en los hallazgos clínicos y en la tomografía computarizada. Actualmente, con las nuevas técnicas de resonancia magnética potenciada en difusión no ecoplanar, sin necesidad de contraste intravenoso, es posible diferenciar entre colesteatoma y tejido de granulación o inflamatorio. Por ello, esta técnica muestra su máxima utilidad en la valoración de recidivas de colesteatoma tras timpanoplastías, sobre todo en técnicas cerradas, ya que puede evitar un alto porcentaje de cirugías de revisión. Otras indicaciones de la técnica son los casos de diagnóstico complejo y el colesteatoma congénito. El objetivo de este estudio es valorar la validez (sensibilidad y especificidad) y la seguridad (valor predictivo positivo y valor predictivo negativo) de la secuencia de difusión PROPELLER, una de las técnicas potenciadas en difusión no ecoplanar en el diagnóstico del colesteatoma.

Métodos: Estudio prospectivo de 52 pacientes con sospecha de colesteatoma en el que se correlacionan hallazgos clínicos y quirúrgicos con los obtenidos del estudio de resonancia magnética, que incluía una secuencia potenciada en difusión no ecoplanar (PROPELLER) de oídos.

Resultados: La sensibilidad de la prueba para el grupo fue del 92,85%, la especificidad del 92,30%, el valor predictivo positivo del 92,85% y el valor predictivo negativo del 92,30%.

Conclusiones: La resonancia magnética con imagen potenciada en difusión no ecoplanar utilizando la secuencia PROPELLER, es una técnica eficaz en el control del colesteatoma, permitiendo diagnosticar lesiones mayores de 2 mm.

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Introduction

Cholesteatoma is a pseudotumoural lesion composed of an active matrix which forms accumulations of keratinised, stratified epithelium in its interior and which grows in the form of concentric layers. This expansive growth entails the destruction of surrounding bone structures. If the disease progresses, it may affect the facial nerve and inner ear, and cause intracranial complications.1

For this reason, early diagnosis and detection of tumour recurrence in operated patients are essential for an adequate treatment of the disease.

The diagnosis of cholesteatoma is based on clinical findings, in which otoscopy and otomicroscopy play a major role in conjunction with radiological findings. Computed tomography (CT) is the technique of choice.

CT enables visualisation of bone structures with high spatial resolution, detecting minimal erosions on the ossicles and walls of the tympanic cavity. Such findings are highly specific of cholesteatoma and lead to a correct diagnosis in most cases of acquired cholesteatoma. However, its lower tissue resolution compared with magnetic resonance imaging (MRI) does not enable the nature of soft tissues to be identified (inflammatory, granulation or scar tissue and cholesteatoma).2

Classically, MRI has only been indicated for the diagnosis of complications: abscesses, meningitis, lateral sinus thrombophlebitis, etc.

In cases of acquired cholesteatomas in atypical locations or those without clear bone erosion, congenital cholesteatomas and especially in ear surgery, where bone references are lost, a technique with a high capacity of tissue discrimination, such as MRI, acquires a high diagnostic value.

MRI diffusion techniques, whose use is now widespread in brain studies, were first used in the late 90s for the diagnosis of acute cerebral ischaemia.3 Subsequently, they showed high specificity in the diagnosis of pyogenic abscesses and intracranial epidermoid cysts. They are based on measuring molecular diffusion (Brownian motion), a random motion observed in some microscopic particles within a fluid medium.4 The speed of movement of water molecular diffusion is markedly restricted under certain conditions, such as ischaemia or acute pyogenic abscesses. This restriction is manifested as an intense brightness or shine in diffusion sequences, which can be quantified using image post-processing techniques. These result in an apparent diffusion coefficient (ADC) for each of the pixels which form the diffusion-enhanced image (DEI), known as ADC maps. In addition to restricting diffusion, the residual T2 brightness of some lesions may result in DEI hyperintensity. Obtaining ADC maps enables the 2 causes of DEI hyperintensity to be differentiated. As described below, such differentiation is of great interest in the differential diagnosis between cholesteatoma (which restricts diffusion) and middle ear cholesterol granulomas (which do not show restriction of diffusion and, conversely, show a residual T2 brightness).

Cholesteatomas, like intracranial epidermoid cysts, are characterised by their intense brightness in diffusion sequences (Fig. 1), which is therefore highly specific for these entities. The literature contains multiple discussions on whether this hyperintensity is due to the restriction of molecular diffusion in the interior or to T2 residual brightness.3,5,6 ADC values are clearly inferior to those of other entities, such as inflammatory granulation tissue or middle ear cholesterol granuloma, and this point indicates at least some degree of diffusion restriction. In any case, in the appropriate clinical context and location, this is a
highly specific technique for the diagnosis of cholesteatoma or epidermoid cysts.

Until recently there were no imaging techniques which enabled the diagnosis of recurrent cholesteatomas in tympanoplasties, mainly in closed techniques which preserved the posterior wall of the external ear canal. Therefore, their diagnosis and treatment required a second surgical intervention known as 'second-look'. Some authors recommend the implementation of a second-look systematically, between 6 months and 1 year after undergoing closed tympanoplasty.7,8

Diagnosis and monitoring of cholesteatoma have recently become possible, based on diffusion techniques capable of distinguishing small-sized lesions and establishing a differential diagnosis with inflammatory and scar-type lesions. These techniques also enable the detection of some lesions which are difficult to diagnose due to such lesions' location and, in the particular case of congenital cholesteatomas, lesions are found behind an intact tympanum.

In our specific case, the non-echo-planar imaging (non-EPI) diffusion technique employed was the PROPELLER sequence (Periodically Rotated Overlapping Parallel Lines with Enhanced Reconstruction sequence). There are very few references on the use of this sequence for the diagnosis and monitoring of cholesteatoma.9-11

The purpose of this study was to establish whether diffusion MRI with the PROPELLER technique is effective for the diagnosis and monitoring of cholesteatoma, correlating clinical and surgical findings with radiological ones.

Materials and Methods

We conducted a prospective study which included a series of patients with suspected cholesteatoma who underwent ear diffusion MRI using a non-EPI PROPELLER sequence between March 2008 and September 2011. The total number of patients was 52, with a mean age of 46.30 years and a range between 1 and 81 years. The gender distribution was 31 males (59.62%) and 21 females (40.38%).

Of these patients, 4 presented involvement of both ears. Therefore, the total number of ears was 56.

Two patients were excluded for various reasons: in 1 case the PROPELLER diffusion image was not assessable due to artefacts caused by dental prosthetic material and 1 patient was lost during the follow-up period.

The final number of studied ears was 54 (23 right ears and 31 left ears), of which 21 had been intervened previously. The diagnosis was based on clinical history, otomicroscopic exploration and intraoperative findings in those patients who were intervened.

Patients were classified into 4 categories, true positive, false positive, true negative and false negative, depending on the result obtained in the diffusion MRI. They were then entered into a 2 x 2 table in order to obtain the sensitivity, specificity, positive predictive value and negative predictive value, which determine the diagnostic efficacy of a technique.

Results

The clinical and radiological concordance was 92.59%.

The distribution of patients among the various categories is shown in Table 1. These data were used to calculate the sensitivity (92.85%), specificity (92.30%), positive predictive value (92.85%) and negative predictive value (92.30%) for the entire group. The percentage of both false positives and false negatives reached 3.7%.

Among our results we found 2 false negatives. One was the result of aspiration of the cholesteatoma during an otomicroscopic exploration prior to the completion of the MRI scan. The other case was due to the presence of a

<table>
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<th>Table 1</th>
<th>Clinical and Radiological Correlation. Distribution of Cases.</th>
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<td></td>
<td>Cholesteatoma</td>
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<tr>
<td>Positive diffusion</td>
<td>26 TP</td>
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<tr>
<td>Negative diffusion</td>
<td>2 FN</td>
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<td>FN, false negatives; FP, false positives; TN, true negatives; TP, true positives.</td>
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spontaneously self-evacuated cholesteatoma, which left an epidermal pouch attached to the bone walls of the middle ear; this is known as mural cholesteatoma\(^2\) (Fig. 2).

Of the 2 false positives detected (Fig. 3), 1 was found in a patient with symptoms of simple chronic otitis media and a central perforation without cholesteatoma in the otomicroscopy. Diffusion showed an intense brightness on the mastoid antrum, with significant restriction of the ADC\(^12\) (Fig. 3A and B). The surgery did not find cholesteatoma, so it was considered as a false positive and the image was attributed to the presence of purulent content within the mastoid at the time of the radiological examination.

The second case (Fig. 3C and D) was due to a possible recurrence following closed tympanoplasty, presenting a double lesion partitioned by a bone spur on the CT scan. This double image shone in diffusion and had a size of 2 mm. It was considered positive, so a second-look was carried out which did not find cholesteatoma.

**Discussion**

The application of diffusion techniques for the diagnosis of cholesteatoma started in the 90s with echo-planar image (EPI) diffusion techniques, which offered good results for the diagnosis of lesions larger than 5 mm, as shown in series published by various authors.\(^13\),\(^14\) However, the technique yielded poor results and low sensitivity for smaller masses due to poor spatial resolution and to the presence of susceptibility artefacts inherent to the EPI technique in the petrosal region, caused by the presence of air and bone structures.\(^5\),\(^15\),\(^16\)

New, non-EPI diffusion techniques can diagnose cholesteatomas of up to 2 mm in diameter, with specificity similar to EPI techniques, by minimising the artefacts in the region of the temporal bone, thus obtaining greater spatial resolution. The name varies according to the different manufacturers, although, they have similar characteristics with minor variations. The most commonly used and referenced by most publications is the SS-TSE-DWI technique (HASTE-DWI, Siemens, Erlangen, Germany), which provides both axial and coronal planes. This technique has led to results with 100% specificity.\(^17\)–\(^20\) Other, non-EPI diffusion sequences include the PROPELLER sequence (GE Healthcare, Milwaukee, WI, USA) and the BLADE-DWI (Siemens, Erlangen, Germany).

The PROPELLER technique only provides axial planes, using morphological coronal sequences enhanced in T1 and/or T2 for a better location of the lesion in the cranio-caudal axis.

The usual morphological techniques of T1- and T2-enhanced MRI are very nonspecific for the diagnosis of middle ear inflammatory condition. The appearance of cholesteatoma, chronic otitis media or granulation tissue is variable in these sequences, which are unable to differentiate between these entities with sufficient reliability. The exception is cholesterol granuloma, which offers a pathognomonic, hyperintense image on T1\(^{11}\) (Fig. 4).

Before the use of diffusion, MRI was used with intravenous gadolinium to obtain delayed, T1-enhanced images for the diagnosis of cholesteatoma. Both inflammatory tissue and scar tissue are vascularised and uptake contrast, as opposed to cholesteatoma, which is a collection of non-vascularised keratin and therefore shows no uptake in its interior. Hence, peripheral uptake can be observed in the surrounding inflamed mucosa, but not in the interior of the lesion. Since granulation tissue can be very fibrous and poorly vascularised, the technique requires images to be obtained with a time delay (45–60 min after intravenous administration of gadolinium) in order to be effective in differentiating cholesteatoma (avoiding false positives caused by lack of prompt uptake by scar tissue). Although some good results were reported at the time with these techniques,\(^22\),\(^23\) even similar to those obtained subsequently with non-EPI diffusion techniques, the need for contrast and the time required for the study increased its cost. The administration of intravenous gadolinium involves risks and the interpretation of images is much more complex than with the diffusion technique. Given their speed, low cost and ease of interpretation, non-EPI diffusion techniques have replaced delayed
contrast techniques for the diagnosis of cholesteatoma. The use of the latter does not increase sensitivity or specificity (diagnostic efficacy) with respect to non-EPI techniques. If non-EPI diffusion techniques are not available, then the use of MRI techniques with delayed contrast improves the sensitivity of EPI diffusion, enabling detection of lesions smaller than 5 mm.

The different MRI patterns for the differential diagnosis of middle ear inflammatory condition are described in Table 2.

Studies published using the PROPELLER technique are scarce and their results are ambiguous. Lehmann et al. used a 3 T MRI unit and included 35 patients, obtaining sensitivity and negative predictive values between 89% and 100%, depending on the radiologist who interpreted the results, and specificity and positive predictive values of 100% for lesions of 3 mm or larger.

In our study, performed with this technique and a 1.5 T device, we obtained similar results. The sensitivity (92.85%), specificity (92.30%), positive predictive value (92.85%) and negative predictive value (92.30%) corresponded to the total patients studied.

However, if we only analyse the group of patients who had been intervened previously (n=21), then the clinical and surgical findings were correlated with the outcome of the diffusion MRI in all cases except for 1 (a false positive case, as previously mentioned). This exception corresponded to a patient who presented 2 punctate hyperintensities of 2 mm in the DEI. The second look revealed an absence of cholesteatoma. If this diffusion result had been considered as negative, the specificity and positive predictive values for this group would have been 100%. The experience gained in our work is that lesions with a size of 2 mm or smaller should be controlled through imaging in order to determine their growth and, initially, do not represent an indication for surgery.

The most common causes of false positives described were: cholesterol granulomas, purulent content or abscesses in the middle ear (such as the patient described in our series), the presence in the middle ear of materials containing silicone, such as Silastic®, bone dust used to seal a semicircular canal fistula, haematomas following recent surgery, ear wax in the EAC and artefacts secondary to dental implants.

We found a mural cholesteatoma among the 2 false negative results. This type of lesions, along with cholesteatomas under 2 mm, are the most common causes of false negatives published, decreasing the sensitivity of some series conducted with non-EPI techniques. In order to avoid false negatives due to emptying of the contents of the
cholesteatoma, we recommend not performing microaspiration during consultation if the radiological examination is to be conducted soon thereafter.

Among patients diagnosed correctly, 2 were congenital cholesteatoma. One of them was a rare case of Kabuki syndrome, which is a congenital disease named after the facial resemblance with a Kabuki mask presented by individuals with this disease. It is characterised by heart problems (30%), urinary tract abnormalities, hearing loss (50%), hypertonia and postnatal growth deficiency (83%).

Upon suspicion of a congenital cholesteatoma, we consider that, in addition to performing an MRI scan to diagnose the nature of the lesion, it is important to perform a CT scan to identify potential erosions in the bone walls and in the ossicular chain, as well as to provide a bone map prior to a possible surgical intervention.

This same diagnostic strategy applies to cholesteatomas associated with malformations of the external and middle ear, where it is sometimes impossible to visualise the tympanic membrane. This was the case in 1 of our patients, who presented a membranous atresia of the external auditory canal and a nonspecific occupation in the CT scan, diagnosed as cholesteatoma through a diffusion MRI scan.

The currently used radiological protocol includes T1 and T2 coronal images without contrast – useful for the spatial guidance of the lesion and the diffusion sequence. After some initial cases, we ceased to use delayed T1 images with contrast, thus reducing scan time and the potential adverse effects caused by the administration of gadolinium chelates, and also improving the cost–benefit efficiency.

As mentioned by other authors17,18,20,27 using different diffusion techniques, MRI with non-EPI DEI, such as the PROPELLER sequence used by us, is becoming established as a good diagnostic alternative to systematic surgical review of cholesteatoma.

Conclusion

Non-EPI diffusion MRI using the PROPELLER sequence is as effective as other diffusion techniques for the diagnosis and monitoring of cholesteatoma.

Conflict of Interests

The authors have no conflict of interests to declare.

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