The role of diffusion-weighted imaging in differentiation of hepatic alveolar echinococcosis and intrahepatic cholangiocarcinoma

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Available online 27 July 2016

Abstract

Objective: A technique is proposed for evaluating the utility of apparent diffusion coefficient (ADC) measurements in the differentiation of type 4 hepatic alveolar echinococcosis (HAE) from the mass-forming type of intrahepatic cholangiocarcinoma (IHCC), using diffusion-weighted magnetic resonance imaging (DW-MRI).

Methods: This study, conducted from November 2013 to January 2015, was approved by the ethics committee of First Affiliated Hospital of Xinjiang Medical University. All patients were given written informed consent. A total of 11 patients underwent T1WI, T2 fat-saturation, and a respiratory triggered DWI sequence by a 1.5T MR imaging system. An experienced radiologist measured the ADC in both alveolar echinococcosis and cholangiocarcinoma lesions. DWI was performed with a b-value gradient of 0 and 600. The mean ADC values of type 4 hepatic alveolar echinococcosis were compared with those of mass-forming type cholangiocarcinoma, in order to determine variations between the two. Differences in ADC between lesion types were determined by using an independent samples t-test and a statistically significant (P < 0.05) difference was observed.

Results: Mean ADC values for IHCC were 1.24 ± 0.23 × 10⁻³ mm²/s, which was significantly lower than the 1.71 ± 0.23 × 10⁻³ mm²/s observed for HAE. These results supported the use of this technique as a mechanism for lesion differentiation.

Conclusions: Lower ADC in DW-MRI represents restricted diffusion. Due to multicellularity being higher in IHCC than HAE, the mean ADC values for IHCC were lower than for HAE.

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Keywords: Alveolar echinococcosis; Apparent diffusion coefficient; Cholangiocarcinoma; Diffusion-weighted imaging; Liver

1. Introduction

To distinguish intrahepatic cholangiocarcinoma (IHCC) and hepatic alveolar echinococcosis (HAE) is an important task for radiologists. IHCC is an adenocarcinoma derived from bile ducts. Fibrous stroma and coagulative necrosis present in the center of IHCC lesions [1]. Cholangiocarcinoma is divided into three types: mass-forming, periductal-infiltrating, and intraductal-growing variations [2]. In contrast, alveolar echinococcosis is typically surrounded by an exuberant granulomatous response, which includes both fibrosis and necrosis. Pathological changes play a major role in determining imaging features, for example, signal intensity depends on structural components in the lesion. As a result, magnetic resonance images acquired of IHCC and HAE may share some common traits, making lesion differentiation difficult. The purpose of this study is to differentiate type 4 hepatic alveolar echinococcosis and mass-forming type intrahepatic cholangiocarcinoma by using diffusion-weighted magnetic resonance imaging. The image features for IHCC are not specific. They represent an ill-defined irregular mass, which is hypo-intense on T1-weighted image (T1WI), with heterogeneous hyper-intensity on T2-weighted image (T2WI).
central fibrous stroma may be T2 hypo-intense, which makes diagnosis difficult. In contrast, HAE appears as an infiltrative and destructive mass with ill-defined outlines. It is hypo-intense on T1WI and heterogeneous on T2WI. The typical AE is a multi-vesicular structure and is often described as a "bunch of grapes" located at the periphery of the lesion [3]. The differential diagnosis for typical IHCC and HAE is easy to be carried out, but differentiation between special types of the two is more difficult. Abdominal diffusion-weighted imaging (DWI) has recently become a possible option as it can reduce the effect of respiration and cardiac movement [4,5]. Diffusion-weighted imaging can also reflect the diffusive movement of water molecules and can be used as a supplement to conventional magnetic resonance imaging. DWI plays an important role in the evaluation of liver disease because of its qualitative and quantitative assessment of tissue diffusivity. Becce et al. have reported that the mean apparent diffusion coefficient (ADC) total for type 4 HAE was 1.15 ± 0.42 × 10^{-3} mm²/s and that there were significant differences between type 4 HAE and other types. Type 4 HAE had a significantly lower ADC max [6]. In other word, type 4 HAE featured the lowest ADC values, as it was more like a tumor. As such, it is meaningful to identify type 4 HAE and IHCC.

The primary aim of this research is to evaluate the role of diffusion-weighted magnetic resonance imaging (DW-MRI) in the characterization of special types of hepatic alveolar echinococcosis and cholangiocarcinoma. ADC values measured in DW-MRI are key parameters of this study. To our knowledge, DW-MRI has not been studied to differentiate type 4 hepatic alveolar echinococcosis and mass-forming type intrahepatic cholangiocarcinoma. In this research, b values of 0 and 600 s/mm² were applied to conventional sequences.

2. Materials and methods

2.1. Patients

This study, conducted between November 2013 and January 2015, included 11 patients who were examined using MRI and were given a pathologic diagnosis for both of HAE and IHCC. The inclusion criteria were as follows. All cases featured: a pathologically proven IHCC or HAE, an abdominal MRI following standard protocol including DWI sequence, a lesion with a diameter greater than 2 cm, and satisfactory image quality requirements. Six of the patients were male and five were female. Their ages ranged between 13 and 72 years (with an average of 47 years). Six of the patients were diagnosed with type 4 HAE and five were diagnosed with mass-forming IHCC. A total of 13 lesions were evaluated in this research, each had a diameter greater than 2 cm on T2WI. Cases were rejected if they included: cystic content in the lesion affecting post-processing results, or a history of specific treatments relating to the lesion. The average maximum diameter of HAE lesions was 9.75 cm and the average maximum diameter for IHCC was 5.27 cm. The diagnosis of HAE was performed by biopsy and positive serological test results. The diagnosis of IHCC was also performed via biopsy.

2.2. MRI protocol and imaging analysis

All patients were examined with a 1.5 T MR scanner (Siemens and Magnetom Avanto). Patients were positioned supinely on a spine coil and covered with a phased-array body coil. The range of scanning included the upper abdomen. Routine MRI protocol consisted of coronal T2WI, an axial T1-weighted image, axial T1W-weighted fat saturation, axial fat-saturated fast-spin echo T2-weighted images, and DW sequences. Diffusion-weighted images were obtained by using single-shot echo-planar spin echo sequences with b values of 0 and 600 s/mm². All DWI images were set in the transverse plane and performed in free breathing mode. DW imaging parameters were as follows: TR: 3800 ms; TE: 59—72 ms; number of excitations: 1; matrix size: 128 × 128; section thickness: 6; scanning time: 2'24''.

2.3. Image analysis

An experienced radiologist evaluated the images independently and was not given any pathological information about the patients. In the case of multiple lesions presented in a single patient, all of them were selected as target lesions. The regions of interest (ROIs) were set in the solid portions. In order to avoid the partial volume averaging effect, and to reduce inaccuracies, the region of interest was positioned larger than 0.5 cm of solid portions in the lesion and kept away from major blood vessels. ADC maps were generated from DW images. The evaluation was performed on a post-processing workstation. The software calculated the ADC of ROI automatically. The average of three measurements was listed as the final ADC value. Mean ADC values for type 4 HAE and mass-forming IHCC were compared.

2.4. Statistical analysis

Statistical analysis of data was carried out by using the SPSS 18 software package (SPSS Inc., Chicago, USA). Apparent diffusion coefficient (ADC) values were listed in the form of mean ± standard deviation. The difference in mean ADCs between HAE and IHCC were evaluated using a group t-test. A P-value below 0.05 was considered to indicate a statistically significant difference.

3. Results

11 cases were examined in this study with an average patient age of 47 years (range, 13—72 years). All cases were confirmed by histopathological examination. This study included 8 lesions from 6 cases of type 4 HAE and 5 lesions from 5 cases of mass-forming IHCC. The average lesion size (maximum diameter) of HAE was 9.75 cm (range, 5.05 cm—12.99 cm). Lesion characterization information was listed in Table 1. Lesion distribution for HAE was as follows: 87.5% of lesions were located in the right lobe and 12.5% of lesions were located in the left lobe. Vascular invasion was found in 5 cases, 83% of HAE patients, whereas all cases...
featured an invasion of intrahepatic bile ducts. In contrast, the average lesion size (maximum diameter) of IHCC was 5.27 cm (range, 2.89–7.22 cm). The lesion distribution for IHCC was as follows: 80% of lesions were located in the right lobe and 20% of lesions were located in the left lobe. Vascular invasion was found in 2 cases, 40% of IHCC patients, whereas all 5 cases (100%) featured an invasion of the intrahepatic bile ducts. The ADC values for IHCC (1.24 ± 0.23 × 10⁻³ mm²/s) were significantly lower than the ADC values for HAE (1.71 ± 0.23 × 10⁻³ mm²/s) (See Figs. 1 and 2). The difference in ADC between type 4 HAE and mass-forming IHCC was statistically significant (P < 0.05).

### Table 1
Reference information of each lesion.

<table>
<thead>
<tr>
<th>Lesion number</th>
<th>Gender</th>
<th>Age</th>
<th>Pathological diagnosis</th>
<th>Maximum diameter</th>
<th>Location</th>
<th>Vascular invasion</th>
<th>Bile ducts invasion</th>
<th>Average ADC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>40</td>
<td>IHCC</td>
<td>2.89 cm</td>
<td>Right lobe</td>
<td>No</td>
<td>Yes</td>
<td>1.11 × 10⁻³ mm²/s</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>72</td>
<td>IHCC</td>
<td>5.76 cm</td>
<td>Right lobe</td>
<td>No</td>
<td>Yes</td>
<td>0.99 × 10⁻³ mm²/s</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>68</td>
<td>IHCC</td>
<td>7.22 cm</td>
<td>Left lobe</td>
<td>Yes</td>
<td>Yes</td>
<td>1.53 × 10⁻³ mm²/s</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>65</td>
<td>IHCC</td>
<td>5.10 cm</td>
<td>Right lobe</td>
<td>No</td>
<td>Yes</td>
<td>1.14 × 10⁻³ mm²/s</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>57</td>
<td>IHCC</td>
<td>5.38 cm</td>
<td>Right and left lobe</td>
<td>Yes</td>
<td>Yes</td>
<td>1.43 × 10⁻³ mm²/s</td>
</tr>
<tr>
<td>6</td>
<td>Female</td>
<td>13</td>
<td>HAE</td>
<td>11.34 cm</td>
<td>Right lobe</td>
<td>Yes</td>
<td>Yes</td>
<td>1.48 × 10⁻³ mm²/s</td>
</tr>
<tr>
<td>7</td>
<td>Male</td>
<td>45</td>
<td>HAE</td>
<td>12.24 cm</td>
<td>Right lobe</td>
<td>No</td>
<td>Yes</td>
<td>1.38 × 10⁻³ mm²/s</td>
</tr>
<tr>
<td>8</td>
<td>Female</td>
<td>61</td>
<td>HAE</td>
<td>12.99 cm</td>
<td>Right lobe</td>
<td>Yes</td>
<td>Yes</td>
<td>1.86 × 10⁻³ mm²/s</td>
</tr>
<tr>
<td>9</td>
<td>Female</td>
<td>39</td>
<td>HAE</td>
<td>9.87 cm</td>
<td>Right lobe</td>
<td>Yes</td>
<td>Yes</td>
<td>1.92 × 10⁻³ mm²/s</td>
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<tr>
<td>10</td>
<td>Female</td>
<td>39</td>
<td>HAE</td>
<td>7.98 cm</td>
<td>Right lobe</td>
<td>Yes</td>
<td>Yes</td>
<td>1.62 × 10⁻³ mm²/s</td>
</tr>
<tr>
<td>11</td>
<td>Female</td>
<td>13</td>
<td>HAE</td>
<td>6.97 cm</td>
<td>Left lobe</td>
<td>Yes</td>
<td>Yes</td>
<td>1.97 × 10⁻³ mm²/s</td>
</tr>
<tr>
<td>12</td>
<td>Female</td>
<td>13</td>
<td>HAE</td>
<td>5.05 cm</td>
<td>Left lobe</td>
<td>Yes</td>
<td>Yes</td>
<td>1.89 × 10⁻³ mm²/s</td>
</tr>
<tr>
<td>13</td>
<td>Female</td>
<td>44</td>
<td>HAE</td>
<td>11.57 cm</td>
<td>Right lobe</td>
<td>Yes</td>
<td>Yes</td>
<td>1.58 × 10⁻³ mm²/s</td>
</tr>
</tbody>
</table>

4. Discussion and conclusion

Ultrasoundography is the first-step exam for hepatic diseases [7]. CT and MRI are also useful to observe vascular and biliary invasion, as well as involvement of adjacent organs. Conventional imaging examinations often perform diagnoses by measuring the size and observing the shape and internal

![Fig. 1. Type 4 hepatic alveolar echinococcosis. An axial T1-weighted MR image (A) and an axial T2-weighted MR image (B) showed the lesion in the right lobe. A diffusion-weighted MR image (C) showed relatively low signal intensity compared to liver parenchyma. An apparent diffusion coefficient (ADC) map (D) showed the ADC values.](image-url)
structure of the lesion. However, conventional imaging methods can only display general pathological morphology and cannot represent biological changes in a lesion. Recently, functional MRI has seen increasingly common application to the diagnosis of hepatic diseases.

DWI is a non-invasive magnetic resonance imaging modality which can reflect the diffusive conditions of water molecules. In recent years, DWI has become a promising technique for performing abdominal MRI [8,9]. This study focused on low incidence diseases and the rare type of each was chosen. DWI sequences include several characteristics: they are conducted without the use of a gadolinium agent, both respiratory-triggered and breath-hold can be used. Diffusion is related to cellularity, cell membrane integrity, and lipophilicity [6]. Water molecules diffuse more freely in a diffusion-sensitive gradient direction; the diffusion distance will then be greater and the signal attenuation will be more obvious. DWI sequences can detect molecular water diffusion states by measuring signal intensity changes before and after applying diffusion-sensitive gradient fields. In other words, the signal intensity for DWI is determined by the degree of signal attenuation. A higher signal intensity in DWI represents restricted diffusion and lower signal intensity represents free diffusion. DWI sequences can allow for both qualitative and quantitative analysis to reflect the diffusion characteristics of lesions. Quantitative analysis is performed using ADC values. Up to now, DWI has been used for differentiation of benign and malignant focal hepatic lesions. Onur et al. came to the conclusion that ADC values for solid benign lesions were significantly higher than for solid malignant lesions at b values of 100, 600, and 1000 gradients [10]. In our research, DWI images were obtained by respiratory triggering acquisition, because of its high signal-to-noise ratio. At the same time, it required a longer scan time and was not suitable for irregularly-breathing patients.

There is no difficulty in distinguishing typical HCE and IHCC via imaging methods. Alveolar echinococcosis primarily consists of cystic and solid components. The solid components consist of coagulation necrosis, granuloma, and calcifications [11]. Type 4 AE lesions are solid components without cysts which mimic tumors. They comprise 4% of all HAE lesions [11]. On the other hand, IHCC is an adenocarcinoma arising from the biliary ducts with the presence of central fibrous stroma and foci of coagulative necrosis [12]. Cholangiocarcinoma is divided into three types: mass-forming, periductal-infiltrating, and intra-ductal growing variations [2]. From what has been discussed above, imaging characteristics for HAE and IHCC may have something in common. There are some difficulties presenting in distinguishing type 4 HAE from mass-forming IHCC. First of all, MRI cannot display calcification definitively. As such, calcification cannot be the identifying point for HAE and IHCC on MRI. Secondly, HAE and IHCC can both cause dilation of the biliary tract which will increase diagnostic difficulty [13]. Thirdly, both HAE and IHCC exhibit the tendency to invade extensive regions of the liver, such as the porta hepatic [14–16]. Finally, in some AE lesions, enhancement of the peripheral area is intense and long lasting [3]. On the other hand, in the arterial
phase, IHCC shows peripheral enhancement and on the delayed phase it shows central enhancement [12]. But in clinical practice, the central enhancement may not be seen during the delayed phase. From what has been discussed above, the diagnosis of IHCC and HAE by conventional imaging remains a challenge. Our study demonstrated that ADC can be used to distinguish the two types.

Thus far, there is no agreement on the selection of b values. High b values (b ≥ 500 s/mm²) can reflect more characteristics of focal hepatic lesions than low b values [17]. Mahmoud et al. found that ADC values measured with b = 500 and b = 1000 diffusion gradients were useful in differential diagnosis of benign and malignant lesions [18]. In this research, b values of 0 and 600 s/mm² were applied to conventional sequences. We compared the diffusion characteristics of IHCC and HCE by using ADC values. In this research, the mean ADC for solid components of IHCC and HAE were 1.24 ± 0.23 × 10⁻³ mm²/s and 1.71 ± 0.23 × 10⁻³ mm²/s, respectively. Higher tissue cellularity leads to less diffusion and lower ADC values [19]. Intrahepatic cholangiocarcinoma as an adenocarcinoma leads to an increased cell density and decreased extracellular gap. This restricts molecular water movement, increasing the DWI signal and decreasing the ADC values. There are similarities between our research and other studies. It was concluded that benign hepatic lesions had higher ADC values than malignant lesions in several studies [5,10,20,21]. In our research, there was an overlap between ADC values of type 4 HAE and mass-forming IHCC. This is also in agreement with other studies [22].

Our study had several limitations. First, the number of patients was relatively small. This was because the incidence of these two kinds of diseases was low and a rare type of both was chosen. Secondly, ADC measurements included large variability, because they were too sensitive to molecular water diffusion. Thirdly, this was a retrospective study and a prospective study needed to examine the technique in further detail.

In conclusion, DWI improved the diagnosis and differentiation of type 4 HAE and mass-forming IHCC. A statistically significant relationship was found between the apparent diffusion coefficient values of mass-forming IHCC and type 4 HAE. The mean ADC of mass-forming IHCC was significantly lower than type 4. This was due to higher tissue cellularity of IHCC than HAE.

Acknowledgment

Grant Support: The National Natural Science Foundation of China (number: 81260232).

References