Diffusion-weighted MRI and FLAIR sequence for differentiation of hydatid cysts and simple cysts in the liver

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HIGHLIGHTS

• DWI signal characteristics are useful in differentiating between hydatid cysts and simple cysts.
• ADC values (b600 and b1000) can distinguish hydatid cyst and simple cyst.
• FLAIR sequence contributes to the differentiation of type 2 hydatid and simple cysts.

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ABSTRACT

Purpose: The contribution of DWI and FLAIR to the differential diagnosis of type 1, 2, and 3 hydatid cysts and simple liver cysts was investigated according to the Gharbi classification. This study is the first report using FLAIR sequence for the differential diagnosis of liver hydatid cysts in this regard.

Methods: A total of 82 hydatid cysts and 40 simple cysts were scanned with DWI (in b600-b1000 values) and FLAIR sequence. In 64 patients included in the study, a total of 122 cystic lesions were diagnosed histopathologically or during follow-up. FLAIR and DWI signal characteristics were evaluated, and ADC values were calculated.

Results: The mean ADC value of hydatid cysts on DWI (b600) was $3.07 \pm 0.41 \times 10^{-3} \text{s/mm}^2$, while it was $3.91 \pm 0.51 \times 10^{-3} \text{s/mm}^2$ for simple cysts and the difference was statistically significant ($p < 0.05$). On b1000 DWI, the mean ADC values of hydatid and simple cysts were $2.99 \pm 0.38 \times 10^{-3} \text{s/mm}^2$ and $3.43 \pm 0.29 \times 10^{-3} \text{s/mm}^2$, respectively ($p < 0.05$). The qualitative evaluation of the signal intensity on $b600–1000$ DWI demonstrated the difference between the simple and hydatid cyst groups ($p < 0.05$). Type 2 hydatid cysts alone were distinguished from type 2-3 hydatid and simple cysts by FLAIR ($p < 0.05$).

Conclusions: ADC values can distinguish between hydatid cyst and simple cyst. FLAIR contributes to the differentiation of type 2 hydatid and simple cysts.

1. Introduction

Hydatid cyst of the liver still continues to be an important public health problem in developing countries [1]. Hydatid cyst often remains silent for a lifetime and does not cause clinical symptoms. But if clinical symptoms exist, blunt right upper quadrant pain is the most common complaint in patients. Weakness, fever, dyspepsia, and nausea are the other nonspecific findings. In complicated hydatid cysts, fever, jaundice, and rarely anaphylactic reactions can be seen. The diagnosis is mostly made incidentally as a result of imaging procedures performed for another reason. Approximately 50–70 % of cysts settle in the liver [2]. They were classified by Gharbi in 1981 [3]. Recently, in 2003, the World Health Organization (WHO) Informal Working Group on Echinococcus updated a new classification of cystic echinococcosis based on

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ultrasonographic findings of hepatic hydatid cyst. Abdel Razek et al. published a new version of the WHO classification based on magnetic resonance imaging (MRI) findings in 2009 [4–6]. Among the imaging methods, ultrasonography (US) especially is an easily accessible method that should be applied first [7,8]. Computed tomography and MRI often offer the possibility to better define anatomic relations. MRI is also used for diagnosis and treatment follow-up in some centers [9].

Diffusion-weighted imaging (DWI) is a method sensitive to molecular diffusion in tissues and is widely used in brain imaging. Müller et al. first used diffusion MRI for focal and diffuse diseases of the liver, spleen, renal lesions, and muscle tissue, and obtained significant results [10]. In the following years, many researchers published studies about the applications of DWI in the liver, kidneys, and other abdominal organs [11,12]. However, there are a limited number of studies investigating the role of DWI in hydatid cyst disease of the liver [13,14].

Fluid-attenuated inversion recovery (FLAIR), which is an inversion recovery (IR) sequence, is one of the routine sequences in neuroradiology. This special sequence removes the signal from cerebrospinal fluid in the resulting images. Cerebral tissues on FLAIR appear similar to T2-WI with gray matter brighter than white matter but fluids are dark instead of appearing white. Due to this high sensitivity and excellent suppression of the cerebrospinal fluid signal, FLAIR is used routinely for neuroimaging [15].

In this study, the contribution of DWI and FLAIR sequences to the differential diagnosis of type 1, 2, and 3 hydatid cysts and simple liver cysts according to the Gharbi classification was investigated. This study is the first report using the FLAIR sequence for the differential diagnosis of liver hydatid cysts.

2. Methods

2.1. Patient selection

After approval from Erciyes University Clinical Research Ethics Committee (2012/79), the study included patients with liver hydatid cyst (type 1, 2, 3) or simple cyst previously detected by US and computed tomography retrospectively. After the informed consent form was obtained, an MRI examination including FLAIR sequence and DWI was performed. Hydatid cysts were classified according to the Gharbi classification, and type 1, 2, and 3 hydatid cysts were included in the study. Type 4 hydatid cysts were excluded from the study due to their solid character and type 5 hydatid cysts are solid and contain peripheral calcification. Cysts smaller than 2 cm were excluded because of the limit of DWI resolution. Patients with hydatid cysts who could not tolerate MRI and simple cyst cases without long-term follow-up were excluded from the study.

Of the 64 patients (27 men, 37 women) included in the study, 22 patients had a total of 40 simple cysts, and 42 patients had a total of 82 hydatid cysts (122 cystic lesions in total). While 10 of 40 simple cysts were diagnosed histopathologically as isointense, peripheral hyperintense, moderately hyperintense, and hyperintense compared to liver parenchyma. The measurements were made by placing the region of interest (ROI) on the cysts covering 2/3 of the lesion. If there was an image of the lesion in consecutive sections, ADC measurements were made from these, and the average ADC value was calculated. The average ADC values were measured, and the diagnoses of the patients were compared.

Cyst signal intensity was classified as hypointense, isointense, and hyperintense compared to liver parenchyma on FLAIR images.

All evaluations were qualitatively and quantitatively evaluated for each cyst by an academic radiologist (20 years’ experience) unaware of the final diagnosis.

2.2. Imaging technique

Routine upper abdominal MRI was performed using a 1.5 T MRI device (Philips Gyroscan Intera, Best, The Netherlands) with a 4-phase channel body coil. For routine examination, axial and coronal T2-weighted single-shot turbo spin-echo (TSE) (TR/TE 700/80, FA: 90°, slice thickness 7 mm, gap 1 mm, FOV: 35–40 cm) and axial T2-weighted TSE with fat-suppression, T1-weighted gradient echo (in phase and out of phase) (TR/TE 80/4.2–3.6, FA: 80°, slice thickness 7 mm), axial T1-weighted spoiled gradient-echo (fast-field echo [FFE]) images with and without fat suppression (TR/TE 169/4, FA: 90°, slice thickness 7 mm, gap 1 mm) and FLAIR sequence (TR/TE 6000/120, TI: 2000, slice thickness 7 mm, gap 1 mm) were obtained. Fat suppression was obtained using the spectral pre-saturation with inversion recovery (SPIR) technique. DWI was obtained by applying diffusion sensitive gradients at different b values (b0, b600, b1000 sec/mm2) in the axial plane in single-shot spin-echo planar sequence (TR 3656, TE 89 mm (b1000), TR 2673, TE 60 (b600), matrix: 256 × 128, FOV 35–40 cm, slice thickness 7 mm, interleave gap 1 mm). Fat-suppressed pulses were used to avoid serious chemical-shift artifacts. ADC maps of isotropic images were created automatically by the device. ADC values for the lesions were calculated on ADC maps created in the second MRI console (View Forum R5.x, Philips Medical Systems). After DWI, contrast-enhanced dynamic imaging was obtained with an axial gradient-echo T1-weighted MRI sequence after the administration of gadopentetate dimeglumine at a dose of 0.1 mmol/kg of body weight as a bolus injection of 25 s (arterial), 60 s (portal), 120 s (equilibrium), and 5 min. The MRI parameters used are summarized in Table 1.

| Sequences                                      | Parameters                                      |
|------------------------------------------------|------------------------------------------------|
| Axial and coronal T2-weighted                 | TR/TE 700/80, FA: 90°, slice thickness 7 mm, gap |
| sing-shot TSE                                 | 1 mm, FOV: 35–40 cm                            |
| Axial T2-weighted TSE with fat-suppression    | TR/TE 700/80                                   |
| Axial T1-weighted gradient                    | TR/TE 80/4.2–3.6, FA: 80°, slice thickness 7 mm |
| dual-echo                                      | gap 1 mm                                       |
| Axial T1-weighted spoiled gradient-echo       | TR/TE 169/4, FA: 80°, matrix: 256 × 128, slice |
| FLAIR                                          | thickness 7 mm, gap 1 mm                       |
|                                                | TR/TE 6000/120, TI: 2000, slice thickness 7 mm |
|                                                | gap 1 mm                                       |

TR/TE: repetition/time/echo time, FOV: Field of view, FA: Flip Angle, TSE: Turbo Spin Echo, FFE: Fast-Field Echo, FLAIR: Fluid-Attenuated Inversion Recovery, TI: Time Inversion.

2.3. Image analysis

The sizes of the cysts were recorded. Cyst signal intensity on DWI was evaluated as isointense, peripheral hyperintense, moderately hyperintense, and hyperintense compared to liver parenchyma. The measurements were made by placing the region of interest (ROI) on the cysts covering 2/3 of the lesion. If there was an image of the lesion in consecutive sections, ADC measurements were made from these, and the average ADC value was calculated. The average ADC values were measured, and the diagnoses of the patients were compared.

Cyst signal intensity was classified as hypointense, isointense, and hyperintense compared to liver parenchyma on FLAIR images.

All evaluations were qualitatively and quantitatively evaluated for each cyst by an academic radiologist (20 years’ experience) unaware of the final diagnosis.

2.4. Statistical analysis

“SPSS 15.0 for Windows” program was used for statistical evaluation. Normal distribution of data was checked with the Kolmogorov-Smirnov test. Measurable (quantitative) data were defined as x ± SD. The difference between the two groups was examined using the Student t-test or Mann-Whitney U test. Countable data (qualitative) were defined as percentages, and statistical analysis between groups was performed with the chi-square test. The sensitivity and specificity of the diagnostic criteria were calculated. The significance level in the evaluation was taken as p < 0.05. Receiver Operating Characteristic (ROC) analysis was performed to find the threshold ADC value for the characterization of the lesions.
3. Results

The mean age of 42 patients with hepatic hydatid cyst was 36.8 ± 20.2 years (between 8–71), and the mean age of 22 patients with liver simple cyst was 58.5 ± 11.9 years (between 32–79). While 16 (38.1%) of the hydatid cyst cases were male and 26 (61.9%) were female, 11 (50%) of the simple cyst cases were male and 11 (50%) were female. There was a statistically significant difference in age distribution between the two groups (p < 0.05), but no difference in terms of gender (p > 0.05). Of the 122 lesions, 40 were simple cysts and 82 were hydatid cysts (type 1: 41, type 2: 20, type 3: 21). The demographic characteristics of the groups are given in Table 2.

The average size of simple cysts was 33.8 ± 15.5 mm (20–94 mm). The mean size of all hydatid cysts was 70.6 ± 8.3 mm (20–230 mm). The average size was 85.2 ± 45.4 mm for type 1 hydatid cysts, 47.7 ± 15.9 mm for type 2 hydatid cysts, and 63.9 ± 23.8 mm for type 3 hydatid cysts. Paired comparisons were made between these groups in order to determine which groups caused the significant statistical difference in terms of mean dimension values. A statistically significant difference was found between the simple cyst and hydatid cyst groups (p < 0.05) (Table 2).

3.1. DWI and ADC findings

Signal intensity in b600 DWIs was compared with normal liver parenchyma and evaluated as isointense, moderately hyperintense, hyperintense in the periphery, and hyperintense. While 31 (77.5%) lesions were moderately hyperintense in the simple cyst group, 19 (23.2%) lesions were moderately hyperintense in the hydatid cyst group (Fig. 1). Peripheral hyperintensity was not observed in the simple cyst group, whereas peripheral hyperintensity was observed in 53 (64.6%) lesions in the hydatid cyst group (Fig. 2). A statistically significant difference was found between the simple cyst and hydatid cyst groups according to the signal intensity (p < 0.05) (Table 3).

When the average ADC (b600) values are evaluated according to cyst types, the average value is $3.15 \pm 0.32 \times 10^{-3}$ s/mm² for type 1 hydatid cysts, $4.77 \pm 1.59 \times 10^{-3}$ s/mm² for type 2 hydatid cysts, and $6.39 \pm 2.38 \times 10^{-3}$ s/mm² for type 3 hydatid cysts.
cysts, 3.13 ± 0.57 × 10^{-3} s/mm^2 for type 2 hydatid cysts, and 2.88 ± 0.33 × 10^{-3} s/mm^2 for type 3 hydatid cysts. The mean value for all hydatid cysts was 3.07 ± 0.41 × 10^{-3} s/mm^2. The ADC (b600) mean value of simple cysts was found to be 3.91 ± 0.51 × 10^{-3} s/mm^2 (Table 3). Paired comparisons were made between the groups in order to determine which groups caused the statistically significant difference in average ADC (b600) values. A statistically significant difference was found between all types of hydatid cysts and simple cysts and between

Table 3
Signal characteristics of hydatid and simple cysts in b600 DWI and average ADC (b600) values.

| DWI                        | Isointense | Moderately hyperintense | Moderately hyperintense in the periphery | Hyperintense | ADC b600 (x10^{-3} s/mm^2) |
|----------------------------|------------|--------------------------|------------------------------------------|--------------|-----------------------------|
| Simple Cyst (n/%)          | 2 (5)      | 31 (77.5)                | 0 (0)                                    | 7 (17.5)     | 3.91 ± 0.51                 |
| Hydatid Cyst (n/%)         | 6 (7.3)    | 19 (23.2)                | 53 (64.6)                                | 4 (4.9)      | 3.07 ± 0.41                 |
| Type 1                     | 0          | 1                        | 40                                       | 0            | 3.15 ± 0.32                 |
| Type 2                     | 4          | 11                       | 1                                       | 4            | 3.13 ± 0.57                 |
| Type 3                     | 2          | 7                        | 12                                       | 0            | 2.88 ± 0.33                 |

Bold texts indicate hydatid and simple cyst numbers in the table.

Fig. 3. Simple cyst with b1000 DWI (a) and ADC map (b). It is isointense on DWI compared to the liver parenchyma. ADC value; 3.60 × 10^{-3} s / mm^2.

Fig. 4. Type 1 hydatid cyst with b1000 DWI (a) and ADC map (b). The cyst is moderately hyperintense in the periphery and isointense in the center. ADC value; 3.05 × 10^{-3} s / mm^2.

Table 4
Signal characteristics of hydatid and simple cysts in b1000 DWI and average ADC (b1000) values.

| DWI                        | Isointense | Central isointense, moderately hyperintense in the periphery | Moderately hyperintense | Hyperintense | ADC b1000 (x10^{-3} s/mm^2) |
|----------------------------|------------|---------------------------------------------------------------|--------------------------|--------------|-----------------------------|
| Simple Cyst (n/%)          | 34 (85)    | 1 (2.5)                                                       | 4 (10)                   | 1 (2.5)      | 3.43 ± 0.29                 |
| Hydatid Cyst (n/%)         | 24 (29.3)  | 44 (53.6)                                                     | 10 (12.2)                | 4 (4.9)      | 2.99 ± 0.38                 |
| Type 1                     | 8          | 33                                                            | 0                        | 0            | 3.01 ± 0.27                 |
| Type 2                     | 10         | 1                                                             | 5                        | 4            | 3.02 ± 0.45                 |
| Type 3                     | 6          | 10                                                            | 5                        | 0            | 2.90 ± 0.32                 |
lesions were moderately isointense in the hydatid cyst group (Fig. 4). In lesions were isointense in the simple cyst group (Fig. 3), 24 (29.3%) in the simple cyst group, peripheral hyperintensity was observed in 1 (2.5%) lesion, while in the hydatid cyst group, peripheral hyperintensity was observed in 44 (53.6%) lesions. A statistically significant difference was found between type 2 hydatid cysts and type 1, type 3 hydatid cysts and simple cysts (p < 0.05) (Table 4).

B600 and b1000 ROC analyses were performed to find the threshold value for differentiation between hydatid cyst and simple cyst (Fig. 5a, b).

3.2. FLAIR findings

The signal intensity was evaluated as hypointense, isointense, and hyperintense by comparing with normal liver parenchyma (Table 5). Paired comparisons were made between the groups in order to determine which groups caused the statistically significant difference in signal intensity. A statistically significant difference was found between type 2 hydatid cysts and type 1, type 3 hydatid cysts and simple cysts (p < 0.05) (Fig. 6).

4. Discussion

Hydatid cyst is most common in the 3rd and 4th decade and is localized at a rate of 50–70% in the liver, 11–17% in the lungs, 2.4–5.3% in soft tissues, 0.5–3% in the heart, 5% in the pericardium, and 0.5–4.7% in muscle and subcutaneous tissues [16, 17]. Hydatid cysts in the liver can be millimetric or can reach 50 cm in size. Average size is 5–6 cm [18–20]. Simple liver cysts originate from intrahepatic bile ducts and are commonly seen in the 5th-7th decades. Size is approximately 3 cm [21]. In our study, the larger size of hydatid cysts compared to simple cysts was attributed to the viability of the hydatid cyst walls and continuous fluid production. The appearance of simple cysts at a later age was attributed to their smaller size and being asymptomatic.

DWI is an MRI technique that can measure the diffusion of water molecules in biological tissues quantitatively and noninvasively. High b values (greater than 400 s/mm²) should be selected for accurate ADC measurements in abdominal evaluation [11, 22, 23]. The most suitable b values were reported as b500–600 sec/mm² [24]. Normal liver parenchyma has a short T2 relaxation time, so the b value should not be greater than 1000s/mm² [25]. Inan et al. [13] found a significant difference in b1000 values but not a significant difference in b500 values in their study of hydatid cysts and simple cysts. For these reasons, b600 and b1000 values were used in this study.

Studies show that the ADC values for benign liver lesions are significantly higher than for malignant lesions. This difference was attributed to benign lesions often having lower cellularity than malignant lesions [26–28]. There are limited studies in the literature regarding the use of DWI for the differential diagnosis and classification of hydatid cysts from other cystic lesions that are benign liver lesions [29, 30]. Oruc et al. [14] used b1000 value in their study with hydatid cyst, abscess and simple cyst, and ADC values were 2.84 ± 0.38, 3.05 ± 0.17, 1.70 ± 0.44, 2.92 ± 0.63, 1.26 ± 0.42, and 3.08 ± 0.76 × 10⁻³ s/mm², respectively for type 1, 3, 4, 5 hydatid cyst, abscess, and simple cyst. While simple cysts and abscesses can be distinguished from type 1-2-3 hydatid cysts by ADC values, type 1 and type 3 hydatid cysts cannot be differentiated from simple cysts. The low
number of cases and the absence of a type 2 hydatid cyst case were stated as serious limitations of the study.

Çeçe et al. [29] used the b1000 value in their study and ADC values were $2.48 \pm 0.16$, $2.80 \pm 0.34$, $2.70 \pm 0.34$, $2.02 \pm 0.01$ and $2.18 \pm 0.1 \times 10^{-3} \text{mm}^2/\text{s}$ for type 1, 2, 3, 4 and 5 hydatid cysts, respectively. In terms of mean ADC values, a statistically significant difference was found between types 1, 2, 3, and types 4, 5, and the sensitivity was 90.9 % and specificity was 90.9 %.

Sonmez et al. [30] found no statistically significant difference between $b_0$ and $b_{500}$ in their study with type 1 and 2 hydatid cysts and simple cysts. ADC values at b1000 were calculated as $2.22 \pm 0.24 \times 10^{-3} \text{mm}^2/\text{s}$ for all hydatid cysts and $2.67 \pm 0.04 \times 10^{-3} \text{mm}^2/\text{s}$ for simple cysts. According to the ADC values, a distinction was made between the whole hydatid cyst group and simple cysts, with sensitivity of 60 % and specificity of 95 %.

In our study, when the threshold value in ROC analysis for $b_{600}$ was considered as $3.7 \times 10^{-3} \text{mm}^2/\text{sec}$, sensitivity was found as 83 % and specificity was 84 %. With b1000, when the threshold value was accepted as $3.2 \times 10^{-3} \text{mm}^2/\text{sec}$ in ROC analysis, sensitivity was found to be 80 % and specificity was 77 %. It was shown that ADC values are lower in hydatid cysts compared to simple cysts. This difference is based on the serous fluid content of simple cysts; the value for hydatid cysts was attributed to their denser content consisting of scolex, sodium chloride, proteins, glucose, ions, lipids, and polysaccharides [31,32].

The numerical differences between the ADC values in different studies are due to variations in in the b values used, the device and parameters used, gradient changes, and shooting technique used [33]. However, as in both studies by Çeçe et al. and Sonmez et al., the common point was that ADC value decreases as the cyst content increases, as we found in our study.

As one of the routines in neuroradiological imaging, the long duration of the FLAIR sequence was a disadvantage in abdominal MRI applications, but it has become applicable with fast sequences developed recently [34,35]. In the literature, there are few studies about the FLAIR sequence in abdominal MR applications [36–38]. Without contrast studies, the distinction between hemangioma and simple cyst, which are benign liver lesions, cannot be always reliably made.

Sasaki et al. [37] investigated the contribution of the FLAIR sequence to differential diagnosis in a study conducted with patients with simple cysts and hemangiomas and reported that 96.3 % of simple cysts were hypointense compared to liver parenchyma, and 98.2 % of hemangiomas were hyperintense compared to liver parenchyma. The appearance of simple cysts that are not monitored as hypointense may be due to protein or hemorrhagic content. In another study, simple cyst and metastases were compared, and 97.3 % of simple cysts were hypointense compared to liver parenchyma, and 94.9 % of metastases were hyperintense, and the FLAIR sequence was a safe modality for differential diagnosis [36]. In these two studies, the TI value was selected as 2265 ms, and the fact that simple cysts could be distinguished with the FLAIR sequence was attributed to the difference in the TI values of the lesions [39,40]. Naganawa et al. [38] chose the TI value as 920 ms for the FLAIR sequence and stated that simple cysts were suppressed, unlike hepatocellular carcinoma, hemangioma, and liver metastases, and were observed as hypointense compared to liver parenchyma.

In the literature, there is no study conducted with FLAIR sequence for hydatid cysts. Our work on this subject is a unique study. In our study, 33 (82.5 %) simple cysts became hypointense compared to liver parenchyma by being suppressed on FLAIR sequence, while 7 (17.5 %) simple cysts were observed as iso-hyperintense and not suppressed. Five (12.5 %) of the simple non-suppressed cysts were proven to be

Fig. 6. FLAIR sequence (a) simple cyst, (b) type 1 hydatid cyst, (c) type 2 hydatid cyst, (d) type 3 hydatid cyst. While simple cysts, type 1 and type 3 hydatid cysts are hypointense with suppression, type 2 hydatid cyst is not suppressed and is observed as hyperintense.
hydatid cysts (type 1-2-3) are isointense on DWI with b1000, and 
were not included in the study. The distribution of the number of pa 

4.1. Limitations

The parallel imaging method or respiratory triggered imaging 
method, which are techniques to increase image quality, were not used. 
Therefore, signal-to-noise ratio was low. Anatomical details decreased 
especially on DWIs with b1000 value; therefore, lesions smaller than 
2 cm were not included in the study. Type 4 and type 5 hydatid cysts 
were not included in the study. The distribution of the number of pa 

4.2. Conclusion

Simple cyst and hydatid cyst (type 1-2-3) distinctions can be made 
with ADC measurements at b600 and b1000 values. Simple cysts and 
hydatid cysts (type 1-2-3) are isointense on DWI with b1000, and pe 

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hypointense on T1W images and surgically hemorrhagic. Two simple 
cysts were observed to be isointense compared with the liver on FLAIR 

Kursad Yalcinoz: Resources, Conceptualization, Methodology, Formal 
analysis, Investigation, Writing - original draft. Turkan Ikizceli: 
Formal analysis, Data curation, Writing - review & editing. Servet 
Kahveci: Data curation, Investigation, Methodology. Okkes Ibrahim 
Karahan: Supervision, Project administration.

Declarations of Competing Interest

The authors report no declarations of interest.

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