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ABDOMINAL IMAGING

ORIGINAL ARTICLE

The value of diffusion-weighted imaging and apparent diffusion coefficient quantification in the diagnosis of perforated and nonperforated appendicitis

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PURPOSE
We aimed to evaluate the effectiveness of diffusion-weighted magnetic resonance imaging (DW-MRI) and apparent diffusion coefficient (ADC) values in the diagnosis of acute appendicitis and differentiation of perforated and nonperforated appendicitis cases, with histopathologic correlation.

MATERIALS AND METHODS
Sixty consecutive patients (34 males, 26 females; mean age, 35.6±15.5 years; range, 17–83 years) with a presumptive diagnosis of acute appendicitis were included in this prospective study. With a 1.5 Tesla MRI unit, DW-MRI examinations were performed with b values of 50, 400, and 800 s/mm^2. The mean ADC values of case and control groups, as well as in perforated and nonperforated groups were compared.

RESULTS
Of the 60 cases, 44 had a radiological diagnosis of acute appendicitis, and 16 were regarded as normal. Of the 40 patients who underwent surgical operation, 12 had a histopathological diagnosis of perforated appendicitis, and 28 had nonperforated appendicitis. Mean ADC value in patients with acute appendicitis (1.01±0.26×10^{-3} mm^2/s) was lower than the control group (1.85±0.13×10^{-3} mm^2/s) ($P < 0.001$). Mean ADC value of the perforated group (0.79±0.19×10^{-3} mm^2/s) was lower than the nonperforated group (1.11±0.22×10^{-3} mm^2/s) ($P < 0.001$). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy rate of DW-MRI in the diagnosis of acute appendicitis were 97.5%, 100%, 97.5%, 100%, and 98.1%, respectively.

CONCLUSION
DW-MRI and ADC quantification are effective in the diagnosis of acute appendicitis, both in perforated and nonperforated cases.

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Magnetic resonance imaging (MRI) is the radiological imaging technique offering the highest soft tissue contrast resolution. Currently, in addition to conventional MRI, other MRI techniques are commonly and routinely used, including diffusion-weighted MRI (DW-MRI). DW-MRI is a functional imaging technique that relies on the measurement of the accelerated or slowed microscopic diffusion movements of protons of water molecules. The images are obtained in short interval times and without the requirement for any contrast medium (1).

Recently, studies have reported the use of DW-MRI to show active inflammatory lesions in the bowel. In these reports, the mean apparent diffusion coefficient (ADC) of the inflamed bowel segments were compared with the ADC of normal segments, and statistically significant difference was demonstrated (1, 2). Only one study has been investigated the use of DW-MRI for the diagnosis of patients with acute appendicitis (3). However, this study did not focus on the differential diagnosis of perforated and nonperforated appendicitis cases.

The aim of this study was to evaluate the effectiveness of DW-MRI and quantitative measurement of ADC values in the diagnosis of acute appendicitis, and in the differentiation between perforated and nonperforated appendicitis cases, with histopathologic correlation.

Materials and methods

Patient selection

This prospective study was performed between March 2009 and February 2010. Sixty consecutive patients (34 males, 26 females; mean age, 35.6±15.5 years; age range, 17–83 years) having right lower abdominal pain with a clinically suspected diagnosis of acute appendicitis were included in the study. Twenty individuals (nine females, 11 males; mean age, 37.7±15.8 years; range, 18–73 years) who underwent abdominal MRI examination for reasons other than suspected appendicitis constituted the control group.

Approval by the ethics committee and informed consent from all patients were obtained for the study.

Imaging

Abdominal MRI examinations of the study and control groups were performed with Magnetom Symphony 1.5 Tesla (Siemens AG Medical Solutions, Erlangen, Germany) using body coil. The gradient force of the superconductive (niobium-titanium) magnet was 30 mT/m, and the maximum field-of-view (FOV) width was 400 mm.

Before the single shot echo-planar DW-MRI examination of the 80 patients constituting the study and control groups, a T2-weighted True-fast imaging with steady state precession (True-FISP) sequence in the axial plane (TR, 4.4 s; TE, 2.2 s; average, 2; flip angle, 80°; matrix, 256×256; slice number, 25; slice thickness, 5 mm; slice gap, 15%), a T2-weighted True-FISP sequence in the coronal plane (TR, 4.3 s; TE, 2.15 s; average, 1; slice number, 35; slice thickness, 4 mm; slice-gap, 15%) followed by axial and coronal turbo inversion-recovery in magnitude (TIRM) (TR, 7660 s; TE, 100 s; flip angle, 80°; matrix, 256×256; slice number, 35; slice thickness, 4 mm; average, 1; gap, 15%) with breath holding were obtained. The diffusion-weighted single shot echo-planar sequence and chemical shift selective fat suppression were obtained without breath holding and without using contrast medium (TR/TE, 300/94 s; matrix, 128×128; slice number, 25; slice gap, 15%; slice thickness, 5 mm; FOV, 350–380 mm; time, 2.26 min; PAT factor, 2; PAT mode, generalized autocalibrating partially parallel acquisitions [GRAPPA]). The protocol used in our clinic for echo-planar DW-MRI was as follows: 0 s/mm², 50 s/mm², 400 s/mm², 800 s/mm², and ADC.

Image analysis

Once obtained, the TIRM, True-FISP, and DW-MRI sequences were transferred to an independent workstation (Leonardo Syngo 2002B, Siemens AG Medical Solutions) to evaluate the DW-MRI data and remodel the ADC maps. One radiologist assessed the data. The DW-MRI examinations were evaluated, and the mean ADC values were calculated from ADC maps.

The patient was diagnosed as acute appendicitis if the appendix lumen displayed a high signal on DW-MRI and a low signal on ADC map. Using axial and coronal TIRM and True-FISP images as references, the most hyperintense area of the inflamed appendix on DW-MRI was determined, and a region of interest (ROI) was placed at the same localization on the ADC map. ROI areas were defined between 9 and 25 mm² according to the application area. For each patient, three measurements were performed at the lesion area and the mean ADC values were calculated. The b value was 800 s/mm², and the inflamed appendices were hyperintense on DW-MRI compared to the cecum, and hypointense on ADC maps.

As it was not possible to define precise appendix localization on DW-MRI for the control group, the ADC measurements were obtained from cecum using free hand ROI over 3 to 6 mm². All ADC measurements in patient and control groups were calculated by the same observer.

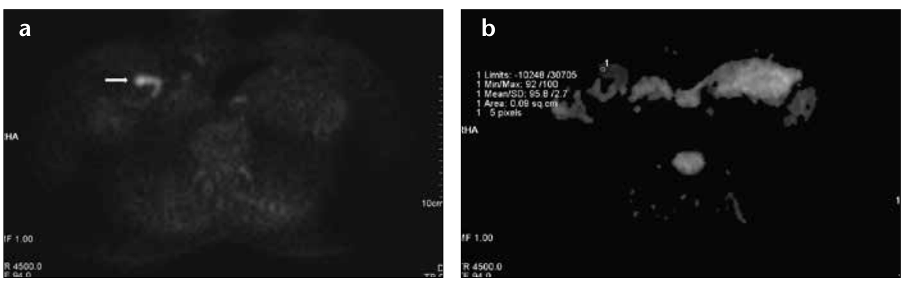

Figure 1. a, b. Nonperforated appendicitis in a 23-year-old man. The appendix shows restricted diffusion (*arrow*) on DW-MRI **(a)**, and is hypointense on ADC map **(b)**. The mean ADC value is 0.95×10^{-3} mm²/s.

Statistical analysis

The defining statistics related to the characteristics of interest were expressed as mean, median, standard deviation, and minimum and maximum values. In order to determine the difference between the ADC values of the appendicitis group and the control group, an independent sample t test was used. In order to evaluate any differences among the ADC values of the patients with appendicitis, without appendicitis, and in the control group, a one-way analysis of variance (ANOVA) was administered. A chi-square test was used for comparison between the mean ADC values of the perforated and nonperforated appendicitis subgroups. The significance level used was $P < 0.05$, and calculations were performed using a commercially available software (Statistical Package for Social Sciences, version 13.0, SPSS Inc., Chicago, Illinois, USA).

In addition, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy rate of DW-MRI in the diagnosis of appendicitis were determined.

Results

Of the 60 patients, 39 who were diagnosed to have appendicitis based on DW-MRI (Figs. 1–4) and one patient having strong clinical suspicion of appendicitis despite any DW-MRI finding (23 males, 17 females; mean age, 33.6±16.2 years; range, 17–83 years) underwent surgical operation. The histopathological diagnosis in these patients was appendicitis. The five patients who were diagnosed with appendicitis based on DW-MRI but did not accept surgical operation were excluded from the study. Unfortunately, the clinical course of these five patients could not be followed-up. Fifteen patients not diagnosed with appendicitis on DW-MRI did not under-

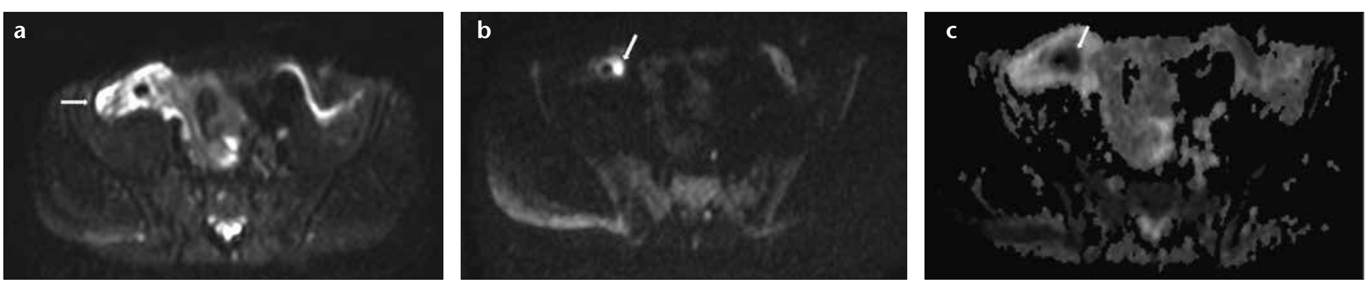

Figure 2. a–c. Perforated appendicitis in a 22-year-old man. On the axial True-FISP image **(a)**, heterogeneity consistent with inflammation in peri-appendicial fat tissue and the thickened appendix are visualized (*arrow*). The appendix shows restricted diffusion (*arrow*) on DW-MRI **(b)**, and is hypointense (*arrow*) on ADC map **(c)**.

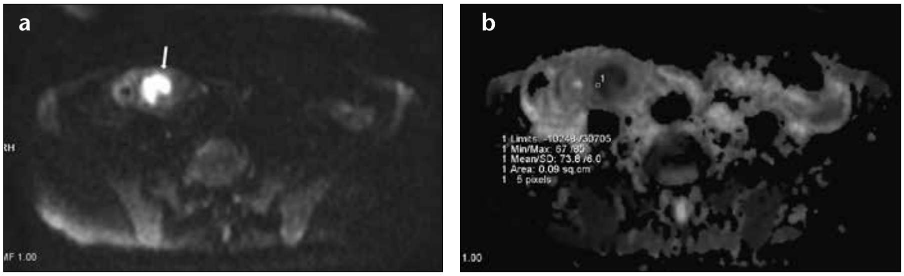

Figure 3. a, b. Perforated appendicitis in a 41-year-old woman. The appendix shows restricted diffusion (*arrow*) on DW-MRI **(a)**, and is hypointense on ADC map **(b)**.

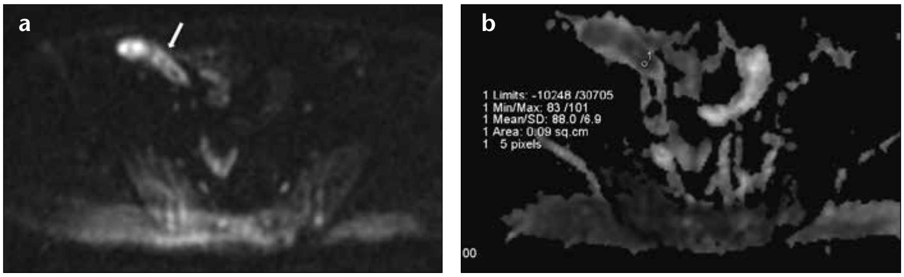

Figure 4. a, b. Nonperforated appendicitis in a 32-year-old man. The appendix shows restricted diffusion (*arrow*) on DW-MRI **(a)**, and is hypointense on ADC map **(b)**.

Table. The mean ADC values (range) of the study groups

	n	ADC (10^{-3} mm²/s)
Control	20	1.85 (1.75–2.11)
No appendicitis	15	1.82 (1.65–2.04)
Appendicitis	39	1.02 (0.42–1.44)

go operation, and as their symptoms disappeared at the end of the clinical observation period, the cases were not considered as appendicitis. There was no diagnosis other than appendicitis (such as ovarian torsion, inflammatory bowel disease, etc.), and there was not any retroceacal appendicitis.

The mean ADC values of the 39 patients with a diagnosis of appendicitis on DW-MRI together with histopathological approval were statistically compared with the mean ADC values of the control group. The mean ADC values of the 15 patients who were not diagnosed with appendicitis based on DW-MRI and clinical follow-up were compared with the mean ADC values of the appendicitis and control groups. Among the 40 cases with histopathologically proven appendicitis, 12 were perforated while 28 were nonperforated.

The mean ADC value in patients with appendicitis was significantly lower than the control group; $1.01 \pm 0.26 \times 10^{-3}$ mm²/s (range, $0.42–1.44 \times 10^{-3}$ mm²/s) and $1.85 \pm 0.13 \times 10^{-3}$ mm²/s (range, $1.75–2.11 \times 10^{-3}$ mm²/s), respectively ($P < 0.001$).

The mean ADC value in patients with appendicitis ($1.01 \pm 0.26 \times 10^{-3}$ mm²/s; range, $0.42–1.44 \times 10^{-3}$ mm²/s) was significantly lower than patients without appendicitis (1.82×10^{-3} mm²/s; range, $1.65–2.04 \times 10^{-3}$ mm²/s) ($P < 0.001$) (Table).

There was no statistically significant difference between the mean ADC values of the patients without appendicitis (1.82×10^{-3} mm²/s; range, $1.65–2.04 \times 10^{-3}$ mm²/s) and the control group ($1.85 \pm 0.13 \times 10^{-3}$ mm²/s; range, $1.75–2.11 \times 10^{-3}$ mm²/s) ($P > 0.05$) (Table).

The mean ADC value of the perforated appendicitis cases was significantly lower than the nonperforated cases; $0.79 \pm 0.19 \times 10^{-3}$ mm²/s (range, $0.42–1.08 \times 10^{-3}$ mm²/s) and $1.11 \pm 0.22 \times 10^{-3}$ mm²/s (range, $0.82–1.44 \times 10^{-3}$ mm²/s), respectively ($P < 0.001$).

The sensitivity, specificity, NPV, PPV, and accuracy rate of DW-MRI in the diagnosis of appendicitis were found to be 97.5%, 100%, 93.75%, 100%, and 98.18%, respectively.

On receiver operator characteristics (ROC) curve analysis based on ADC, the cut-off value for the diagnosis of appendicitis was 1.54×10^{-3} mm²/s, with a sensitivity and specificity of 100%. The cut-off value for the differential diagnosis of perforated and nonperforated appendicitis was 0.98×10^{-3} mm²/s, with a sensitivity of 77.8% and specificity of 91.7% (Fig. 5).

Discussion

Computed tomography (CT) is currently used for the differential diagnosis of acute abdomen such as appendicitis (4), especially in patients with inconclusive ultrasonography (US) findings. MRI can be used for pregnant women or children in whom CT is contraindicated when radiation must be avoided. T1- and T2-weighted turbo spin echo sequences and inversion recovery turbo spin echo sequence as much as T1-weighed sequences can be used with MRI (5, 6). In a comparative study, İncesu et al. (7) applied abdominal MRI and US to 60 patients potentially suffering from appendicitis, and a higher performance of MRI technique was statistically demonstrated. DW-MRI is a feasible and applicable imaging modality under emergency settings, owing to its short acquisition time, and lack of need for contrast material administration.

DW-MRI has several technical limitations; for example, respiratory, cardiac or peristaltic physiological movements can decrease the quality of the images due to the sensitivity of this technique to movement, thus impairing the examination. Because of this limitation, DW-MRI was previously only used for brain imaging until the development of fast MRI techniques. The development of echo planar imaging (EPI), one of the fast MRI techniques, eliminated the long imaging time of conventional sequences and the associated artifacts, thus making DW-MRI usable for abdominal examinations (8–11).

The studies on diffusion in the abdomen were performed using ultrafast sequences, allowing data to be obtained in one breath. This decreased the number of artifacts due to respiration, arterial beating, and bowel movements, further decreasing the signal-noise ratio. These ultrafast sequences were EPI sequences that collected data in approximately 30–60 ms. Thus, artifacts associated with macroscopic physiological movements could be eliminated (8–11).

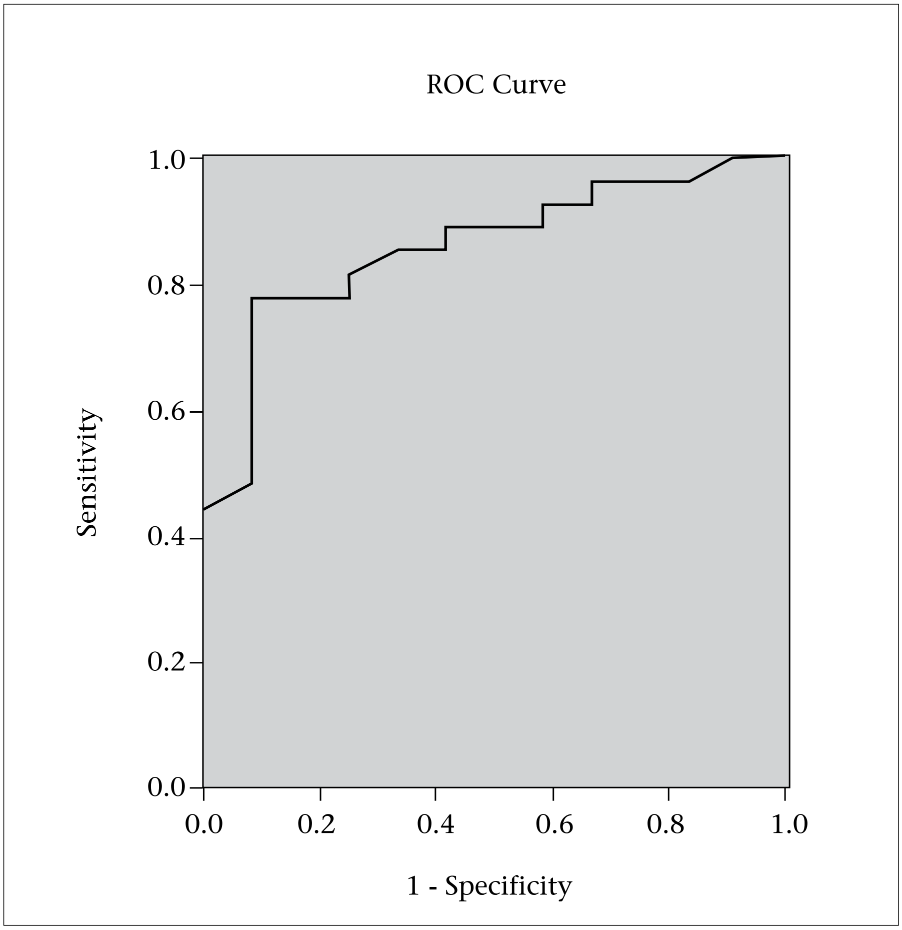

Figure 5. On ROC curve analysis based on ADC, the cut-off value for the differential diagnosis of perforated and nonperforated appendicitis is 0.98×10^{-3} mm^2/s, with a sensitivity of 77.8% and specificity of 91.7%.

The studies on abdominal diffusion mostly consist of single shot EPI (SSEPI). With this technique, images are obtained in a time period shorter than one second, so physiological movements are frozen. By the addition of a breath-hold to EPI, respiratory artifacts are prevented, and ADC measurements can then be performed in the abdomen (10). We also used the SSEPI technique in our study and did not include the breath-hold during DW-MRI, allowing for the possibility to analyze elderly and obese patients who may have difficulty with breath holding. We did not observe any artifacts associated with respiratory movement, vessel beat, or bowel movement in the DW-MRI of our patients.

ADC is a quantitative parameter calculated from DW-MRI images and an indicator of the combined effect of water diffusion and capillary perfusion in extracellular and extravascular space (11).

Selecting the specific b value to use during DW-MRI is crucial. If the b value is 400 s/mm^2 or less, the images obtained are not only affected by water molecule diffusion but also by blood microcirculation and the associated perfusion in tissue capillaries. Thus, by specifying a low b value, the perfusion effects on ADC value will be higher. In this case, called pseudo-diffusion, the ADC value will be higher than in normal tissue because of capillary perfusion (8–10). Ichikawa et al. (12) used low b values, such as 1, 6, 16, and 55 mm^2/s, which led to high ADC values for abdominal organs. As mentioned in their study, in selecting low b values, factors such as perfusion and T2-weighted shine-through had more of an impact on the ADC measurements. Thus, the authors stated that b values over 400 mm^2/s would be more appropriate to determine ADC values in abdominal diffusion studies. In our study, we used b values of 50, 400, and 800 mm^2/s, which allowed us to obtain sufficient imaging quality on DW-MRI.

In our study, while no hyperintense signal was observed on DW-MRI, one patient with strong clinical suspicion for appendicitis underwent surgical operation, and the histopathological diagnosis was nonperforated appendicitis. In this patient, the mean ADC value obtained from cecum was 1.68×10^{-3} mm^2/s, which was higher than the cut-off value of 1545×10^{-3} mm^2/s defined for the distinction of appendicitis on ROC curve analysis. This case constituted the false negative data of our study. There was no reasonable explanation for the absence of high signal on DW-MRI in this patient. In the present study, all the appendicitis cases except one were easily discernible with a hyperintense signal on DW-MRI and hypointense signal on ADC maps. Increased cell volume on the inflamed appendix wall with the lumen filled with purulent material, which has a high viscosity and cellularity, might be the cause of restriction in diffusion in appendicitis cases. Very low ADC accounts for signal hyperintensity on DW-MRI and signal hypointensity on ADC maps (13). In our study, the mean ADC values of the perforated cases were significantly lower than the nonperforated cases, and we speculate that this may be related to the degree of the inflammatory process.

Up to date, only one study has used DW-MRI and ADC measurements in appendicitis cases. The study by İnci et al. (3) on 119 appendicitis and 50 control cases reported a mean ADC value of 2.02±0.19×10^{-3} mm^2/s in the control group and a significantly lower ADC of 1.28±0.18×10^{-3} mm^2/s in the inflamed appendix group. The results in our study are consistent with these results, and further demonstrate a statistically significant cut-off ADC value for the differentiation of perforated and nonperforated appendicitis cases.

In segments without active inflammation, high intensity signals were obtained using DW-MRI in large bowel, thus decreasing the specificity. In parallel, the ADC value in large bowel was lower than in small bowel. Increased DW-MRI signal intensity and decreased ADC value in inactive segments of colon could be partly due to the bowel content (1).

When ADC values are considered, our results are similar to those of İnci et al. (3), Oto et al. (2), and Kiryu et al. (1). These studies showed that the mean ADC values obtained for appendicitis cases are lower than the mean ADC values obtained in inflamed bowels in Crohn's disease. We speculate that these results are most likely due to the advanced stage of inflammation in appendicitis cases compared to edema and inflammation in Crohn's disease.

In our study, the sensitivity, specificity, and accuracy rate values of DW-MRI were similar to those of İnci et al. (3); interestingly, in their study, one appendicitis case was also not detected on DW-MRI. However, lower statistical values were reported by Kiryu et al. (1) and Oto et al. (2). These results suggest that DW-MRI may be more effective in the diagnosis of appendicitis compared to its ability to display inflammatory areas in Crohn's disease.

In many studies, the inverse proportionality between diagnostic certitude and appendix perforation has been demonstrated (1, 7). While mortality is low for nonperforated appendicitis (0.1%), it can reach 3% in perforated appendicitis (7). The ADC value can be used for the discrimination between perforated and nonperforated appendicitis. In our study, from the ROC curve analysis performed to discriminate between perforated and nonperforated groups, the ADC cut-off value was 0.98×10^{-3} mm²/s, with a sensitivity of 77.8% and specificity of 91.7%.

There were a few limitations in our study. First, the ADC measurements were operator dependent, and obtained from the cecal wall in the control group. Only one case underwent operation among the patients with negative DW-MRI findings. Further, DW-MRI was not compared with other MRI sequences, such as post-gadolinium T1-weighted images. Lack of interobserver variability should also be indicated as a limitation of our study. The cost-effectiveness of the method should be evaluated with further studies combining US and CT examinations.

In conclusion, DW-MRI is a noninvasive, fast imaging technique that does not require contrast medium or involve ionizing radiation. DW-MRI shows high sensitivity and specificity in the diagnosis of appendicitis, and ADC values can be useful in the differentiation of perforated and nonperforated appendicitis. We suggest the use of DW-MRI in routine practice for the evaluation of patients with suspected appendicitis.

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Kiryu S, Dodanuki K, Takao H, et al. Free-breathing diffusion-weighted imaging for the assessment of inflammatory activity in Crohn's disease. J Magn Reson Imaging 2009; 29:880–886. [CrossRef]
2. Oto A, Zhu F, Kulkarni K, Karczmar GS, Turner JR, Rubin D. Evaluation of diffusion-weighted MR for detection of bowel inflammation in patients with Crohn's disease. Acad Radiol 2009; 16:597–603. [CrossRef]
3. İnci E, Kılıçkesmez O, Hocağlu E, Aydın S, Bayramoğlu S, Cimilli T. Utility of diffusion-weighted imaging in the diagnosis of acute appendicitis. Eur Radiol 2011; 21:768–775. [CrossRef]
4. Forsted DH, Kalbhen CL. CT of pregnant women for urinary tract calculi, pulmonary thromboembolism and acute appendicitis. AJR Am J Roentgenol 2002; 178:1285.
5. Oto A, Ernst RD, Shah R, et al. Right-lower-quadrant pain and suspected appendicitis in pregnant women: evaluation with MR imaging--initial experience. Radiology 2005; 234:445–451. [CrossRef]
6. Pedrosa I, Levine D, Eyvazzadeh AD, Siewert B, Ngo L, Rofsky NM. MR imaging evaluation of acute appendicitis in pregnancy. Radiology 2006; 238:891–899. [CrossRef]
7. İncesu L, Coşkun A, Selçuk MB, Akan H, Sozubir S, Bernay F. Acute appendicitis: MR imaging and sonographic correlation. AJR Am J Roentgenol 1997; 168:669–674.
8. Avcu S, Koseoglu MN, Ceylan K, Bulut MD, Unal O. The value of diffusion-weighted MRI in the diagnosis of malignant and benign urinary bladder lesions. Br J Radiol 2011; 84:875–882. [CrossRef]
9. Müller MF, Prasad P, Siewert B, Nissenbaum MA, Raptopoulos V, Edelman RR. Abdominal diffusion mapping with use of a whole-body echo-planar system. Radiology 1994; 190:475–478.
10. Ebisu T, Tanaka C, Umeda M, et al. Discrimination of brain abscess from necrotic or cystic tumors by diffusion-weighted echo planar imaging. Magn Reson Imaging 1996; 14:1113–1116. [CrossRef]
11. Unal O, Koparan HI, Avcu S, Kalender AM, Kisli E. The diagnostic value of diffusion-weighted magnetic resonance imaging in soft tissue abscesses. Eur J Radiol 2011; 77:490–494. [CrossRef]
12. Ichikawa T, Haradome H, Hachiya J, Nitatori T, Araki T. Diffusion-weighted MR imaging with single-shot echo-planar imaging in the upper abdomen: preliminary clinical experience in 61 patients. Abdom Imaging 1999; 24:456–461. [CrossRef]
13. Chan JH, Tsui EY, Luk SH, et al. MR diffusion-weighted imaging of kidney: differentiation between hydronephrosis and pyonephrosis. Clin Imaging 2001; 25:110–113. [CrossRef]