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Accuracy, criteria, and clinical significance of visual assessment on diffusion-weighted imaging and apparent diffusion coefficient quantification for diagnosing acute appendicitis

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Abstract

Purpose To assess the accuracy, criteria, and clinical significance of diffusion-weighted imaging (DWI) signal intensity and apparent diffusion coefficient (ADC) quantification for diagnosing acute appendicitis.

Methods Fifty-one patients with right lower abdominal pain [uncomplicated appendicitis ($n = 25$), complicated appendicitis ($n = 10$), and non-appendicitis ($n = 16$)] who underwent MR examination were enrolled in this retrospective study. Two radiologists independently measured appendiceal diameter and wall thickness. They assessed whether a wall defect, an abscess, extraluminal air, or an appendicolith was present on axial T2WI; evaluated intensity on DWI using a 5-point scale; and determined the ADC values of the appendix and peri-appendiceal tissue. Statistical analysis was performed to assess imaging findings for the diagnosis of appendicitis and complicated appendicitis. Cut-off values were determined using receiver operating characteristic analysis.

Results For diagnosing acute appendicitis, the accuracy improved from 78.4% using only T2WI to 86.3% using combined T2WI and DWI for reader 1 and from 82.4 to 86.3% for reader 2. For the appendix, the cut-off ADC values that diagnosed appendicitis were 1.41×10^{-3} and 1.26×10^{-3} mm^2/s with accuracies of 78.4% and 76.5%, respectively. For the peri-appendiceal tissue, these values of 1.03×10^{-3} and 0.91×10^{-3} mm^2/s differentiated between uncomplicated and complicated appendicitis with an accuracy of 97.1%.

Conclusions Combined DWI and T2WI provided high accuracy for diagnosing appendicitis. The inflamed appendix had lower ADC value than the normal appendix. The peri-appendiceal tissue presenting low ADC value was a notable finding of complicated appendicitis.

Keywords Magnetic resonance image · Diffusion-weighted image · Apparent diffusion coefficient · Acute appendicitis

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Introduction

Acute appendicitis is a common condition requiring emergent surgery with an estimated lifetime risk of 7–8%, and it predominantly occurs in the second or third decade of life [1]. Currently, computed tomography (CT) plays a pivotal role in the diagnosis of acute abdomen and is recommended in adult patients with right lower abdominal pain [2, 3]. Conversely, ultrasonography (US) is recommended as the first-line imaging approach for pediatric and pregnant female patients suspected with acute appendicitis, as ionizing radiation exposure should preferably be avoided in these patients [3]. However, US requires skilled, well-trained personnel for satisfactory examination, and it frequently indeterminate findings are observed, requiring additional imaging examinations [4].

In abdominal imaging, magnetic resonance imaging (MRI) has been mostly used for diagnosing biliary and gynecological pathologies [5, 6]; moreover, it has been more frequently used in pediatric and pregnant patients [2]. However, recent technological advances have enabled the imaging of the gastrointestinal tract using MRI, and its high ability to demonstrate both a normal and an inflamed appendix has been reported [7]. According to published studies, MRI is advocated as a first-line or second-line imaging modality after US for diagnosing acute appendicitis as it has an accuracy comparable to that of CT and prevents exposure to ionizing radiation [8–11]. Moreover, it has been used for evaluating other gastrointestinal diseases associated with acute abdominal pain [12–16]. The advantages of MRI over CT include excellent tissue contrast, even without the use of a nephrotoxic contrast agent, and no radiation exposure during scanning, which make MRI an attractive imaging modality, particularly for pediatric and pregnant patients who should avoid radiation exposure.

A normal appendix appears as a tubular, blind-ending structure originating from the cecum, with a diameter less than 7 mm and a wall thickness less than 2 mm [12] on MRI and with better visualization on T2-weighted imaging (T2WI) [17, 18]. On the other hand, an inflamed appendix is more distended with a thicker wall, and fat-suppressed T2WI (FS-T2WI) is more sensitive to edema and inflammation of the appendix and peri-appendiceal tissue [12]. In addition, an inflamed appendix shows hyperintensity on diffusion-weighted imaging (DWI), which helps in the diagnosis of acute appendicitis [19, 20] and improves diagnostic sensitivity, especially among inexperienced readers [21]. Moreover, apparent diffusion coefficient (ADC) quantification has been reported to be able to distinguish between perforated and non-perforated appendicitis [22]. However, there are few reports on the use of DWI and ADC quantification for the diagnosis of appendicitis, and the criteria of DWI and value of ADC quantification regarding the diagnosis of acute appendicitis are unclear. Therefore, the purpose of this study was to investigate the diagnostic accuracy of MRI and determine the accuracy, criteria, and clinical significance of visual assessment on DWI and ADC quantification for diagnosing acute appendicitis and for distinguishing between complicated and non-complicated appendicitis.

Materials and methods

Patients

This retrospective study was approved by our institutional review board, and the requirement of written informed consent was waived. According to the MR indication for acute abdominal pain at our institution, a pregnant female, a female suspected of pregnancy, and pediatric patients aged less than or equal to 18 years are firstly assessed by ultrasound. MR examination is performed if the diagnosis is not made. Patients aged between 18 and 30 years and patients with renal function impairment or iodine contrast allergy undergo non-contrast CT. When the diagnosis could not be established and when complicated or uncomplicated appendicitis could not be determined, MR examination is performed instead of contrast-enhanced CT to reduce radiation exposure and avoid the adverse effects of iodine contrast media, respectively. We identified 55 consecutive patients who underwent MR examination for the assessment of right lower abdominal pain with suspicion of acute appendicitis between June 2017 and April 2018. In four patients, the appendix was not identified because of previous appendectomy, and these patients were excluded. Finally, 51 patients (24 male and 27 female patients; mean age, 35.1 years; age range, 6–90 years) were enrolled. This study cohort including 14 pediatric patients (9 male and 5 female patients; mean age 11.8 years; age range 6–18 years, body mass index (BMI) 17.1 ± 3.2), 11 female patients suspected of pregnancy (mean age 29.4 years; age range 23–40 years; BMI 22.3 ± 5.6), 9 patients who were not confidently diagnosed with non-contrast CT (6 male and 3 female patients; mean age 25.2 years; age range 20–37 years; BMI 20.8 ± 2.0), and 17 patients with renal function impairment or iodine contrast allergy (7 male and 10 female patients; mean age 63.2 years; age range 39–90 years; BMI 23.6 ± 2.0). CT was performed within 24 h after MRI in adult patients. Among the 51 patients, a surgical diagnosis was made in 25 patients, with complicated appendicitis diagnosed in 10 patients and uncomplicated appendicitis diagnosed in 15 patients. The diagnosis was made according to CT findings and the clinical course in the remaining 26 patients, with uncomplicated appendicitis diagnosed in 10 patients and other conditions diagnosed in 16 patients [bacterial colitis ($n = 2$), ischemic colitis ($n = 1$), eosinophilic gastroenteritis ($n = 1$), Meckel diverticulitis ($n = 1$), colonic diverticulitis ($n = 1$), mesenteric lymphadenitis ($n = 1$), endometriosis ($n = 1$), vasculitis ($n = 1$), acetonemic vomiting ($n = 1$), and nonspecific causes ($n = 6$)].

MR protocol

MR examinations were performed using a 1.5T MR scanner (Magnetom Aera, Siemens, Muenchen, Germany) with an 18-channel surface coil (1.5T Tim coil, Siemens). Neither intravenous nor intraluminal contrast medium was used in the MR study. Axial and coronal T2WI [half-Fourier acquisition single-shot turbo spin-echo (HASTE); repetition time (TR): 700 ms, echo time (TE): 70 ms, field of view

(FOV): 320 mm and 400 mm for axial and coronal images, respectively, matrix: 512 × 512 mm, slice thickness: 5 mm] and DWI (TR: 7300 ms, TE: 68 ms, FOV: 320 mm, matrix: 150 × 120 mm, slice thickness: 5 mm, b value: 50 and 800 s/mm^2) were performed.

Image analysis

All images were independently reviewed by two radiologists (K.T. and N.N. with 10 and 30 years of experience reading MRI images, respectively) who were aware of patient age, sex, and chief complaints but were blinded to any other clinical information, and they evaluated the signal intensity of the appendix. First, the two readers identified the appendix on MRI using axial and coronal T2WI, and they measured the appendiceal diameter and appendiceal wall thickness on axial T2WI and recorded whether an appendiceal wall defect, a peri-appendiceal phlegmon or abscess, extraluminal air, or an extraluminal appendicolith was present. Second, they visually evaluated the signal intensity of the appendix on DWI by using a 5-point scale as follows: score 1, no signal intensity; 2, lower signal intensity than that of the small bowel; 3, similar signal intensity to that of the small bowel; 4, higher signal intensity than that of the small bowel; and 5, extremely high signal intensity (Fig. 1). Third, the average ADC values of the appendix and peri-appendiceal tissue were measured using regions of interest (ROI) at 20–40 mm^2, referring to the axial and coronal T2WI findings to identify the appendix (Figs. 2, 3, 4). In placing ROI in the peri-appendiceal tissue, ROI was put on focal fluid collection if any existed (Fig. 3), on low intensity area on ADC map around the appendix without fluid collection (Fig. 4).

Statistical analysis

Statistical comparisons of quantitative evaluation items were performed between non-appendicitis ($n = 16$) and appendicitis ($n = 35$) and between uncomplicated appendicitis ($n = 25$) and complicated appendicitis ($n = 10$). The unpaired *t* test was used for the appendiceal diameter and wall thickness and for the ADC values of the appendix and peri-appendiceal tissue. The Mann–Whitney *U* test was used for the signal intensity of the appendix on DWI. A *p* value of 0.05 or less was considered to indicate a statistically significant difference. Cut-off values and areas under the curve (AUCs) were determined using receiver operating characteristic (ROC) curve analysis for quantitative items, and their sensitivities, specificities, positive-predictive values, negative-predictive values, and accuracies for the diagnosis of appendicitis and complicated appendicitis were calculated. The diagnostic accuracies of respective T2WI findings, combined T2WI findings, and combined T2WI and DWI findings according to cut-off values obtained from the ROC curve analysis were calculated. The diagnosis of appendicitis was made with combined findings when at least one positive finding was noted. Fisher's exact test was used for the imaging findings of an appendiceal wall defect, a peri-appendiceal phlegmon or abscess, extraluminal air, and an extraluminal appendicolith to distinguish between complicated appendicitis and uncomplicated appendicitis. Interobserver agreement was assessed for the findings of an appendiceal wall defect, a phlegmon, an abscess adjacent to the appendix, extraluminal air, and an extraluminal appendicolith, using kappa statistics,

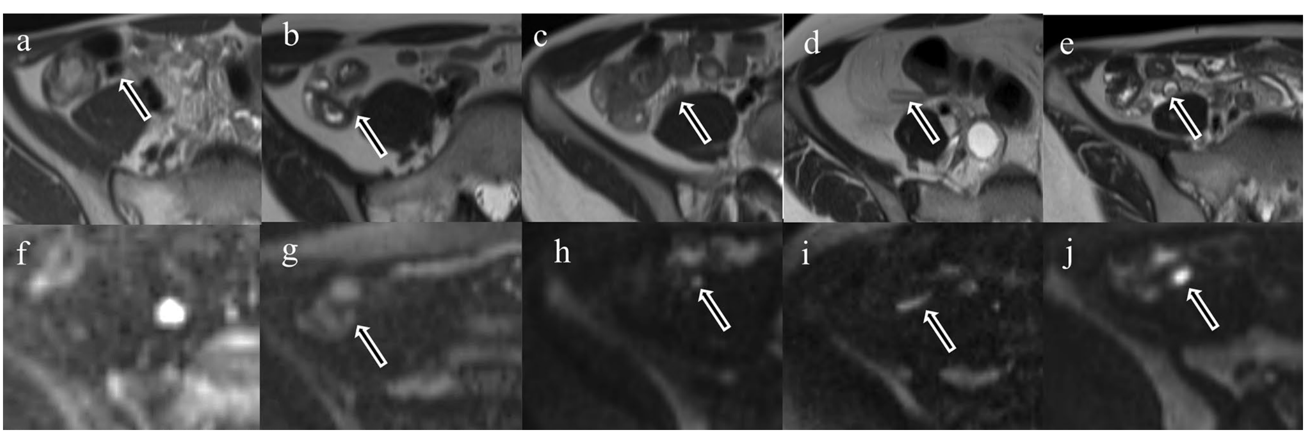

Fig. 1 The signal intensity of the appendix on diffusion-weighted imaging (DWI) using a 5-point scale. The arrows indicate the appendix on T2-weighted imaging (*HASTE* half-Fourier acquisition single-shot turbo spin-echo, *TR* repetition time, 700 ms, *TE* echo time, 70 ms, *FOV* field of view: 320 mm, matrix: 320 × 320 mm, and slice thickness: 5 mm) (**a**–**e**). On DWI (TR: 7300 ms, TE: 73 ms, FOV: 320 mm, matrix: 150 × 120 mm, slice thickness: 5 mm, and b value: 800 s/mm^2), no signal intensity of the appendix is defined as score 1 (**f**), signal intensity lower than that of the small bowel is defined as score 2 (**g**), signal intensity similar to that of the small bowel is defined as score 3 (**h**), signal intensity higher than that of the small bowel is defined as score 4 (**i**), and extremely high signal intensity is defined as score 5 (**j**)

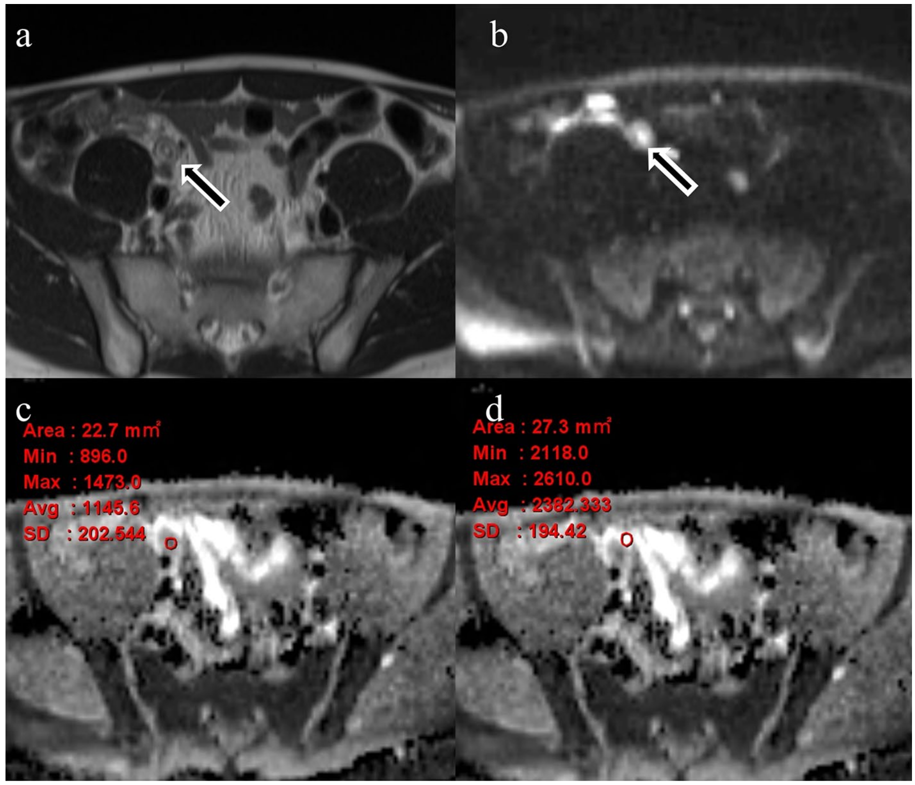

Fig. 2 A 20-year-old man presented with right lower abdominal pain. He was diagnosed with uncomplicated appendicitis on laparotomy. A wall-thickened appendix is shown on T2-weighted imaging (**a**: arrow). An extremely high-intensity appendix is seen on diffusion-weighted imaging (**b**: arrow). The mean ADC value of the appendix is 1.145×10^{-3} mm^2/s (**c**) and that of the peri-appendiceal tissue is 2.382×10^{-3} mm^2/s (**d**). *ADC* apparent diffusion coefficient

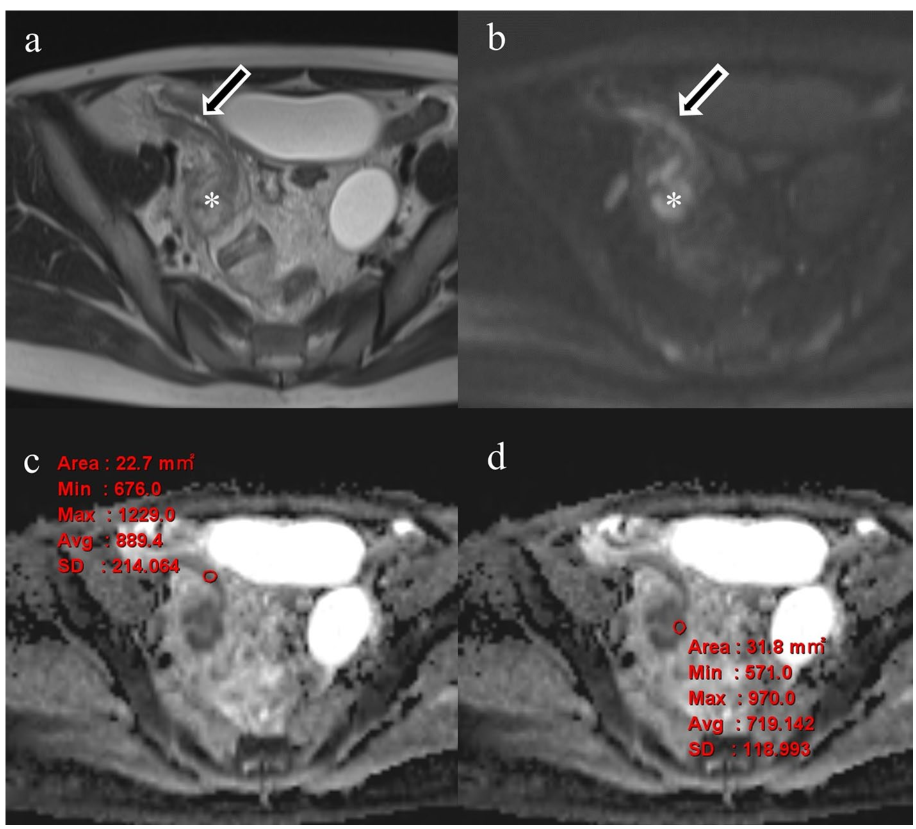

Fig. 3 A 24-year-old woman presented with right lower abdominal pain and nausea. She was diagnosed with complicated appendicitis on laparotomy. A wall-thickened appendix (**a**: arrow) and fluid collection adjacent to the appendix (**a**: asterisk) are shown on T2-weighted imaging. The intensity of the appendix is higher than that of the ileum (**b**: arrow) and fluid collection adjacent to the appendix (**b**: asterisk) shows high intensity on diffusion-weighted imaging. The mean ADC value of the appendix is 0.889×10^{-3} mm^2/s (**c**) and that of the fluid collection is 0.719×10^{-3} mm^2/s (**d**). *ADC* apparent diffusion coefficient. Reproduced from Inoue [35]

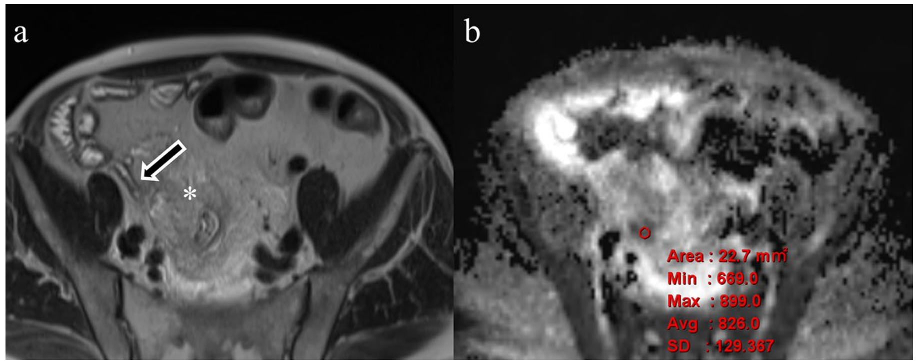

Fig. 4 A 50-year-old man who presented with right lower abdominal pain and disturbance of consciousness. He was diagnosed with complicated appendicitis on laparotomy. The slightly wall-thickened appendix (**a**: arrow) and fat stranding surrounding the appendix (**a**: asterisk) is observed on T2-weighted imaging. The mean ADC value of the peri-appendiceal tissue is 0.826×10^{-3} mm^2/s (**b**)

and it was categorized as poor (< 0.20), fair (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80), and very good (0.81–1.00). All statistical analyses were performed using SPSS statistics 22 (IBM, Chicago, IL, USA).

Results

Table 1 presents the results of the quantitative analysis. On comparing appendicitis and non-appendicitis patients, significant differences were found in the appendiceal diameter ($p < 0.001$, both readers), appendiceal wall thickness

Table 1 Comparisons of quantitative evaluation items between appendicitis and non-appendicitis and between uncomplicated appendicitis and complicated appendicitis

	Non-appendicitis ($n = 16$)	Appendicitis ($n = 35$)	p value
Reader 1			
Appendiceal diameter on T2WI	5.46 ± 1.46	8.09 ± 2.80	<0.001*
Appendiceal wall thickness on T2WI	1.68 ± 0.59	2.64 ± 1.20	<0.001*
Signal intensity on DWI	2.19 ± 1.29	4.31 ± 0.92	<0.001*
ADC value (mm^2/s) of the appendix	$1.15 \times 10^{-3} \pm 0.27 \times 10^{-3}$	$1.57 \times 10^{-3} \pm 0.44 \times 10^{-3}$	0.002*
ADC value (mm^2/s) of the peri-appendiceal tissue	$1.67 \times 10^{-3} \pm 0.71 \times 10^{-3}$	$1.63 \times 10^{-3} \pm 0.62 \times 10^{-3}$	0.832
Reader 2			
Appendiceal diameter on T2WI	5.80 ± 1.19	8.24 ± 3.07	<0.001*
Appendiceal wall thickness on T2WI	1.90 ± 0.57	2.61 ± 1.08	<0.001*
Signal intensity on DWI	2.00 ± 1.32	4.17 ± 0.61	<0.001*
ADC value (mm^2/s) of the appendix	$1.14 \times 10^{-3} \pm 0.26 \times 10^{-3}$	$1.56 \times 10^{-3} \pm 0.41 \times 10^{-3}$	0.001*
ADC value (mm^2/s) of the peri-appendiceal tissue	$1.73 \times 10^{-3} \pm 0.71 \times 10^{-3}$	$1.69 \times 10^{-3} \pm 0.55 \times 10^{-3}$	0.851
	Uncomplicated appendicitis ($n = 25$)	Complicated appendicitis ($n = 10$)	p value
Reader 1			
Appendiceal diameter on T2WI	7.61 ± 2.66	9.29 ± 2.91	0.136
Appendiceal wall thickness on T2WI	2.47 ± 1.12	3.05 ± 1.38	0.258
Signal intensity on DWI	4.36 ± 0.87	4.20 ± 0.98	0.76
ADC value (mm^2/s) of the appendix	$1.19 \times 10^{-3} \pm 0.28 \times 10^{-3}$	$1.05 \times 10^{-3} \pm 0.23 \times 10^{-3}$	0.145
ADC value (mm^2/s) of the peri-appendiceal tissue	$2.03 \times 10^{-3} \pm 0.47 \times 10^{-3}$	$0.76 \times 10^{-3} \pm 0.18 \times 10^{-3}$	< 0.001*
Reader 2			
Appendiceal diameter on T2WI	7.78 ± 2.95	9.56 ± 3.09	0.125
Appendiceal wall thickness on T2WI	2.41 ± 0.78	3.09 ± 1.55	0.218
Signal intensity on DWI	4.12 ± 0.58	4.80 ± 0.64	0.483
ADC value (mm^2/s) of the appendix	$1.17 \times 10^{-3} \pm 0.28 \times 10^{-3}$	$1.08 \times 10^{-3} \pm 0.22 \times 10^{-3}$	0.335
ADC value (mm^2/s) of the peri-appendiceal tissue	$2.01 \times 10^{-3} \pm 0.46 \times 10^{-3}$	$0.77 \times 10^{-3} \pm 0.23 \times 10^{-3}$	< 0.001*

T2WI T2-weighted imaging, *DWI* diffusion-weighted imaging, *ADC* apparent diffusion coefficient

$^*p < 0.05$

($p < 0.001$, both readers), signal intensity of the appendix on DWI ($p < 0.001$, both readers), and ADC value of the appendix ($p = 0.002$, reader 1; $p = 0.001$, reader 2). On comparing uncomplicated and complicated appendicitis patients, a significant difference was found in the ADC value of the peri-appendiceal tissue ($p < 0.001$, both readers). The results for the appendiceal diameter and appendiceal wall thickness on T2WI, appendiceal intensity score on DWI, and ADC value of the appendix did not show any statistical differences.

Table 2 presents the diagnostic values, cut-off values, and AUCs of quantitative evaluation items for distinguishing between non-appendicitis and appendicitis and between uncomplicated appendicitis and complicated appendicitis. For distinguishing between non-appendicitis and appendicitis, the diagnostic accuracies of all items, except for the ADC value of the peri-appendiceal tissue, were 66.7% or higher (range 66.7–88.2%) and the diagnostic accuracies of the appendiceal intensity on DWI and the ADC value of the appendix were higher than the accuracies of the other imaging findings. For distinguishing between uncomplicated and complicated appendicitis, the diagnostic accuracies of all items, except for the ADC value of the peri-appendiceal tissue, were 65.7% or lower (range 28.6–65.7%), whereas the diagnostic accuracy of the ADC value of the peri-appendiceal tissue was high at 97.1%. We measured peri-appendiceal ADC by placing ROI in the focal fluid collection adjacent to the swollen appendix in 6 of 10 cases, as in Fig. 3. In the remaining four cases of complicated appendicitis without fluid collection suggesting abscesses, ROIs were placed in the peri-appendiceal fat tissue presenting low intensity on ADC map adjacent to swollen appendix (Fig. 4). The mean ADC values of the 4 cases were $0.88 \times 10^{-3} \pm 0.26 \times 10^{-3}$, which were also significantly lower than those of the uncomplicated appendicitis cases ($p < 0.05$).

Table 2 Diagnostic values, cut-off values, and areas under the curve of quantitative evaluation items for distinguishing between non-appendicitis and appendicitis and between uncomplicated appendicitis and complicated appendicitis

	Sensitivity	Specificity	PPV	NPV	Accuracy	Cut-off value	AUC
Non-appendicitis versus appendicitis							
Reader 1							
Appendiceal diameter on T2WI	71.4 (25/35)	62.5 (10/16)	80.6 (25/31)	50.0 (10/20)	68.6 (35/51)	5.75	0.816
Appendiceal wall thickness	71.4 (25/35)	62.5 (10/16)	80.6 (25/31)	50.0 (10/20)	68.6 (35/51)	1.85	0.772
Appendiceal intensity on DWI	88.6 (31/35)	87.5 (14/16)	93.9 (31/33)	77.8 (14/18)	88.2 (45/51)	3.5	0.896
ADC value (mm^2/s) of the appendix	85.7 (30/35)	62.5 (10/16)	83.3 (30/36)	66.7 (10/15)	78.4 (40/51)	1.41×10^{-3}	0.811
ADC value (mm^2/s) of the peri-appendiceal tissue	37.1 (13/35)	43.8 (7/16)	59.1 (13/22)	24.1 (7/29)	39.2 (20/51)	1.57×10^{-3}	0.523
Reader 2							
Appendiceal diameter	68.6 (24/35)	75.0 (12/16)	85.7 (24/28)	52.2 (12/23)	70.6 (36/51)	6.1	0.764
Appendiceal wall thickness	68.6 (24/35)	62.5 (10/16)	80.0 (24/30)	47.6 (11/21)	66.7 (34/51)	2	0.729
Appendiceal intensity on DWI	88.6 (31/35)	81.2 (13/16)	91.2 (31/34)	76.5 (13/17)	86.3 (44/51)	3.5	0.888
ADC value (mm^2/s) of the appendix	77.1 (27/35)	75.0 (12/16)	87.1 (27/31)	60.0 (12/20)	76.5 (39/51)	1.26×10^{-3}	0.771
ADC value (mm^2/s) of the peri-appendiceal tissue	45.7 (16/35)	56.3 (9/16)	96.9 (16/23)	32.1 (9/28)	49.0 (25/51)	1.71×10^{-3}	0.511
Uncomplicated versus complicated appendicitis							
Reader 1							
Appendiceal diameter	70.0 (7/10)	64.0 (16/25)	43.8 (7/16)	84.2 (16/19)	65.7 (23/35)	8.15	0.692
Appendiceal wall thickness	80.0 (8/10)	48.0 (12/25)	38.1 (8/21)	85.7 (12/14)	57.1 (20/35)	2.25	0.652
Appendiceal intensity on DWI	80.0 (8/10)	8.0 (2/25)	25.8 (8/31)	50.0 (2/4)	28.6 (10/35)	3.5	0.536
ADC value of the appendix	50.0 (5/10)	68.0 (17/25)	38.5 (5/13)	77.3 (17/22)	62.9 (22/35)	1.09×10^{-3}	0.648
ADC value of the surrounding tissue	90.0 (9/10)	100 (25/25)	100 (9/9)	96.2 (25/26)	97.1 (34/35)	1.03×10^{-3}	0.996
Reader 2							
Appendiceal diameter	70.0 (7/10)	56.0 (14/25)	38.9 (7/18)	82.4 (14/17)	60.0 (21/35)	7.95	0.69
Appendiceal wall thickness	70.0 (7/10)	36.0 (9/25)	30.4 (7/23)	75.0 (9/12)	45.7 (16/35)	2.15	0.6
Appendiceal intensity on DWI	90.0 (9/10)	12.0 (3/25)	29.0 (9/31)	75.0 (3/4)	343 (12/35)	3.5	0.578
ADC value of the appendix	60.0 (6/10)	44.0 (11/25)	30.0 (6/20)	73.3 (11/15)	48.6 (17/35)	$1.15 \times$10-3	0.504
ADC value of the surrounding tissue	90.0 (9/10)	100 (25/25)	100 (9/9)	96.2 (25/26)	97.1 (34/35)	$0.91 \times$10-3	0.992

PPV positive-predictive value, *NPV* negative-predictive value, *AUC* area under the curve, *T2WI* T2-weighted imaging, *DWI* diffusion-weighted imaging, *ADC* apparent diffusion coefficient

Table 3 Diagnostic values of T2-weighted imaging and diffusion-weighted imaging findings for appendicitis

	Sensitivity	Specificity	PPV	NPV	Accuracy
Reader 1					
Swollen appendix	71.4 (25/35)	62.5 (10/16)	80.6 (25/31)	50.0 (10/20)	68.6 (35/51)
Wall thickening	71.4 (25/35)	62.5 (10/16)	80.6 (25/31)	50.0 (10/20)	68.6 (35/51)
Peri-appendiceal findings	60.0 (21/35)	93.8 (15/16)	95.5 (21/22)	51.7 (15/29)	70.6 (36/51)
Combination findings on T2WI	88.6 (31/35)	56.3 (9/16)	81.6 (31/38)	69.2 (9/13)	78.4 (40/51)
Combination findings on T2WI + DWI	100 (35/35)	56.3 (9/16)	83.3 (35/51)	100 (9/9)	86.3 (44/51)
Reader 2					
Swollen appendix	68.6 (24/35)	75.0 (12/16)	85.7 (24/28)	52.2 (12/23)	70.6 (36/51)
Wall thickening	68.6 (24/35)	62.5 (10/16)	80.0 (24/30)	47.6 (11/21)	66.7 (34/51)
Peri-appendiceal findings	62.9 (22/35)	87.5 (14/16)	91.7 (22/24)	51.9 (14/27)	70.6 (36/51)
Combination findings on T2WI	88.6 (31/35)	68.8 (11/16)	86.1 (31/36)	73.3 (11/15)	82.4 (44/51)
Combination findings on T2WI + DWI	100 (35/35)	56.3 (9/16)	83.3 (35/42)	100 (9/9)	86.3 (44/51)

T2WI T2-weighted imaging, *DWI* diffusion-weighted imaging, *ADC* apparent diffusion coefficient

Table 4 The number of true positive, true negative, false positive, and false negative on T2-weighted image and diffusion-weighted image

	TP	TN	FP	FN
Reader 1				
Combination findings on T2WI	31	9	7	4
DWI score	31	14	2	4
Reader 2				
Combination findings on T2WI	31	11	5	4
DWI score	31	13	3	4

T2WI T2-weighted image, *DWI* diffusion-weighted image, *TP* true positive, *TN* true negative, *FP* false positive, *FN* false negative

The diagnostic accuracy improved from 78.4% with only T2WI to 86.3% with combined T2WI and DWI for reader 1 and from 82.4 to 86.3% for reader 2 (Table 3).

The sensitivity and specificity of DWI in the diagnosis of acute appendicitis were 88.6% and 87.5% for reader 1, and 88.6% and 81.2% for reader 2, respectively (Table 2). The specificity of DWI was higher than that of "combined assessment from T2WI findings" with the similar values of sensitivity in both. However, the specificity decreased when "DWI" was combined with "combined assessment of T2WI findings" because false positive in either of the assessments is counted as false positive in the "combined assessment of both T2WI findings and DWI" (Table 3). Table 4 shows true positive, true negative, false positive, and false negative on combination findings on T2WI and DWI score. In both "DWI" and "combined assessment from T2WI findings," false-negative results were found in 4 different patients without overlapping (Table 4), which increased true positive numbers in the "combined assessment of both T2WI findings and DWI," and consequently the sensitivity was improved (Table 3). For reader 1, "DWI" resulted in two cases where "combined assessment from T2WI findings" was similar and corrected five false-positive cases of "combined assessment from T2WI findings" (Table 4) (Fig. 5), which, however, did not change the true negative numbers in "combined assessment of both T2WI findings and DWI" (Table 4). For reader 2, DWI corrected four false-positive cases of "combined assessment from T2WI findings"; however, DWI was false positive in three cases where two of them were true negative in "combined assessment from

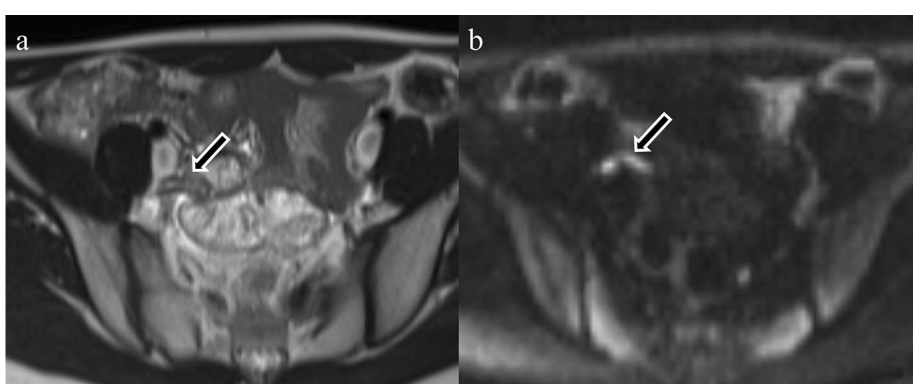

Fig. 5 A 13-year-old female presented with right lower abdominal pain. She was treated with antibiotics therapy. The dilated wall-thickened appendix on T2WI is obscure, and readers 1 and 2 were judged normal on T2WI (**a**). The bright appendix was observed on DWI, and readers 1 and 2 were rated score 5 and 4, respectively (**b**)

T2WI findings" (Table 4). As a result, the true negative numbers in "combined assessment of both T2WI findings and DWI," as well as the specificity, decreased (Table 3). Table 5 presents the results of comparisons between uncomplicated and complicated appendicitis patients. With regard to qualitative assessment, significant differences were noted in the findings of a phlegmon by reader 1 ($p = 0.028$), an appendiceal wall defect by both readers ($p < 0.05$), and an abscess by both readers ($p < 0.001$). The interobserver agreements for the findings were good to very good (appendiceal wall defect, $\kappa = 0.922$; peri-appendiceal abscess, $\kappa = 0.717$; peri-appendiceal phlegmon, $\kappa = 0.940$; extraluminal air, $\kappa = 1.000$; and extraluminal appendicolith, $\kappa = 1.000$).

Discussion

In the diagnosis of acute appendicitis, judgment of the presence of the disease and assessment of the severity of the condition are important. A false-positive diagnosis can result in negative appendectomy, and a false-negative diagnosis can delay management, making the patient prognosis poor. Accurate assessment of the severity of the condition is essential for selecting the appropriate treatment. Various clinical data, including patient complaints, physical findings, and blood test results, are important for diagnosis; however, imaging examinations are required for more precise assessment in most cases [1]. US, CT, and MRI are the imaging modalities of choice, and each modality has strengths and limitations. US is easy to access and least invasive; however, it requires an experienced technique and the results depend on the patient's body habitus [23]. CT is also easily accessible and has the highest accuracy for diagnosing and excluding acute appendicitis [24]. It allows precise assessment of the severity of the condition by demonstrating the presence or absence of a deficit in the appendiceal wall and acute cellulitis or an abscess in the peri-appendiceal tissue [25–27]. It might also provide an alternative diagnosis when acute appendicitis is excluded. However, radiation exposure and side effects from iodinated contrast medium use are drawbacks of CT, and its use in pediatric and pregnant patients and those with renal dysfunction or iodine allergy risks is limited [3]. MRI does not involve radiation exposure and provides excellent tissue contrast without intravenous contrast administration. MRI has recently been demonstrated to have an accuracy similar to that of CT for diagnosing acute appendicitis [28]. In addition, DWI provides very unique and valuable information for diagnosing acute appendicitis [19–21]. However, one of the limitations of MRI is the possible difficulty in differentiating between complicated and uncomplicated appendicitis because a perforated appendiceal wall is not directly demonstrated, as in CT, owing to its spatial resolution.

In imaging diagnosis, it is essential to detect the structure of the appendix initially, and T2WI is the best sequence to depict a normal appendix [17, 29, 30] on MRI. A normal appendix is a tubular and blind-ending structure originating from the cecum and present in various directions and sometimes behind the ascending colon, which is referred to as retrocecal appendix [31]. In acute appendicitis, the inflamed appendix is dilated (> 7 mm) and the wall is thickened (> 2 mm), showing low intensity on T1WI and high intensity on T2WI, and the peri-appendiceal tissue becomes edematous, which is best seen on FS-T2WI [12]. Similar to the findings in previous studies, our study demonstrated that combined MRI findings (T2WI) had high diagnostic accuracy for acute appendicitis, with sensitivities of 88.6% and 88.6%, specificities of 56.3% and 68.8%, and accuracies of 78.4% and 82.4% for readers 1 and 2, respectively, considering the diagnosis of appendicitis when at least one finding is

Table 5 Diagnostic values of imaging findings for distinguishing between uncomplicated appendicitis and complicated appendicitis

	Sensitivity	Specificity	PPV	NPV	Accuracy	*P* value
Reader 1						
Phlegmon	90.0 (9/10)	52.0 (13/25)	42.9 (9/21)	92.9 (13/14)	43.1 (22/51)	0.028*
Wall defect	60.0 (6/10)	92.0 (23/25)	75.0 (6/8)	85.2 (23/27)	56.9 (29/51)	0.0028*
Abscess	60.0 (6/10)	100 (25/25)	100 (6/6)	86.2 (25/29)	60.8 (31/51)	<0.001*
Extraluminal air	20.0 (2/10)	100 (25/25)	100 (2/2)	75.8 (25/33)	52.9 (27/51)	0.0756
Extraluminal appendicolith	10.0 (1/10)	100 (25/25)	100 (1/1)	73.5 (25/34)	51.0 (26/51)	0.286
Reader 2						
Phlegmon	90.0 (9/10)	48.0 (12/25)	40.9 (9/22)	92.3 (12/13)	41.2 (21/51)	0.0548
Wall defect	60.0 (6/10)	96.0 (24/25)	85.7 (6/7)	85.7 (24/28)	58.8 (30/51)	<0.001*
Abscess	60.0 (6/10)	96.0 (24/25)	85.7 (6/7)	85.7 (24/28)	58.8 (30/51)	<0.001*
Extraluminal air	20.0 (2/10)	100 (25/25)	100 (2/2)	75.8 (25/33)	52.9 (27/51)	0.0756
Extraluminal appendicolith	10.0 (1/10)	100 (25/25)	100 (1/1)	73.5 (25/34)	51.0 (26/51)	0.286

PPV positive-predictive value, *NPV* negative-predictive value

*$p < 0.05$

positive. Another important MRI finding in acute appendicitis is signal increase of the appendix on DWI, which can help in the depiction of an inflamed appendix, even in thin patients [19, 20]. A previous study reported that the signal intensity of the appendix on DWI and its ADC value showed significant differences between a normal appendix and an inflamed appendix and that 98.7% of inflamed appendix cases demonstrated high intensity on DWI [19]; however, a clear threshold of the diagnostic criteria was not demonstrated. In this study, we attempted to present objective criteria for assessing the intensity of the appendix on DWI using a 5-point scale with ROC analysis. The visual score of the appendix on DWI was higher in appendicitis than in non-appendicitis ($p < 0.001$). Additionally, when scores of 4 and 5 (appendiceal intensity higher than that of the small bowel) were considered positive, there was high diagnostic accuracy, with sensitivities of 88.6% and 88.6%, specificities of 87.5% and 81.2%, and accuracies of 88.2% and 86.3% for readers 1 and 2, respectively. Furthermore, combined T2WI and DWI had high diagnostic accuracy, with sensitivities of 100% and 100%, specificities of 56.3% and 56.3%, and accuracies of 86.3% and 86.3% for readers 1 and 2, respectively, considering the diagnosis of appendicitis when at least one finding is positive. These results suggest that adding DWI is helpful to improve diagnostic accuracy.

In this study, the ADC value was measured in the appendix and peri-appendiceal tissue separately. The ADC value of the appendix showed a significant difference between appendicitis and non-appendicitis ($p = 0.001$), and its accuracies were 78.4% (cut-off value, 1.41×10^{-3} mm^2/s) and 76.5% (cut-off value, 1.26×10^{-3} mm^2/s) for readers 1 and 2, respectively. The increase in appendiceal signal intensity on DWI and decrease in the ADC value might be explained by the diffusion restriction of water molecules due to inflammatory cell infiltration in the inflamed appendix wall and purulent material in the appendiceal lumen, similar to the mechanism reported for Crohn's disease and cholecystitis [32–34].

The differentiation of uncomplicated appendicitis from complicated appendicitis is clinically important for the selection of the appropriate treatment. The CT findings of an abscess, a phlegmon, extraluminal air, an extraluminal appendicolith, and a focal defect in the enhancing appendiceal wall are considered important for identifying complicated appendicitis [25–27]. Among these findings, a defect in the enhancing appendiceal wall is the most accurate finding for identifying complicated appendicitis, with a sensitivity of 58.8–64.3% and specificity of 85.7–100% on CT with 5–10-mm section thickness [25, 26], and the sensitivity and specificity increased to 95.0% and 96.8%, respectively, on CT with 2 or 3-mm section thickness [27]. On the other hand, MRI has limitations in depicting small wall defects of the appendix because of its spatial resolution and the slice thickness (5 mm) generally used. Actually, phlegmon (one reader), abscess (both readers), and appendiceal wall defect (two readers) findings showed significant differences between uncomplicated and complicated appendicitis on MRI, with diagnostic accuracies of 43.1%, 58.8–60.8%, and 56.9–58.8%, respectively.

In this study, the ADC value of the peri-appendiceal tissue was significantly lower in complicated appendicitis and had a high diagnostic accuracy of 97.1% for differentiating between uncomplicated and complicated appendicitis. The difference in the ADC value of the peri-appendiceal tissue between uncomplicated and complicated appendicitis may be explained by the fact that the change in the peri-appendiceal tissue in acute appendicitis initiates with pure edema in the case of uncomplicated appendicitis, which causes an increase in the ADC value. With disease progression, inflammatory cell infiltration and abscess progress beyond the appendiceal wall and reach the peri-appendiceal tissue in complicated appendicitis, which can decrease the ADC value of the peri-appendiceal tissue. Conversely, ADC value of the appendix did not show a significant difference between uncomplicated and complicated appendicitis in this study. This result may be explained by the severity of appendiceal inflammation, which was similar between uncomplicated and complicated appendicitis groups, although inflammation in the peri-appendiceal tissue was severer in the complicated appendicitis group.

This study demonstrated a high diagnostic accuracy of MRI for the diagnosis of acute appendicitis, in combination with the findings of appendiceal diameter, appendiceal wall thickening, and peri-appendiceal abnormalities. In addition, DWI with visual scale assessment improved the diagnostic accuracy, especially the sensitivity and negative-predictive value, which is quite helpful in clinical management. DWI could reveal appendicitis in patients whose appendix appeared normal on T2WI and in patients with lower BMI or young age. High-intensity inflamed appendix on DWI was helpful in identifying appendicitis even in pediatric patients with little mesenteric fat. In a case with false positive on DWI, the high-intensity swollen lymph node was misread as an inflamed appendix. It is essential to identify swollen appendix and high-intensity tubular structure corresponding with swollen appendix on T2WI and DWI to avoid false positive on DWI. In a case with false negative on DWI, score 3 was rated for the appendix that appeared as appendicitis on T2WI. This may be caused by the degree of the inflammation of the appendix; however, the distinction between score 3 and 4 on DWI is sometimes equivocal, which can be a limitation of visual assessment. In cases with equivocal findings on DWI, comprehensive assessment with T2WI findings might be necessary. MRI diagnosis for distinguishing between uncomplicated and complicated appendicitis according to imaging findings is limited, and on the other hand, the ADC value of the peri-appendiceal tissue has a reasonably high diagnostic accuracy for improving diagnosis. Therefore, MRI is considered as an applicable imaging modality in patients suspected with acute appendicitis, and it has benefits especially in pediatric and pregnant patients. In MRI, DWI and ADC map should be added to the protocol, as reported previously [19–22], and in the evaluation, quantitative assessment will be valuable.

The present study has some limitations. First, the number of enrolled patients was relatively small because of the single-center design. Second, this study might have had potential selection bias because of the retrospective nature. Consecutive patients with right lower abdominal pain who underwent MRI were enrolled in this study; however, some candidate patients in the study period did not undergo MRI because our institution had only one MRI scanner, which was in use for reserved examinations. Third, there were no pregnant patients in the study period, although these patients are appropriate candidates to undergo MRI for acute abdomen. Fourth, the scores on DWI were evaluated by reviewing T2WI for the appendix because it was hard to identify the appendix on DWI in some cases. This might cause bias, although the readers compared with the intensity of the normal small bowel, such as equivocal T2WI findings for appendicitis, have the potential to inflate scores on DWI. Conversely, the bright appendix on DWI helped to identify the appendix on T2WI, especially in pediatric cases. DWI is a helpful pulse sequence to diagnose appendicitis, but it should be noted that the intensity of DWI is subjective and it is essential to observe with combination of T2WI and DWI in clinical practice.

In conclusion, to diagnose acute appendicitis, the accuracy was improved by adding the visual assessment of the appendiceal signal intensity on DWI and the measurement of ADC values of the appendix to conventional MR examination using T2WI. Moreover, the ADC values of the peri-appendiceal tissues were demonstrated as notable finding to identify complicated appendicitis. Therefore, the DWI sequence should be included in the MR examination in this clinical setting and the ADC values should be separately evaluated at the appendix and the peri-appendiceal tissue.

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