MRI in suspected appendicitis

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CHAPTER 5

MRI features associated with acute appendicitis

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ABSTRACT

Objective

To identify MRI features associated with appendicitis.

Methods

Features expected to be associated with appendicitis were recorded in consensus by two expert radiologists on 223 abdominal MRIs in patients with suspected appendicitis. Nine MRI features were studied: appendix diameter $>7$ mm, appendicolith, peri-appendiceal fat infiltration, peri-appendiceal fluid, absence of gas in the appendix, appendiceal wall destruction, restricted diffusion of the appendiceal wall, lumen or focal fluid collections. Appendicitis was assigned as the final diagnosis in 117/223 patients. Associations between imaging features and appendicitis were evaluated with logistic regression analysis.

Results

All investigated features were significantly associated with appendicitis in univariate analysis. Combinations of two and three features were associated with a probability of appendicitis of 88% and 92%, respectively. In patients without any of the nine features appendicitis was present in 2% of cases. After multivariate analysis only an appendix diameter $>7$ mm, peri-appendiceal fat infiltration and restricted diffusion of the appendiceal wall were significantly associated with appendicitis. The probability of appendicitis was 96% in their presence and 2% in their absence.

Conclusion

An appendix diameter $>7$ mm, peri-appendiceal fat infiltration and restricted diffusion of the appendiceal wall have the strongest association with appendicitis on MRI.
INTRODUCTION

If a patient has suspected acute appendicitis prompt and accurate diagnosis is crucial. The availability and use of ultrasound and computed tomography (CT) to aid in the diagnosis of appendicitis has increased over the last decade. Several studies have linked this increased use of preoperative imaging to the decrease in negative appendectomy rates and missed diagnoses. More recently magnetic resonance imaging (MRI) has made its entrance into the emergency department for patients with suspected appendicitis, with a promising high accuracy for acute appendicitis. However, radiologists in the emergency department are not familiar with this relatively new technique for the evaluation of suspected appendicitis. A better understanding of the diagnostic value of specific MRI features can help radiologists to increase their imaging performance. While the imaging features for ultrasound and CT are well known, specific MR features and criteria for diagnosing appendicitis are not yet available in literature.

An enlarged appendix diameter is considered an important feature in the diagnosis of appendicitis. Yet there is significant overlap between the normal and abnormal CT appearance of the appendix; the diameter range of a normal appendix was 3 to 10 mm on CTs in healthy patients, while in 42% of normal appendices the diameter was greater than 6 mm. Consequently, a diagnosis of acute appendicitis should be based not only on the diameter of the appendix but also on the presence of secondary signs. Van Randen et al found that the combination of transducer tenderness, enlarged appendix and peri-appendiceal fat infiltration on ultrasound examinations had a 95% probability of appendicitis. For CT the probability was 96% in patients with an enlarged appendix, peri-appendiceal fat infiltration and appendiceal enhancement. Some of these features can also be evaluated on MRI, but their diagnostic value may be different. In addition, findings of diffusion-weighted MR imaging may further increase MRI sensitivity for acute appendicitis.

The aim of our study was to identify MRI features that are associated with acute appendicitis and to estimate the probability of appendicitis when specific combinations of these features are observed.

MATERIALS AND METHODS

Patients

In a prospective multicentre diagnostic accuracy study in six hospitals we included 230 adult patients (≥18 years) with clinically suspected acute appendicitis. Our study protocol had been approved by the local Medical Ethics Committee before the start of this study. On-call doctors in the emergency department identified patients with suspected appendicitis based on medical history, and on physical and laboratory examination. In two hospitals patients were included seven days a week, between 8 am and 11 pm; the other four hospitals only included patients during office hours. Eligible patients were informed about this study and invited to participate, before medical imaging. Written consent was obtained from all study participants. We excluded pregnant women, patients with a contraindication for MRI, and critically ill patients who needed intensive vital organ function monitoring for life-support. Consenting patients underwent an MRI within 2h of admission to the emergency department. MRI was not used for clinical care; patients were managed based on ultrasound, and on CT in conditional cases with negative
or inconclusive ultrasound findings, according to the Dutch guideline on the diagnosis and treatment of acute appendicitis.¹⁸

MRI protocol
Patients underwent MRI in the supine position using 1.5-T MRI (MAGNETOM Avanto 1.5T MRI, Siemens Medical Systems, Forchheim, Germany or Intera 1.5-T MRI, Philips Medical Systems, Best, The Netherlands). The protocol included the following sequences in the coronal and axial planes: breath-hold single shot half Fourier rapid acquisition with relaxation enhancement (RARE) without and with fat saturation and free-breathing diffusion-weighted images (DWI). Images were obtained with the following parameters for single shot half Fourier RARE: TR 1500 ms, TE 90 ms, flip angle 170°, slice thickness 6 mm, FOV 400 mm, 256x256 matrix; for fat saturated single shot half Fourier RARE: TR 1400 ms, TE 93 ms, flip angle 160°, slice thickness 6 mm, FOV 400 mm, 256x256 matrix. Acquisition for coronal (fat saturated) RARE in 3 stacks of 14s/breathhold, axial (fat saturated) RARE in 5 stacks of 15s/breathhold; Acquisition time of RARE and fat saturated RARE in coronal and axial plane was approximately 7 minutes. Scan parameters for DWI: TR 3900ms, TE 75 ms, slice thickness 6 mm, FOV 400 mm, 192x192 matrix, b-values 50, 400, 800 s/mm². Freebreathing in coronal and axial plane; acquisition time approximately 7 minutes. No intravenous or oral contrast medium or bowel relaxant was administered.

MRI interpretation
Two experienced radiologists (B.W., 16 years of experience and L.C., 14 years of experience, both had reviewed > 500 abdominal MRI for suspected acute appendicitis) evaluated all MRI examinations and reached a consensus on the presence or absence of imaging features expected to be associated with acute appendicitis. Images were observed on a picture archiving and communication system workstation, where clinical information on history and on physical and laboratory examinations was provided for each case. The radiologists were blinded for the patients’ follow up and imaging findings on ultrasound and CT.

First, readers individually examined the conventional sequences ((fat saturated) single shot half Fourier RARE ) and then reached consensus about the following six imaging features: diameter of the appendix (outer to outer wall), presence of an appendicolith, peri-appendiceal fat infiltration, peri-appendiceal fluid, absence of gas in the appendix and destruction of the appendiceal wall structure. The imaging features and final diagnosis were documented in a structured case record form (Appendix A). After this, readers examined the additional diffusion-weighted images (DWI) and recorded the presence or absence of three extra features: presence of the restricted diffusion of the appendiceal wall, restricted diffusion of the appendiceal lumen and restricted diffusion of focal fluid collections. These features were also documented on the case record form, as well as the final overall MRI diagnosis.

Reference standard
An expert panel consisting of two surgeons and one radiologist (expert panel 1; M.W., B.V. and H.E. Expert panel 2; A.H., H.S. and A.S.) decided on the presence of acute appendicitis based on clinical information, imaging findings (except MRI findings), surgery, histopathology,
and 3 months’ follow-up. Disagreements between panel members were resolved during consensus meetings. Members of the expert panel had not been involved in the examination or management of the evaluated cases.

Statistical analysis
The expert panel diagnosis served as the clinical reference standard in evaluating the diagnostic accuracy of the MRI features. Sensitivity and specificity for an overall diagnosis of acute appendicitis, with corresponding confidence intervals, were calculated according to conventional sequences and compared with the same accuracy statistics for an overall diagnosis after additional DWI. Differences in accuracy statistics were tested for significance with the McNemar test statistic. \( P \) values below 0.05 were considered to indicate statistical significance.

The median diameter of the appendix was calculated in the appendicitis group and compared with the group without appendicitis, using the Mann–Whitney U test. Several cut-off values for the appendix diameter were evaluated using receiver operating characteristics and odds ratios.

We evaluated the positive predictive value for acute appendicitis for each MRI feature in isolation and for combinations of MRI features. For these calculations we used a cut-off value of 7 mm for appendix diameter.

Associations between the imaging features and acute appendicitis were evaluated using logistic regression analysis. We calculated the odds ratio with corresponding 95% confidence intervals per feature using univariate logistic regression. Features significantly associated with acute appendicitis in univariate analysis \( (P < 0.05) \) were included in a multivariate logistic regression model. We used a backward elimination method and the Wald test statistic to arrive at a parsimonious model. The significance level for exclusion was set at 0.05. All analyses were performed using SPSS 18.0 (SPSS, Chicago, IL, USA).

RESULTS
Between March 2010 and September 2010, 230 patients were included. In 223 patients the MRI was performed according to the study protocol; in seven patients the MRI could not be performed because of claustrophobia or technical failure, these patients were excluded from data analysis. The mean age of the 223 patients was 38 years (range 18 to 84) and 41% were men. The expert panel assigned acute appendicitis as the final diagnosis in 117 patients, in 112 of these patients results of histopathology were available; in one patient the specimen did not arrive in the pathology department, the other four patients were treated non-operatively with antibiotics (two patients) or percutaneous drainage (two patients). In nine of the remaining 106 patients with other diagnoses than appendicitis histopathology was available, the expert panel assigned diagnoses in these patients based on clinical findings, other imaging modalities, and follow-up.

Two expert radiologists reviewed all 223 MRIs. They were not able to visualise the appendix in 13 patients, 1 of whom had acute appendicitis. In this patient the MRI readers had identified an enlarged adnex with restricted diffusion. The remaining 210 MRI examinations were used for analysis of MRI features potentially associated with acute appendicitis. A flow diagram of patient selection for analysis is presented in Figure 1.
Diagnostic accuracy after conventional images and with diffusion-weighted images

Sensitivity of the overall diagnosis of appendicitis was 0.96 (95% CI: 0.90 to 0.98) according to conventional MRI images versus 0.97 (95% CI: 0.93 to 0.99) according to conventional images and additional DWI. Specificity was 0.94 (95% CI: 0.87 to 0.97) for conventional versus 0.93 (95% CI: 0.85 to 0.96) for both conventional and DWI. None of these comparisons reached statistical significance.

Appendix diameter

The median diameter of an inflamed appendix was 10.5 mm (IQR 9.0 to 13.0 mm); a healthy appendix had a median diameter of 5.5 mm (IQR 5.0 to 6.2 mm; P < 0.001). Different cut-off values of appendiceal diameter are displayed in a receiver-operating characteristic (ROC) space for the diagnosis of appendicitis in Figure 2. A 7-mm cut-off of the appendix diameter provided the highest odds ratio in our study population, i.e. 355 (95% CI 78 to 1617). In 98% of all patients with acute appendicitis a thickened appendix (> 7mm) was visualised, versus 14% of all patients without appendicitis.

MRI features for acute appendicitis

The positive predictive value for appendicitis varied between 0.79 and 0.95 for each MRI feature in isolation (Table 1). Combinations of MRI features were frequently observed on MRIs of patients with acute appendicitis as the final diagnosis; in 97% (113/116) at least three features were present. Combinations of features were less frequent on MRIs of patients without acute appendicitis; in 11% (10/94) three or more features were present. Presence of any one of the nine MRI features had a positive predictive value of 0.75 (115/154, 95% CI 0.67 to 0.81) for
appendicitis. For combinations of any two, three or four features the positive predictive values were 0.87 (114/131, 95% CI 0.80 to 0.92), 0.92 (113/123, 95% CI 0.86 to 0.96) and 0.94 (111/118, 95% 0.88 to 0.97), respectively. If none of the nine features was identified acute appendicitis was the final diagnosis in only 2% of patients (1/56, 95% CI 0 to 9%).

All nine investigated MRI features were significantly associated with acute appendicitis in univariate analysis. The odds ratios of the isolated MRI features varied between 9 for restricted
diffusion of focal fluid collections and 355 for a thickened appendix. In univariate analysis a thickened appendix, peri-appendiceal fat infiltration and restricted diffusion of the appendiceal wall had the strongest association with acute appendicitis. After backwards elimination in multivariate analysis, these three MRI features were also significantly associated with acute appendicitis. The results of univariate and multivariate analysis are listed in Table 1.

**Predictive values for MRI features with a strong association with acute appendicitis**

A thickened appendix (diameter > 7 mm), peri-appendiceal fat infiltration and restricted diffusion of the appendiceal wall (Figures 3, 4 and 5) had the strongest association with acute appendicitis in multivariate analysis; the predictive values of all possible combinations of these three features are shown in Table 2. The positive predictive value for appendicitis was 0.88 if one of these features was present, 0.94 for two of the three features and 0.96 if all three of these features were present. In 112 out of 116 (97%) patients with appendicitis at least two of these MRI features were identified. Absence of these three features almost ruled out appendicitis; with a positive predictive value 0.02 (95% CI 0.01 to 0.09).

<table>
<thead>
<tr>
<th>Presence of MRI features</th>
<th>n</th>
<th>Proportion within appendicitis %, (95%CI)</th>
<th>Positive predictive value TP/TP+FP %, (95%CI)</th>
<th>Negative predictive value TN/TN+FN %, (95%CI)</th>
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<td>All three of three features present</td>
<td>101</td>
<td>84 (97/116)</td>
<td>96 (90-98)</td>
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<td>Any two of three features present</td>
<td>119</td>
<td>97 (112/116)</td>
<td>94 (88-97)</td>
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<td>+ +</td>
<td>117</td>
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<td>(110/117)</td>
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<tr>
<td>Any one of three features present</td>
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<td>85 (99/116)</td>
<td>96 (90-98)</td>
<td>(99/103)</td>
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<tr>
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<td>118</td>
<td>95 (110/116)</td>
<td>93 (87-97)</td>
<td>(110/118)</td>
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<tr>
<td>None of the three features present</td>
<td>81</td>
<td>2 (2/116)</td>
<td>2 (1-9)</td>
<td>(2/81)</td>
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</table>

**DISCUSSION**

This study identified nine MRI features that were each associated with acute appendicitis. Three of these, an enlarged appendix (>7 mm), peri-appendiceal fat infiltration and restricted diffusion
of the appendiceal wall, were significantly associated with appendicitis in multivariate analysis. Their presence gave a high probability of appendicitis whereas their absence almost ruled out appendicitis. If these features were present on abdominal MRI 96% had a final diagnosis of appendicitis, compared with 2% of patients without any of these features. Knowledge of these features can help radiologists to make decisions on the diagnosis of appendicitis and improve diagnostic accuracy when reading abdominal MRI for suspected appendicitis.

A number of potential limitations of this study need to be addressed. All MRIs in our study were reviewed by two expert radiologists. This makes an unconditional generalisation to clinical practice in other hospital settings hazardous. Radiologists with less experience will possibly not be able to identify all MRI features found under the scrutiny of the expert panel. However, identification of only two of the three MRI features with a strong association with acute appendicitis already resulted in a probability of acute appendicitis of 94%.

In this study the addition of diffusion-weighted images did not increase the diagnostic accuracy of the two experienced readers. This is in contradiction with the results of a previous study that found a higher sensitivity for acute appendicitis after viewing additional DWI in 17 novice readers. Authors suggest that the additional DWI helps to locate the inflamed appendix, which is in line with the present finding that restricted diffusion of the appendiceal wall is one of the three features strongly associated with the diagnosis of appendicitis. The addition of DWI is possibly more helpful to less experienced radiologists than to expert radiologists.

We were able to visualise the appendix in 210 out of 223 MRIs (94%); the other 13 MRIs could not be used for the analyses. This could be the result of our relatively thick slice thickness. However, the percentage of visualisation is superior to what is reported in the literature. The reported detection rates of a normal appendix on MRI in healthy volunteers vary between 48% and 90%, depending on study population and imaging protocol, in terms of slice thickness and
detection classification. 20-22 For example, in healthy adult patients imaged at a slice thickness of 5 mm and an intersection gap of 0.5 mm, 90% of appendices were visualised. 22 Non-visualisation of the appendix has also been reported in patients with acute appendicitis, but sample sizes were too small for reliable estimates of the proportion of non-visualisation. 23

We decided to use a fast MRI protocol for this study, without administration of contrast medium or a bowel relaxant. Therefore, the association between contrast enhancement and acute appendicitis could not be assessed. Use of intravenous gadolinium-based contrast media or oral barium-containing contrast agents has resulted in high accuracy for acute appendicitis in previous studies. 24-26 Yet in our study high sensitivity and specificity were also obtained without contrast medium. Absence of a bowel relaxant can be considered as a limitation to this study. However, we did not encounter any artifacts due to bowel movement using single shot turbo spin echo sequences. In an emergency department setting the use of oral contrast agent or bowel relaxant would lead to an unfortunate delay. The associated risk of unnecessary complications, additional discomfort to patients and the costs should be considered as well.

Children and pregnant patients were excluded in this study because the imaging protocol of the original comparative study comprised CT. 7 Children and pregnant patients would probably benefit the most from introduction of MRI in the diagnostic work-up of appendicitis. We expect that results of this study can be extrapolated to these patient groups, however there may be some dissimilarities due to differences in anatomy.

Limited availability and experience with MRI compared to CT is a difficulty in adoption of MRI in the diagnostic work-up of patients with suspected appendicitis. Also the higher costs of MRI may be a drawback for introduction of this technique.

On conventional images an enlarged appendix (> 7 mm) and peri-appendiceal fat infiltration had the strongest association with acute appendicitis. Both features were seen in at least 95% of patients with acute appendicitis. These findings are consistent with known CT features 12,27,28 and

Figure 4. MR features of appendicitis. The axial single shot half Fourier RARE with fat saturation (a) shows a thickened, fluid-filled appendix (arrow) in a 60-year-old man. There is infiltration around the appendix with small fluid collections (arrowheads). The axial DWI (b) (b-value 800 s/mm²) shows restricted diffusion of the wall and content of the appendix (arrow). The small fluid collections around the appendix also show restricted DWI (arrowheads), which is suggestive of abscess/perforation. At surgery a perforated appendix with abscess formation was visualised.
observations in previous MRI studies.\textsuperscript{6,22} Thickening of the appendiceal wall with a dilated lumen and high intensity of peri-appendiceal tissue on (fat saturated) T2-weighted imaging have been linked with acute appendicitis in 29 histopathologically proven cases.\textsuperscript{22} Another study has shown that true-positive MRI examinations each demonstrate two or more signs of appendicitis.\textsuperscript{6} All positive MRIs in that study depicted part or all of an enlarged appendix (> 6 mm), and peri-appendiceal inflammatory changes, usually fat stranding. The median diameter of the inflamed appendix in the present study was 10.5 mm (IQR 9.0–13.0 mm) which is comparable with that in the study by Cobben et al.\textsuperscript{6} In our study population, a 7-mm cut-off value of the appendix diameter provided the highest odds ratio.

On DWI, restricted diffusion of the appendiceal wall had a strong association with acute appendicitis. Hypothetically, the restricted diffusion is caused by increased cell volume in the inflamed appendix wall. This results in high viscosity and cellularity and thus a low apparent diffusion coefficient (ADC) that accounts for signal hyperintensity on DWI and signal hypointensity on ADC maps.\textsuperscript{29} In our study restricted diffusion of the appendiceal wall was present in 87% of all patients with acute appendicitis and the presence of this feature had a probability of acute appendicitis as high as 0.95. A recent prospective study has demonstrated the value of DWI in patients with suspected acute appendicitis.\textsuperscript{16} The study authors found a positive predictive value of 0.99 with DWI (b 500 s/mm\(^2\)) signal intensity quantification. Although additional DWI did not increase diagnostic accuracy in our study, DWI features can be helpful in assigning and ensuring the diagnosis of acute appendicitis. Therefore, DWI seems a valuable technique for the diagnosis of acute appendicitis and may be added to the routine MRI protocols for acute appendicitis.

In conclusion, an enlarged appendix, peri-appendiceal fat infiltration and restricted diffusion of the appendiceal wall have the strongest association with acute appendicitis on MRI. The presence of all three features on an MRI examination leads to a probability of 96%, whereas their absence almost rules out appendicitis (2%). These features can be used in daily practice to diagnose or exclude acute appendicitis on abdominal MRI, and to help radiologists to increase their performance.
REFERENCES


**APPENDIX A: A CASE RECORD FORM WAS COMPLETED FOR EACH MRI EXAMINATION**

<table>
<thead>
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<td>Appendicolith</td>
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<tr>
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</tr>
<tr>
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<td>YES / NO</td>
</tr>
<tr>
<td>Absence of gas in appendix</td>
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</tr>
<tr>
<td>Destruction appendiceal wall</td>
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<table>
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</tr>
<tr>
<td>Restricted diffusion appendiceal lumen</td>
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</tr>
<tr>
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