

Stratified computed tomography findings improve diagnostic accuracy for appendicitis

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larger than 6.0 mm (66.3% vs 37.0%; $P < 0.001$), peri-appendiceal fat stranding (34.1% vs 8.9%; $P = 0.001$), and the absence of intraluminal air (67.6% vs 48.9%; $P = 0.024$) compared to the non-appendicitis group. Furthermore, the presence of two or more of these factors increased the odds ratio to 6.8 times higher than baseline (95%CI: 3.013-15.454; $P < 0.001$).

CONCLUSION: Appendiceal diameter and wall thickening, fat stranding, and absence of intraluminal air can be used to increased diagnostic accuracy for appendicitis with equivocal CT findings.

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Key words: Appendectomy; Appendicitis; Computed tomography; Diagnostic accuracy; Re-evaluation

Abstract

AIM: To improve the diagnostic accuracy in patients with symptoms and signs of appendicitis, but without confirmative computed tomography (CT) findings.

METHODS: We retrospectively reviewed the database of 224 patients who had been operated on for the suspicion of appendicitis, but whose CT findings were negative or equivocal for appendicitis. The patient population was divided into two groups: a pathologically proven appendicitis group ($n = 177$) and a non-appendicitis group ($n = 47$). The CT images of these patients were re-evaluated according to the characteristic CT features as described in the literature. The re-evaluations and baseline characteristics of the two groups were compared.

RESULTS: The two groups showed significant differences with respect to appendiceal diameter, and the presence of periappendiceal fat stranding and intraluminal air in the appendix. A larger proportion of patients in the appendicitis group showed distended appendices

Core tip: When equivocal computed tomography (CT) findings for appendicitis are encountered, the diagnostic accuracy can be enhanced by identifying several characteristic CT features: appendiceal diameter ≥ 6.0 mm, appendiceal wall thickening ≥ 2.0 mm, periappendiceal fat stranding, and the absence of intraluminal air. Therefore, radiologists, surgeons and physicians should apply these criteria when encountering patients with equivocal CT findings for appendicitis.

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INTRODUCTION

Appendectomy is the most common acute abdominal surgical procedure worldwide. Appendicitis is mainly di-

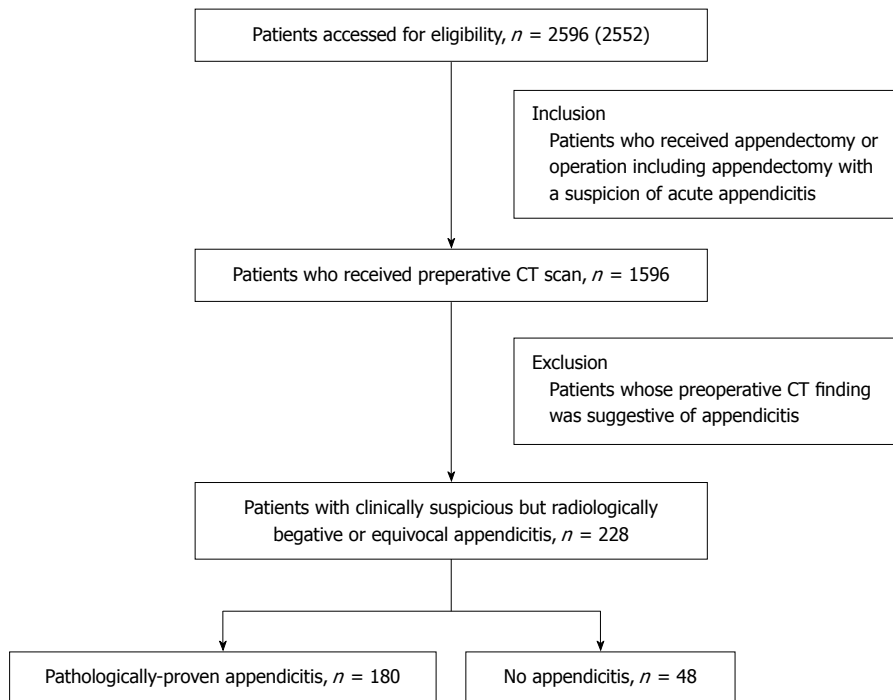


Figure 1 Patient selection flow chart. CT: Computed tomography.

agnosed based on meticulous history taking and physical examination. However, a substantial proportion of patients do not present with classic signs and symptoms^[1-3], and there are many other conditions that resemble appendicitis. The introduction of computed tomography (CT) has dramatically improved the diagnostic accuracy for appendicitis, with a sensitivity of 90%-100% and a specificity of 91%-99%^[4-6]. The CT criteria for appendicitis are mainly comprised of an appendiceal diameter greater than 6^[7-9] or 7 mm^[10-12] with thickening and enhancement of the circumferential wall, which may give a halo or target appearance. Although CT improves diagnostic accuracy, there can still be equivocal findings. Over time, several CT features have been described as indicators for a diagnosis of acute appendicitis. However, their significance and frequencies have not been extensively studied.

The purpose of this study was to systematically stratify CT findings in order to improve the diagnostic accuracy of appendicitis. To achieve this, we first reviewed the literature and searched CT findings relating to appendicitis. Thereafter, we examined the incidences of misdiagnosis within the database from our institution in which CT interpretation was negative or equivocal for appendicitis and re-evaluated them based on the criteria. Finally, we attempted to find the characteristic CT features supporting appendicitis by comparing the final pathologic results.

MATERIALS AND METHODS

Study design and data collection

This study included a cohort of patients who underwent either appendectomy or an operation including appendectomy with the suspicion of acute appendicitis at the

Department of Surgery, Daejeon St. Mary's Hospital between January 2006 and November 2012. The patients were initially identified from a prospectively collected database that included correct diagnoses and treatments. Thereafter, the electronic medical records were thoroughly reviewed to collect additional information, such as patient's histories, laboratory findings, and pathologic results. We obtained approval from the ethics committee of Daejeon St. Mary's Hospital, the Catholic University of South Korea (IRB code: DC13RISI0025).

A total of 2596 patients were screened for eligibility (Figure 1). Of these, we selected 1596 patients with preoperative CT scans. Of these, we excluded 1372 patients whose CT interpretations coincided with the diagnosis. Accordingly, the final study group included 224 patients with negative or equivocal CT findings for appendicitis, and were thereafter operated on for suspected appendicitis. We then stratified these patients into a pathologically proven appendicitis group (PA group; $n = 177$) and a non-appendicitis group (NA group; $n = 47$).

Throughout the study period, only one radiologist (G Park) with more than ten years of experience in abdominal imaging interpreted the CT findings. The diagnostic criteria for appendicitis from CT scans included a distended appendix more than 7 mm in diameter and circumferential wall thickening and enhancement, often shown as a target or halo appearance.

CT scanning: Patterns of use and dosage

During the day, CT images were obtained using a 64-slice multidetector CT (MDCT), and at night, they were obtained using a 6-slice MDCT scanner (Sensation 64 and Emotion 6, respectively; Siemens, Erlangen, Germany).

Oral contrast medium was not administered, instead CT enhancement was accomplished using a 70 s delay after intravenous contrast media infusion, consisting of 110 mL of iopromide (Ultravist; Bayer Healthcare Pharmaceuticals, Berlin, Germany), iodixanol 270 contrast (Visipaque; GE Healthcare, Princeton, NJ), or iohexol (Iobrix 350; Taejoon Pharmaceutical, Kyungkido, South Korea) through an antecubital vein at 4 mL/s. CT parameters for the 6-slice MDCT scanner were collimation 2 mm, pitch 1.2, and rotation time 0.8 s, and the parameters for the 64-slice MDCT scanner were collimation 1.2 mm, pitch 1.4, and rotation time 0.5 s. Axial section data were reconstructed at a thickness of 3 mm with 3 mm increments.

Re-evaluation of CT images

We thoroughly reviewed the literature related to CT features of appendicitis and non-appendicitis^[1-3,6,13,14]. The CT features related with appendicitis included: appendiceal diameter ≥ 6.0 mm, appendiceal wall thickening (≥ 2.0 mm), appendiceal wall enhancement, and presence of appendicolith, periappendiceal fat string, periappendiceal fluid collection, and periappendiceal lymphadenopathy. The CT features related with non-appendicitis included the presence of intraluminal air and/or coexisting inflammatory lesions. To avoid selection bias, the radiologist was not given information about the patient's final diagnosis. The CT images were provided to the radiologist as a random sequence using a PACS (Maroview; Infinitt, Seoul, South Korea) in stack mode.

Appendiceal diameter was defined as the maximum diameter of the appendix observed in full magnification view, and appendiceal wall thickness was defined as a wall thickness of ≥ 2 mm in the full magnification view. Appendiceal wall enhancement was defined as attenuation of the appendiceal wall that was subjectively equal to or greater than that of the normal bowel wall^[15]. Mesenteric lymphadenopathy was defined as at least one lymph node larger than 1.0 cm in the short axis diameter or as a cluster of at least four lymph nodes of any size in the right lower quadrant^[16]. Coexisting inflammatory lesions referred to the inflammatory lesions seen in the CT scan that could be related with right low quadrant pain, such as diverticulitis or ovarian cysts.

Statistical analysis

Numeric data are presented as mean and standard deviation or as median and range. Continuous variables were analyzed with independent *t*-tests, and proportions were compared with Pearson χ^2 or Fisher's exact tests, as appropriate. For data that were not normally distributed, Wilcoxon rank-sum tests were used to examine differences in central tendency. Statistical analyses were performed with SPSS version 18.0 (SPSS Inc., Chicago, IL, United States). Two-tailed *P* values < 0.05 were considered statis-

tically significant.

RESULTS

Patient characteristics and baseline comparison

We analyzed the database of 224 patients who underwent operations with the suspicion of appendicitis based on clinical manifestations despite negative or equivocal CT interpretation. Of these, 177 patients had appendicitis and 47 patients did not. There were 88 men and 136 women with a mean age of 35.3 ± 20.1 years. The mean body mass index was 22.3 ± 3.5 kg/m². Most patients (88.8%) did not present with high fever (≥ 37.8 °C). The mean serum leukocyte count was 10357 ± 4208 /mm³. Baseline and clinical features, including findings obtained from history taking, physical examination, and laboratory results, were similar between the NA and PA groups (Table 1), except for platelet count (*P* = 0.005), creatinine level (*P* = 0.036) and serum bilirubin concentration (*P* = 0.020).

Re-evaluation of CT features

We re-evaluated the CT scans of the 224 patients included in the study (Table 2). Of these, the features indicative of appendicitis were appendiceal visualization, appendiceal diameter ≥ 6.0 mm, appendiceal wall enhancement (Figure 2), appendiceal wall thickening ≥ 2.0 mm (Figure 3), presence of appendicolith, periappendiceal fat stranding (Figure 4), periappendiceal fluid collection, and mesenteric lymphadenopathy. The features excluding appendicitis were the presence of intraluminal air (Figure 5) and coexisting inflammatory lesion(s). Of the features indicating appendicitis, the two groups showed significant differences in appendiceal diameter ≥ 6.0 mm and positive periappendiceal fat stranding (*P* < 0.001). Of the features excluding appendicitis, the two groups showed significant differences in the presence of intraluminal air (*P* = 0.024). There was no significant difference in the presence of co-existing inflammatory lesion(s) between the two groups. Ileocolitis (*n* = 37, 27.6%), terminal ileitis (*n* = 10, 7.5%), and periappendiceal fluid collections (*n* = 4, 3.0%) were the most frequently encountered lesions (Table 3).

Risk estimation of appendicitis in patients with negative or equivocal CT interpretation

Based on the three factors significant for appendicitis in equivocal CT findings, we further evaluated the combination effect of these factors (Table 4). Of all possible combinations, we found that the greatest intergroup difference was seen when they were divided into low-risk (0-1 risk factor) and high-risk groups (2-3 risk factors). The probability of appendicitis in the high-risk group was 6.832 times higher than the low-risk group (95%CI:

Table 1 Patient characteristics *n* (%)

Characteristics	Total population (<i>n</i> = 224)	Negative appendicitis (<i>n</i> = 47)	Pathologically proven appendicitis (<i>n</i> = 177)	<i>P</i> value
Age (yr)				0.052
< 15	26 (11.6)	10 (21.3)	16 (9.0)	
15-64	169 (75.4)	33 (70.2)	136 (76.9)	
≥ 65	29 (13.0)	4 (8.5)	25 (14.1)	
Gender				0.092
Male	88 (39.3)	13 (27.7)	75 (42.4)	
Female	136 (60.7)	34 (72.3)	102 (57.6)	
Body mass index (kg/m ²)				0.635
< 20	52 (27.1)	12 (31.6)	40 (26.0)	
20-25	106 (55.2)	21 (55.2)	85 (55.2)	
> 25	34 (17.7)	5 (13.2)	29 (18.8)	
Comorbidity				0.350
Charlson index = 0	217 (96.9)	47 (100.0)	170 (96.0)	
Charlson index > 0	7 (3.1)	0 (0.0)	7 (4.0)	
Symptom duration before presentation				0.740
< 72 h	129 (58.1)	26 (55.3)	103 (58.9)	
≥ 72 h	93 (41.9)	21 (44.7)	72 (41.1)	
Body temperature (°C)				0.755
< 37.8	119 (88.8)	28 (87.5)	91 (89.2)	
≥ 37.8	15 (11.2)	4 (12.5)	11 (10.8)	
Presenting symptom				0.507
Abdominal pain	219 (97.8)	47 (100.0)	172 (97.2)	
Indigestion	1 (0.4)	0 (0.0)	1 (0.6)	
Fever/chill	4 (1.8)	0 (0.0)	4 (2.2)	
Pain migration				0.507
No	114 (53.3)	26 (57.8)	88 (52.1)	
Yes	100 (46.7)	19 (42.2)	81 (47.9)	
Degree of tenderness				0.383
Mild	4 (1.8)	0 (0.0)	4 (2.3)	
Moderate	217 (96.9)	47 (100.0)	170 (96.0)	
Severe	3 (1.3)	0 (0.0)	3 (1.7)	
RLQ localization of pain				0.559
Discrete	205 (91.5)	42 (89.4)	163 (92.1)	
Obscure	19 (8.5)	5 (10.6)	14 (7.9)	
Lab findings, median (range)				
WBC count (× 10 ³ /mm ³)	9.55 (4.0-29.1)	9.3 (4.6-25.9)	9.6 (4.0-29.1)	0.833
Platelet count (× 10 ³ /mm ³)	250 (157- 564)	277 (202-564)	241 (157-341)	0.005
Creatinine (mg/dL)	0.64 (0.41- 1.11)	0.56 (0.41-0.69)	0.70 (0.46-1.11)	0.036
Albumin (g/dL)	4.30 (3.3-5.4)	4.40 (3.3-5.2)	4.30 (3.3-5.4)	0.989
Total bilirubin (mg/dL)	0.50 (0.2-1.5)	0.55 (0.2-1.5)	0.77 (0.2-2.2)	0.020
Neutrophil fraction				0.359
< 80%	160 (72.4)	36 (78.3)	124 (70.9)	
≥ 80%	61 (27.6)	10 (21.7)	51 (29.1)	

Data from patients receiving operations for suspicion of appendicitis with computed tomography findings that were negative or equivocal for appendicitis. RLQ: Right low quadrant of abdomen; WBC: White blood cells.

3.013-15.454; *P* = 0.001).

DISCUSSION

Although several characteristic CT features for appendicitis have been revealed, their significance and frequencies have not been extensively studied. In this study, we applied these factors individually to the CT scans of which previous interpretations were negative or equivocal for appendicitis. As a result, we could arrange their priority. We identified three factors related to appendicitis: appendiceal diameter ≥ 6.0 mm, periappendiceal fat stranding, and the absence of intraluminal air. The patients who had two or more of these factors showed a significantly higher probability of appendicitis. We think that the

application of our criteria would improve diagnostic accuracy of appendicitis, leading to a reduction in the rates of negative appendectomy and complications associated with delayed appendectomy.

The classical diagnostic criteria of appendicitis include appendiceal diameter of ≥ 7 mm; however, we found that the appendiceal diameter of 6 mm would be more helpful when encountered with equivocal CT findings. Actually, it is possible to have appendicitis with a 5-mm-appendiceal diameter, and to not have appendicitis with a 10-mm-appendiceal diameter. Therefore, appendiceal diameter alone is insufficient in making a diagnosis and should be supported by other more specific features.

Appendiceal wall thickening strongly suggests appendiceal inflammation. Administration of intravenous

Table 2 Reevaluations of computed tomography scans preoperatively interpreted as indeterminate for appendicitis *n* (%)

	Total population (<i>n</i> = 224)	Negative appendicitis (<i>n</i> = 46)	Pathologically proven appendicitis (<i>n</i> = 178)	<i>P</i> value
Appendiceal visualization				1.000
No	6 (2.7)	1 (2.2)	5 (2.8)	
Yes	218 (97.3)	45 (97.8)	173 (97.2)	
Appendiceal diameter				< 0.001
< 6.0 mm	89 (39.7)	29 (63.0)	60 (33.7)	
≥ 6.0 mm	135 (60.3)	17 (37.0)	118 (66.3)	
Thickness of appendiceal wall				0.175
< 2.0 mm	54 (24.1)	15 (32.6)	39 (21.9)	
≥ 2.0 mm	170 (75.9)	31 (67.4)	139 (78.1)	
Appendiceal wall enhancement				0.059
No	138 (63.3)	34 (75.6)	104 (63.3)	
Yes	80 (36.7)	11 (24.4)	69 (39.9)	
Presence of intraluminal air				0.024
No	139 (63.8)	22 (48.9)	117 (67.6)	
Yes	79 (36.2)	23 (51.1)	56 (32.4)	
Presence of appendicolith				1.000
No	206 (94.5)	43 (95.6)	163 (94.2)	
Yes	12 (5.5)	2 (4.4)	10 (5.8)	
Presence of periappendiceal fat stranding				0.001
No	155 (71.1)	41 (91.1)	114 (65.9)	
Yes	63 (28.9)	4 (8.9)	59 (34.1)	
Presence of periappendiceal fluid collection				0.669
No	216 (96.4)	44 (95.7)	172 (96.6)	
Yes	8 (3.6)	2 (4.3)	6 (3.4)	
Presence of periappendiceal lymphadenopathy				1.000
No	200 (89.3)	41 (89.1)	159 (89.3)	
Yes	24 (10.7)	5 (10.9)	19 (10.7)	
Presence of coexisting lesions				0.084
No	169 (75.4)	30 (65.2)	139 (78.1)	
Yes	55 (24.6)	16 (34.8)	39 (21.9)	

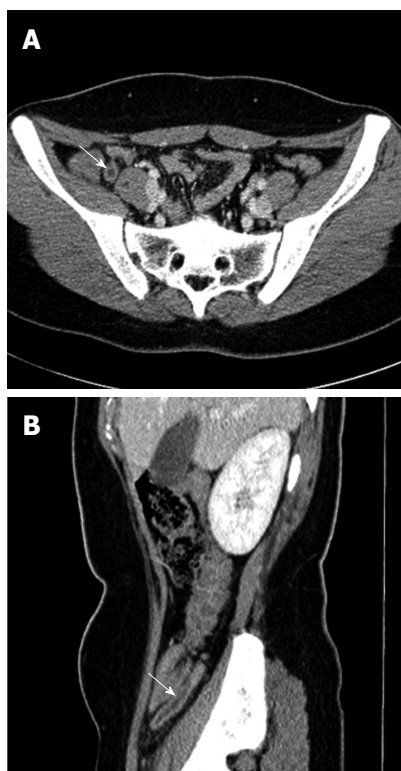
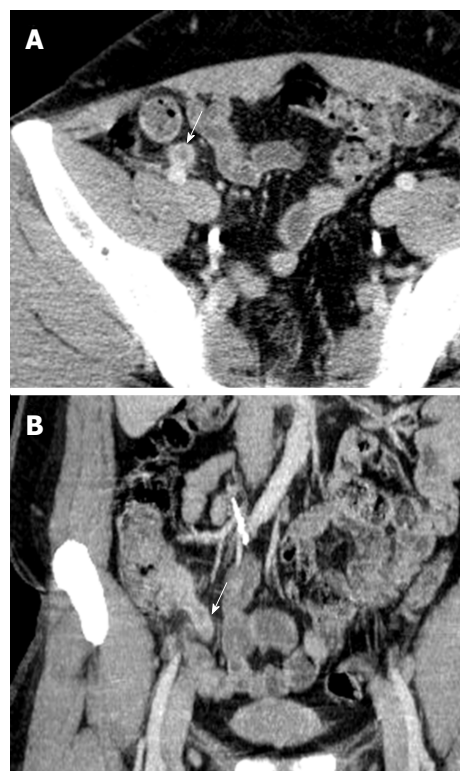
**Figure 2** Enlarged appendix and appendiceal wall enhancement. A: Cross-sectional (arrow); B: Sagittal abdominal computed tomography scans showing increased appendiceal diameter (≥ 6.0 mm) (arrow).**Figure 3** Appendiceal wall thickening. A: Cross-sectional (arrow); B: Coronal abdominal computed tomography scans showing appendiceal wall thickening suggestive of acute appendicitis (arrow).



Figure 4 Fat stranding. A: Cross-sectional (arrow); B: Coronal abdominal computed tomography scans showing periappendiceal fat stranding suggestive of acute appendicitis (arrow).

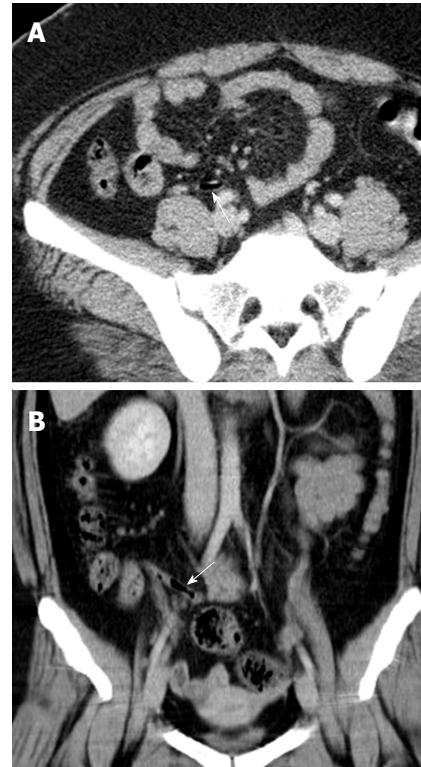


Figure 5 Appendiceal intraluminal air. A: Cross-sectional (arrow); B: Coronal abdominal computed tomography scans showing appendiceal intraluminal air suggestive of normal appendix (arrow).

contrast media is essential for visualizing the appendiceal wall. Because all the patients in this study underwent contrast-enhanced CT scanning, we could estimate the presence of the appendiceal wall thickening. Our results indicate that appendiceal wall thickening did not strongly suggest appendicitis in patients with equivocal CT features. However, we think that further and more intensive study is required to validate this factor.

The extension of appendiceal inflammation to nearby mesenteric fat results in fat inflammation surrounding the appendix. Such fat inflammation is manifested as periappendiceal fat stranding on the CT scan. In previous studies, periappendiceal fat stranding was reported in more than 70% of patients with appendicitis^[13,17,18]. In the present study, we showed that the presence of periappendiceal fat stranding is also a useful differential parameter when other CT findings are equivocal.

We also estimated whether it is helpful to detect intraluminal air in appendicitis when encountered in equivocal CT scans. The luminal obstruction by inspissated stool or lymphoid hyperplasia is believed to be the major cause of appendicitis^[19]. The luminal obstruction promotes bacterial overgrowth and increases mucus secretion, leading to intraluminal distention and wall pressure elevation. Consequently, intraluminal air, which used to be easily observed in the normal appendix, can disappear in patients with appendicitis^[20]. In a previous report, appendiceal intraluminal air was detected in 86% of patients without appendicitis and 15% of patients with appendicitis^[14]. In this study, we also found that the presence of intralumini-

Table 3 Incidence of coexisting inflammatory lesions

Coexisting lesions	Incidence (n)	% (n = 224)
Ileocolitis	37	17.0
Terminal ileitis	10	4.5
Periappendiceal fluid collection	4	1.0
Pelvic inflammatory disease	2	0.9
Epiploic appendicitis	1	0.4

Data refer to patients who underwent operation with suspicion of appendicitis based on clinical manifestations despite negative or equivocal computed tomography interpretation.

nal air was a useful indicator for appendicitis in situations with the equivocal CT scans.

We acknowledge that this study had several limitations. First, because it was a retrospective study, our results should be confirmed by prospective trials. Next, due to the nature of this study, the study population size was relatively small ($n = 224$). However, the use of a single radiologist eliminates the possibility for differences in CT interpretation. Even when the patients suspicious for appendicitis visited the hospital after work hours and were immediately evaluated by the on-duty radiologist, the CT findings were re-assessed and confirmed by the radiologist in charge.

In conclusion, we found that when we encountered equivocal CT findings for appendicitis, the diagnostic accuracy would be enhanced by several characteristic CT features: appendiceal diameter ≥ 6.0 mm, appendiceal

Table 4 Risk estimations *n* (%)

Groups	Number of risk factors ¹	Patients with positive appendicitis	OR	95%CI	P value
Low-risk group	0-1	73 (65.8)	1.000		
High-risk group	2-3	105 (92.9)	6.832	3.013-15.454	0.001

¹Risk factors include: appendiceal diameter ≥ 6.0 mm, presence of periappendiceal fat stranding, and intraluminal air in the appendix. Data refer to patients who underwent operation for suspicion of appendicitis based on clinical manifestations despite negative or equivocal computed tomography interpretation.

wall thickening ≥ 2.0 mm, periappendiceal fat stranding, and the absence of intraluminal air, rather than presence, as an indicator for appendicitis. By the application of these criteria, we could improve the diagnostic accuracy of appendicitis up to 6.8 times in patients with equivocal CT features. These characteristic CT features are not difficult to detect with instruction. Therefore, we recommend that not only radiologists, but also surgeons and physicians, could improve diagnostic accuracy of appendicitis by using these criteria.

COMMENTS

Background

The introduction of computed tomography (CT) has improved the diagnostic accuracy of appendicitis. However, CT may overlook about 10% patients with appendicitis because of its limited sensitivity and specificity. Therefore, clinicians frequently encounter patients who show equivocal CT findings for appendicitis, but who also have clinical manifestations of appendicitis.

Research frontiers

Since CT scanning became widely used in the diagnosis of appendicitis, several CT features indicating appendicitis have been proposed; however, they have been used rather sporadically to date. Systematic utilization of these CT features would provide better discrimination between patients with and without appendicitis.

Innovations and breakthroughs

First, this study population was specifically chosen, and therefore well suited to the study. Of the 2596 patients who underwent appendectomy during a 6-year period, the authors selected 224 patients who showed negative or equivocal CT findings for appendicitis, but thereafter were operated on for suspected appendicitis. Next, they thoroughly reviewed the literature concerning CT features of appendicitis, and determined the most reliable parameters. Thereafter, they systematically applied these features to the patient population. Finally, all the related CT images were re-evaluated by one radiologist with specialist experience in abdominal imaging. To avoid selection bias, the radiologist who re-evaluated CT images was not given information about the patient's final diagnosis.

Applications

The authors have developed criteria which are useful when encountering patients with equivocal CT features: Appendiceal diameter ≥ 6.0 mm, appendiceal wall thickening ≥ 2.0 mm, periappendiceal fat stranding, and the absence of intraluminal air. By the application of these criteria, they could improve the diagnostic accuracy of appendicitis up to 6.8 times in patients with equivocal CT features.

Peer review

The original article is well presented. The application of these criteria helps to improve the diagnostic accuracy in patients with symptoms and signs of appendicitis.

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