Original Article

Value of Additional Ultrasound Examination in Patients with Equivocal Computed Tomography Findings of Acute Appendicitis: Comparison with Computed Tomography Reassessment

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Abstract

Objectives: The objective of this study was to find the diagnostic values of additional ultrasound (US) in patients with equivocal computed tomography (CT) findings of acute appendicitis, compared to CT reassessment. **Materials and Methods:** Patients with equivocal CT findings of acute appendicitis (n = 115), who underwent the US, were included in the study. Two abdominal radiologists reviewed CT scans independently. They analyzed CT findings and made a diagnosis of acute appendicitis. The patients were categorized into positive and negative appendicitis based on the previous US reports. The diagnostic performance, interobserver agreement of CT findings, and appendicitis likelihood were calculated. **Results:** The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of US (100%, 92.1%, 79.5%, and 100%, respectively) were higher than those of CT reassessment (reviewer 1: 51.9%, 87.5%, 56.1%, and 85.6%; reviewer 2: 66.7%, 85.2%, 58.1%, and 89.3%, respectively). In the coexistent inflammation group, the sensitivity, specificity, PPV, and NPV of US (reviewer 1: 100%, 98%, 91.5%, and 100%; reviewer 2: 100%, 98%, 87.7%, and 100%, respectively) were higher than those of CT reassessment (reviewer 1: 27.3%, 94.1%, 49.9%, and 85.8%; reviewer 2: 14.3%, 98.0%, 50.5%, and 88.9%, respectively). **Conclusion:** In patients with equivocal CT findings of acute appendicitis, US shows better diagnostic performance than CT reassessment, and helps differentiate with periappendicitis.

Keywords: Appendicitis, appendix, diagnostic tests, ultrasonography, X-ray computed tomography

Introduction

Acute appendicitis is one of the most common causes of acute abdominal pain and is an urgent condition that requires prompt surgical intervention. Although numerous studies attest to the high sensitivity (90%–100%) and specificity (91%–99%) of computed tomography (CT)-based diagnosis of appendicitis,[1] there is also an increase in the number of patients with equivocal CT findings.[2] The reported incidence of equivocal CT findings of acute appendicitis ranges from 5% to 13.1%.[2-7] Appendicitis is present in up to 30% of patients, whose CT findings are considered equivocal.[2] Whereas, an equivocal appearance of appendicitis can occur in up to 6.6% of the normal population in the control study.[8] In addition, when patients have a coexistent inflammatory lesion, it can be difficult to differentiate acute appendicitis from periappendicitis.[9,10]

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Received: 22-04-2018 **Accepted:** 26-06-2018 **Available Online:** 07-05-2019

Access this article online

Quick Response Code:

Website: www.jmuonline.org

DOI: 10.4103/JMU.JMU_52_18

How to cite this article: Sim JY, Kim HJ, Jang SK, Yeon JW, Jeon BG, Ha YR, *et al*. Value of additional ultrasound examination in patients with equivocal computed tomography findings of acute appendicitis: Comparison with computed tomography reassessment. J Med Ultrasound 2019;27:75-80.

Therefore, making a correct diagnosis of acute appendicitis continues to be a challenge for radiologists, when presented with equivocal CT findings. The current management of equivocal CT findings of acute appendicitis is still controversial. It includes active observation, using alternate imaging modalities, diagnostic laparoscopy, or immediate appendectomy.[11] However, a prompt, accurate diagnosis is important to avoid appendiceal perforation, which is associated with increased rates of morbidity and mortality.[1]

For patients with equivocal CT findings of acute appendicitis, ultrasound (US) reevaluation could improve diagnostic accuracy and decrease negative appendectomy rate.[12]

The purposes of this study were to find diagnostic values of additional US in patients with equivocal CT findings of acute appendicitis, compared to CT reassessment.

Materials and Methods

Patient population

This retrospective, single-institution study was approved by the Institutional Review Board, and the need for informed consent was waived.

Between April 2011 and October 2012, a total of 316 consecutive patients underwent both CT and appendix US for suspected acute appendicitis. Initial CT reports were presented as a five-grade system for likelihood appendicitis (G1, definitely absent; G2, probably absent; G3, indeterminate; G4, probably present; and G5, definitely present). Of these, 158 were excluded based on the initial CT reports as follows: absent appendicitis (G1 or G2, n = 117) and present appendicitis (G4 or G5, n = 41). The remaining 158 patients had equivocal CT findings (indeterminate appendicitis, G3) of acute appendicitis in the initial CT reports. Of these, 43 were excluded from the study as follows: lost to follow-up (n = 25), underwent US before CT (n = 9), time interval over 4 days between US and CT (n = 5), and transfer to another hospital (n = 4). Finally, 115 patients (mean age ± standard deviation [SD], 32.1 ± 17.5 years; age range, 7–81 years) were included in this retrospective, single-center study: 75 women (34.9 ± 17.7 years, 10–81 years), and 40 men (27.0 ± 16.0 years, 7–72 years).

Among the current study population, 40 patients were included in a previous study investigating the added diagnostic value of US in patients with equivocal CT findings of acute appendicitis.[12]

Imaging techniques

Intravenous contrast-enhanced portal-venous phase CT scans were performed using 16-(Brilliance, Philips, Cleveland, Ohio) or 64-detector-row machines (Somatom Sensation, Siemens, Forchheim, Germany). An intravenous iodinated contrast agent (2 mL/kg) was administered at a rate of 3.0 mL/s.

All US examinations were performed with an iU22 US system (Philips Healthcare, Eindhoven, The Netherlands) using 5–8 MHz curved or 5–12 MHz linear probes. Color Doppler US was performed using a low-velocity scale (pulse repetition frequency, 1500 Hz) and a low wall filter (100 Hz).

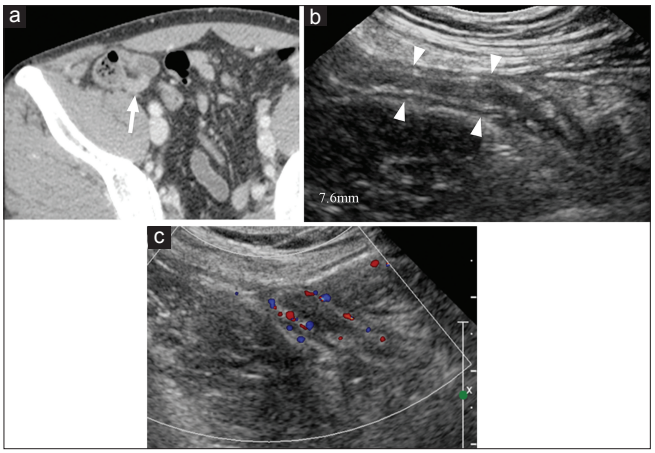

Figure 1: A 35-year-old male diagnosed as a normal appendix on both reviewers' computed tomography reassessment. Contrast enhanced computed tomography image (a) shows appendiceal dilatation without other findings of acute appendicitis. Grayscale ultrasound (b) shows increased appendix diameter (7.6 mm) and mild appendiceal wall thickening. Colo Doppler ultrasound (c) shows mild mural hyperemia. The ultrasound diagnosis was acute appendicitis. The patient underwent appendectomy, and acute appendicitis was histopathologically confirmed

Computed tomography analysis

All CT scans were independently reassessed by two radiologists (13 and 4 years of dedicated abdominal imaging experience, respectively). The two reviewers were aware that the CT scans were acquired for suspected acute appendicitis and that the initial CT reports indicated an equivocal appendix. The reviewers were also aware of laboratory data. The reviewers were, however, unaware of surgical, pathological reports, or physical examination results. All axial and coronal reformatted images were presented on the picture archiving and communications system (Piview Star, Infinitt Healthcare, Seoul, Korea).

Reviewers analyzed four CT findings – appendiceal wall enhancement, appendiceal wall thickening, intraluminal air in the appendix, and coexistent inflammatory lesion. Appendiceal wall enhancement and wall thickening were determined subjectively compared to the normal bowels. Coexistent inflammatory lesion was considered as positive, when the findings indicated an inflammation-causing right lower quadrant pain in other organs except the appendix. The reviewers made a binary conclusion whether a patient had acute appendicitis or not.

Ultrasound analysis

In our institution, we routinely recommend the additional US evaluation for patients with equivocal CT findings of acute appendicitis. All US examinations were performed by one experienced abdominal radiologist (10 years of experience) and two residents (2 and 3 years of training, respectively). If the US examinations were initially performed by the residents, the experienced abdominal radiologist reviewed and confirmed the results. Acute appendicitis was diagnosed

and reported according to a structured report form used at our institution [Supplementary Table E1]. We reviewed the initial, structured US reports and categorized all patients into positive and negative appendicitis. The patients with a low probability of appendicitis were categorized as negative appendicitis.

Time interval analysis between ultrasound and computed tomography

We investigated the effect of time interval between the initial CT scan and the US on the diagnostic performance of US. Based on this time interval, the patients were classified into five groups, and analyzed diagnostic performance in each groups. (<6 h, $n = 56$; 6–12 h, $n = 11$; 12–18 h, $n = 24$; 18–24 h, $n = 6$; >24 h, $n = 18$).

Definitive diagnosis

For patients who underwent surgery, a definitive diagnosis was made on the basis of the pathological findings. Otherwise, congestions were considered negative appendicitis. For patients who did not undergo surgery, final diagnosis was retrieved from medical records.

Statistical analysis

The area under the receiver operator characteristic curve (AUC), sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracies of CT reassessment and US were calculated for the entire study group and for the coexistent inflammation group. Comparison of receiver operator characteristic curves between CT reassessment and US was done using the method of DeLong *et al*.[13] Sensitivity and specificity of CT reassessment and US were compared using the McNemar test. Interobserver agreement was analyzed using Cohen's kappa coefficient (κ) and reported as a point estimate with a 95% confidence interval (CI). We also conducted predefined subgroup analyses for the diagnostic performance based on the time interval between the initial CT and the US, and the presence or absence of a coexistent inflammatory lesion other than appendicitis. $P < 0.05$ was considered statistically significant difference. All analyses were performed using MedCalc® software (Version 12.1.4; MedCalc Software, Mariakerke, Ostend, Belgium).

Results

Definite diagnosis

Among 115 patients, 34 patients underwent surgery. Twenty-seven patients were pathologically confirmed as acute appendicitis [Figure 1a-c]. Seven patients were pathologically confirmed as negative appendicitis and the pathologic reports were fecalith impaction only ($n = 1$), fecalith impaction with serosal congestion ($n = 1$), fecalith impaction with lymphoid hyperplasia and congestion ($n = 1$), congestion ($n = 2$), and serosal congestion ($n = 2$) [Figure 2a-c]. The other 81 patients were successfully treated by conservative therapy or improved symptom at follow-up.

Figure 2: A 44-year-old male diagnosed as acute diverticulitis with negative appendicitis on both reviewers' computed tomography reassessment and ultrasound report. Contrast-enhanced coronal reformatted computed tomography images (a and b) show cecal diverticulitis (arrow) and periappendicitis (arrowhead). On grayscale US (c), appendiceal diameter is within the normal range (4.3 mm). The patient underwent appendectomy by surgeon's decision. The pathological report was serosal congestion (negative appendicitis) period

Computed tomography reassessment result

Table 1 shows frequency and interobserver agreement of each CT findings and diagnosing appendicitis. Appendiceal wall enhancement, intraluminal air in the appendix, and coexistent inflammatory lesions demonstrated good interobserver agreement (κ = 0.62, 0.69, and 0.65, respectively). Interobserver agreement of diagnosing appendicitis was moderate (κ = 0.44).

Diagnostic performances of computed tomography reassessment and ultrasound

The diagnostic performance of CT reassessment by two reviewers and US for acute appendicitis is summarized in Table 2. The sensitivity, specificity, PPV, and NPV from CT reassessment were 51.9% (95% CI: 31.9%–71.3%), 87.5% (95% CI: 78.7%–93.6%), 56.1% (95% CI: 35.0%–75.6%), and 85.6 (95% CI: 76.5%–92.1%), respectively, as estimated by reviewer 1, and 66.7% (95% CI: 46.0%–83.5%), 85.2% (95% CI: 76.1%–91.9%), 58.1 (95% CI: 39.1%–75.5%), and 89.3% (95% CI: 80.6%–95.0%), respectively, as estimated by reviewer 2. The sensitivity, specificity, PPV, and NPV of US were 100% (95% CI: 87.2%–100%),

92.1% (95% CI: 84.3%–96.7%), 79.5 (95% CI: 61.9%–91.5%), and 100% (95% CI: 95.6%–100%), respectively. The sensitivity and specificity are higher than the corresponding values from CT reassessment ($P < 0.001$ for both, McNemar test). The differences in the AUC were also statistically significant (reviewer 1, CT vs. US $P < 0.0001$ and reviewer 2, CT vs. US $P = 0.0001$).

Coexistent inflammation group

Reviewer 1 categorized 62 patients and reviewer 2 categorized 56 patients as belonging to the coexistent inflammation group. The diagnostic performance of CT reassessment and US in coexistent inflammation group is presented in Table 3. The sensitivity, specificity, PPV, and NPV of US (reviewer 1: 100%, 98%, 91.5%, and 100%; reviewer 2: 100%, 98%, 87.7%, and 100%, respectively) were higher than those of CT reassessment (reviewer 1: 27.3%, 94.1%, 49.9%, and 85.8%; reviewer 2: 14.3%, 98.0%, 50.5%, and 88.9%, respectively). The differences between the AUC were also statistically significant in the coexistent inflammation group.

Effect of the time interval between initial computed tomography and ultrasound

The time interval between initial CT and US ranged between 32 min and 3 days 17 h 33 min (mean time interval ± SD: 14 h 51 min ± 19 h 59 min). As the time interval increased, the diagnostic performance of US generally increased, except 12–18 h [Table 4]. In addition, there were only true negative cases in the time interval group of over 24 h.

Discussion

In this study, in patients with equivocal CT findings of appendicitis, the sensitivity, specificity, PPV, and NPV of US were higher than CT reassessment. A previous study reported that US reevaluation could decrease negative appendectomy rate.[12] These results suggest that US can improve diagnostic accuracy and prevent delayed complicated appendicitis in patients with equivocal CT findings of appendicitis. US provides many advantages. It has been demonstrated that the graded compression US technique is helpful in distinguishing acute appendicitis from dilatation due to fluid or feces.[12,14] The spatial resolution of bowel wall in high-frequency US images is better than that of CT. In addition, US probe-induced tenderness over the appendix is also an important finding that can improve the accuracy of diagnosis of acute appendicitis.

We also compared the diagnostic performance of US and CT reassessment in patients with coexistent inflammation because

Table 1: Frequency of individual computed tomography findings, diagnosis of acute appendicitis, and interobserver agreement

	Reviewer 1*	Reviewer 2*	Interobserver agreement†
Appendiceal wall enhancement	35 (30.4)	38 (33.0)	0.62 (0.47-0.77)
Appendiceal wall thickening	64 (55.7)	61 (53.0)	0.32 (0.14-0.49)
Intraluminal air in appendix	54 (47.0)	56 (48.7)	0.69 (0.55-0.82)
Coexistent inflammatory lesion	62 (53.9)	56 (48.7)	0.65 (0.52-0.79)
Diagnose acute appendicitis	25 (21.7)	31 (27.0)	0.44 (0.25-0.62)
Alternative diagnosis	58 (52.2)	60 (52.2)	0.51 (0.36-0.67)

*Data are numbers of patients (percentages), †Data are kappa (95% CIs) CT: Computed tomography, CIs: Confidence intervals

Table 2: Diagnostic performance of computed tomography reassessment and ultrasound

	CT (reviewer 1)	CT (reviewer 2)	US
Outcome results*			
Positive	25 (21.7)	31 (27.0)	34 (29.6)
Negative	90 (78.3)	84 (73.0)	81 (70.4)
True positive	14 (12.1)	18 (15.7)	27 (23.5)
True negative	77 (66.9)	75 (65.2)	81 (70.4)
False positive	11 (9.6)	13 (11.3)	7 (6.1)
False negative	13 (11.3)	9 (7.8)	0
Performance			
Sensitivity (%)	51.9 (31.9-71.3)	66.7 (46.0-83.5)	100 (87.2-100)
Specificity (%)	87.5 (78.7-93.6)	85.2 (76.1-91.9)	92.1 (84.3-96.7)
PPV (%)	56.1 (35.0-75.6)	58.1 (39.1-75.5)	79.5 (61.9-91.5)
NPV (%)	85.6 (76.5-92.1)	89.3 (80.6-95.0)	100 (95.6-100)
Accuracy (%)	79.1 (71.7-86.6)	80.1 (73.7-88.1)	93.9 (89.5-98.3)
AUC	0.697 (0.604-0.779)	0.759 (0.671-0.834)	0.960 (0.906-0.988)

*Data are numbers of patients (percentages). Data in brackets are 95% CI. PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under the receiver operator characteristic curve, CT: Computed tomography, US: Ultrasound, CI: Confidence interval

Table 3: Diagnostic performance of computed tomography reassessment and ultrasound in coexistent inflammation group

	Coexistent inflammation		The other group	
	CT reassessment	US	CT reassessment	US
Reviewer 1				
Sensitivity (%)	27.3 (6.0-61.0)	100 (71.5-100)	68.8 (41.3-89.0)	100 (79.4-100)
Specificity (%)	94.1 (83.8-98.8)	98.0 (89.6-100)	78.4 (61.8-90.2)	87.8 (68.0-93.8)
PPV (%)	49.9 (11.8-88.1)	91.5 (59.5-99.8)	58.0 (33.6-79.8)	78.0 (54.1-93.1)
NPV (%)	85.8 (73.7-93.7)	100 (92.9-100)	85.3 (68.7-95.2)	100 (89.1-100)
Accuracy (%)	82.3 (72.8-91.8)	98.4 (95.6-100)	75.5 (63.9-87.1)	88.7 (80.2-97.2)
AUC	0.607 (0.475-0.729)	0.990 (0.924-1.000)	0.736 (0.596-0.847)	0.919 (0.811-0.976)
Reviewer 2				
Sensitivity (%)	14.3 (0.4-57.9)	100 (59.0-100)	85.0 (62.1-96.8)	100 (83.2-100)
Specificity (%)	98.0 (89.1-99.9)	98.0 (89.1-99.9)	69.2 (52.4-83.0)	84.6 (69.5-94.1)
PPV (%)	50.5 (0.04-100)	87.7 (44.2-99.8)	58.6 (38.9-76.5)	76.9 (56.3-91.0)
NPV (%)	88.9 (77.3-95.8)	100 (92.6-100)	90.0 (73.1-98.0)	100 (98.1-100)
Accuracy (%)	87.5 (78.8-96.2)	98.2 (94.8-100)	74.6 (63.5-85.7)	90.8 (83.7-97.8)
AUC	0.561 (0.422-0.694)	0.990 (0.917-1.000)	0.771 (0.643-0.870)	0.923 (0.823-0.976)

Data in brackets are 95% CI. PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under the receiver operator characteristic curve, CT: Computed tomography, US: Ultrasound, CI: Confidence interval

Table 4: Diagnostic performance of US according to time interval

	≤6 h (*n*=56)	6-12 h (*n*=11)	12-18 h (*n*=24)	18-24 h (*n*=6)	>24 h (*n*=18)*
Sensitivity (%)	100 (79.4-100)	100 (29.2-100)	100 (54.1-100)	100 (15.8-100)	NA
Specificity (%)	85.0 (70.294.3)	100 (63.1-100)	94.4 (72.7-99.9)	100 (39.8-100)	100 (88.5-100)
Accuracy (%)	89.3 (81.2-97.4)	100 (100-100)	95.8 (87.8-103.8)	100 (100-100)	NA
AUC	0.925 (0.822-0.978)	1 (0.715-1.000)	0.972 (0.810-1.000)	1 (0.541-1.000)	NA

*Insufficient data for AUC. Data in brackets are 95% CI. AUC: Area under the ROC curve, ROC: Receiver operator characteristic, CT: Computed tomography, US: Ultrasound, NA: Not available, CI: Confidence interval

it is usually difficult to differentiate between appendicitis and periappendicitis in the presence of a coexistent inflammatory lesion, both clinically and radiologically. This study shows that the sensitivity, specificity, PPV, and NPV of US were also higher than CT reassessment in patients with coexistent inflammation.

In this study, CT specificity was high enough; however, sensitivity was low in the entire study group and the coexistent inflammation group. It was more pronounced in coexistent inflammation group since coexistent inflammation known as a finding of negative appendicitis.[15] In our opinion, US may play a complementary role to the CT's low sensitivity since real-time probe-induced tenderness can indicate the regions of maximum tenderness on the appendix or other inflammatory lesions. In addition, evaluation of the compressibility of the appendix may help to differentiate appendicitis from periappendicitis filled with fluid.

The analysis of the effect of time interval between initial CT and the US shows that the diagnostic performance of US improves with increasing time interval. In addition, the rate of negative appendicitis gradually increased over time, and all the patients who underwent the US after 24 h showed negative appendicitis. These results may suggest that short-term (<24 h) active observation using the US should be enough for the diagnosis in patients with equivocal radiologic or clinical findings of appendicitis.

The result shows that the interobserver agreement to diagnose acute appendicitis was not high as well as diagnostic accuracy. The interobserver agreement to diagnose acute appendicitis ($\kappa = 0.44$) was lower than those of three of CT findings ($\kappa = 0.62$, 0.69, and 0.65, respectively). We thick that the reason of low interobserver agreement is that only equivocal cases of acute appendicitis were included, while most patients had one or two positive CT findings, and even each of the CT findings were subtle.

This study has several limitations. This is a retrospective study. There is a selection bias since we excluded the patients with equivocal CT findings of appendicitis without US. Some of these patients with a high clinical suspicion of appendicitis underwent surgery without US. Others with a low clinical suspicion of appendicitis were observed without US. The final diagnosis of patients who did not undergo surgery was made on the basis of a medical record review. We also excluded patients who did not visit our hospital for follow-up after undergoing CT and US, further contributing to the selection bias. We did not evaluate the correlation between US accuracy and patient obesity because there was only one obese patient with a sagittal abdominal diameter over 25 cm (mean 18.2 cm, range 11.6–27.7 cm). The time interval between initial CT and US varied. We excluded patients with a time interval of over 4 days, 86% (99/115) of the patients underwent the

Supplementary Table E1: US diagnostic criteria for acute appendicitis of our institution

Likelihood of acute appendicitis	Diagnostic criteria
Acute appendicitis	Noncompressible enlarged appendix >6 mm
	Wall thickening, compared to other normal bowel wall
	US-guided localized tenderness
	Increased periappendiceal fat echogenicity
	Increased color flows within the appendiceal wall on Doppler US
Low possibility of appendicitis	Nonvisible appendix without any periappendiceal inflammatory changes
	Slightly increased appendiceal diameter (6-7 mm) without other positive findings
Normal appendix	Normal appendix*, diameter <6 mm

*Compressible tubular structure with a blind end and without wall thickening, localized tenderness, or other periappendiceal inflammatory changes.
CT: Computed tomography, US: Ultrasound

US within 24 h after the initial CT. Finally, the study period was relatively short, and the study population was small. A prospective, randomized controlled trial comprising a large population of patients with equivocal CT findings of appendicitis is required to confirm our results.

Conclusion

For patients with equivocal CT findings of acute appendicitis, US shows better diagnostic performance characteristics than CT reassessment. The US is also helpful in the accurate diagnosis of acute appendicitis in patients with coexistent inflammatory lesions causing symptoms of suspected appendicitis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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