Diagnostic performance of US re-evaluation for patients with equivocal CT findings of acute appendicitis; comparison with CT re-assessment

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Authors: H. Kim, J. Sim, J. W. Yeon, S. K. Jang; Seongnam-si/KR
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Aims and objectives

I. INTRODUCTION

Acute appendicitis is one of the most common causes of acute abdominal pain, and it is an urgent condition that requires prompt surgical intervention. Although numerous studies attest to the high sensitivity and specificity of CT, which are reported to range from 90-100% and 91-99%, respectively [1], the number with equivocal CT findings has increased [2]. The reported incidence of equivocal CT findings of acute appendicitis ranges from 5-13.1% [3-6]. Appendicitis is present in up to 30% of patients whose CT findings are considered equivocal [2], while an equivocal appearance of the appendix can also occur in up to 6.6% of the normal population [7].

The current management of equivocal CT findings of acute appendicitis is inpatient observation [1]. The prompt accurate diagnosis is important because the mortality and morbidity is 0.24% and 6.1% for acute uncomplicated appendicitis but increased as 1.7% and 19% for perforated appendicitis [1]. On the other hand, unnecessary appendectomy carries potentially major risks and substantial costs. There were many studies to improve diagnostic accuracy of acute appendicitis. Kim et al. [8] reported that knowledge of the identified CT findings can improve diagnostic accuracy of patients with equivocal preoperative CT interpretation. And we reported that for patients with equivocal CT findings of acute appendicitis, US reevaluation can improve diagnostic accuracy and decreased negative appendectomy rate. [9]

The purpose of this study was to compare diagnostic performance between CT reassessment and US reevaluation for patients with equivocal CT findings of acute appendicitis.
Methods and materials

Study population

Our Institutional Review Board approved this retrospective single center study and waived informed consent. Between April 2011 and October 2012, 316 patients underwent CT and US for suspected acute appendicitis. Of these, 158 patients who had equivocal CT findings of acute appendicitis were enrolled in the study. Of these patients, 43 were excluded because of lost to follow-up (n=25), underwent US before CT (n=9), over 1 week time interval between US and CT (n=5) and transfer to another hospital (n=4). The remaining 115 patients (mean age ± standard deviation, 32.1 ± 17.5 years; age range, 7 - 81 years) finally formed the study population (Figure 1). The study group consisted of 75 female patients (34.9 ± 17.7 years, 10 - 81 years) and 40 male patients (27.0 ± 16.0 years, 7 - 72 years). Of these patients, 40 enrolled previous study [9].

Figure 1. Patients flow diagram.

```
158 initially eligible^a
  25 lost to follow up
    9 US before CT
    5 time interval between US and CT over 1 week
    4 transfer to another hospital
  115 finally included
  34 underwent surgery
  81 did not undergo surgery
```

^aUnderwent CT and US for suspected acute appendicitis and the initial CT reports were equivocal appendix.

Fig. 1: Figure 1. Patients flow diagram. Eligible criteria: underwent CT and US for suspected acute appendicitis and the initial CT reports were equivocal appendix.

References: Radiology, Daejin medical center, Bundang Jesaeng hospital - Seongnam-si/KR

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

All ultrasound examinations were performed with an iU22 ultrasound system (Philips Healthcare) using 5-8 MHz curved or 5-12 MHz linear probes. Color Doppler US was performed at the end of the gray-scale US examination using a low-velocity scale (pulse repetition frequency, 1,500 Hz) and a low wall filter (100 Hz) to evaluate blood flow.

**CT analysis**

All CT images were retrospectively and independently reassessed by two radiologists with 11 and 4 years of dedicated abdominal imaging experience. These two reviewers were aware that all CT examinations were taken for suspected acute appendicitis and the initial reports were equivocal appendix. But they were unaware of surgical, pathological report, laboratory data or physical examination result. All axial and coronal reformatted images were presented to the reviewers using a PACS (Piview Star, Infinitt Healthcare, Seoul, Korea) in stack mode. They were informed that appendiceal wall enhancement, appendiceal wall thickening, intraluminal air in appendix, and inflammatory lesion other than appendicitis were significant CT findings to improve diagnostic accuracy in patients with equivocal CT findings of appendicitis on previously reported study. [8]

Regardless of whether appendicitis is exist or not, when there was fat infiltration or the other findings indicated inflammation in other organ except appendix, reviewers were asked to categorize into coexistent inflammation group, and the rest of patients categorized into appendicitis proper group. Then, reviewers analyzed seven following CT findings for appendicitis; appendiceal diameter, appendiceal wall enhancement, appendiceal wall thickening, periappendiceal fat infiltration, intraluminal air in the appendix, cecal apical wall thickening, and mesenteric lymphadenopathy. The diameter of appendix was measured at the greatest portion of the visible appendix with on axial enhanced sections. Appendiceal wall enhancement, wall thickening and cecal apical wall thickening were determined subjectively when affected bowel wall enhancement or thickening was more prominent compared with the normal small or large bowels. Mesenteric lymphadenopathy was defined as enlarged lymph node with more than 1cm in short diameter or clustered lymph nodes more than 4 in the right lower quadrant.

The reviewers also reassessed whether it is acute appendicitis or normal appendix. If there was alternative diagnosis, reviewers asked to record the alternative diagnosis.

**Ultrasound analysis**
We reviewed all patients previous US reports. In our institution, we recommended US reevaluation for patients who have equivocal CT findings of acute appendicitis. *Appendix figure 1* shows the diagnostic algorithm for acute appendicitis of our institution and *Table 1* shows the ultrasound diagnostic criteria for acute appendicitis. All US examinations included in this study were performed by one experienced abdominal radiologist (10 years' experience) and two residents (2 and 3 years' training). If residents initially performed the US examinations, the experienced abdominal radiologist immediately reviewed and confirmed the results. Off-hour studies were performed by two residents (2 and 3 years' training), and the expert abdominal radiologist reviewed and confirmed the results on the morning of the next business day.

**Appendix figure1. Diagnostic flow chart for patient with suspected acute appendicitis in our institution**

![Diagnostic flow chart](image)

*Fig. 7: Appendix figure1. Diagnostic flow chart for patient with suspected acute appendicitis in our institution*

**References:** Radiology, Daejin medical center, Bundang Jesaeng hospital - Seongnam-si/KR
Table 1. US diagnostic criteria for acute appendicitis of our institution

<table>
<thead>
<tr>
<th>Likelyhood of acute appendicitis</th>
<th>Diagnostic criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute appendicitis</td>
<td>Non-compressible enlarged appendix &gt;6mm</td>
</tr>
<tr>
<td></td>
<td>Wall thickening, compared with other normal bowel wall</td>
</tr>
<tr>
<td></td>
<td>US-guided localized tenderness</td>
</tr>
<tr>
<td></td>
<td>Increased periappendiceal fat echogenicity</td>
</tr>
<tr>
<td></td>
<td>Increased color flows within the appendiceal wall on Doppler US</td>
</tr>
<tr>
<td>Low possibility of appendicitis</td>
<td>Non-visible appendix without any periappendiceal inflammatory changes</td>
</tr>
<tr>
<td></td>
<td>Slightly increased appendiceal diameter (6-7mm) without other positive findings</td>
</tr>
<tr>
<td>Normal appendix</td>
<td>Normal appendix*, diameter &lt;6mm</td>
</tr>
</tbody>
</table>

*a visible compressible tubular structure with a blind end without wall thickening, localized tenderness or other periappendiceal inflammatory changes

Table 1: Table 1. US diagnostic criteria for acute appendicitis of our institution
Normal appendix is visible compressible tubular structure with a blind end without wall thickening, localized tenderness or other periappendiceal inflammatory changes.

References: Radiology, Daejin medical center, Bundang Jesaeng hospital - Seongnam-si/KR
The time interval of CT and US reevaluation were range 32 minutes to 3 days 17 hours 33 minutes (mean time interval ± standard deviation : 14hours 51minutes ± 19hours 59 minutes).

Obesity measurement

Because US evaluation may influenced by patient obesity, we tried to categorized obese patients and non-obese patient. But in many patients, body weight and height were omitted in their medical charts, we could not calculate patients BMI. Instead BMI, the presence of abdominal obesity was determined on each CT study by measurement of the sagittal abdominal diameter. Sagittal abdominal diameter values of greater than 25 cm have been determined to be indicative of obesity [10]. In another study, the mean sagittal abdominal diameter values of 24.5 cm in women and 23.7 cm in men have been shown to correspond to BMI values of 31.4 and 29.0 kg/m2, respectively [11]. This distance was measured by resident (4 years training), between the anterior and posterior skin at the level of the fourth to fifth lumbar vertebra.

Definitive diagnosis
For patients who underwent surgery, a definitive diagnosis of appendicitis was made on the basis of the surgical and pathological findings. Pathological diagnosis of acute appendicitis was based on neutrophil infiltration of the submucosa or muscularis propria. Periappendicitis is defined as neutrophil infiltration of the appendiceal serosa and subserosa without mucosal involvement. For all patients who did not undergo surgery, a final diagnosis was made on the basis of information retrieved from medical records.

**Statistical analysis**

The sensitivity, specificity, PPV, NPV, and accuracy for each reviewers CT reassessment and US reevaluation were calculated. Comparison of ROC curves between CT reassessment and US reevaluation was done with the method of DeLong et al. Interobserver agreement on nominal data was analyzed using Cohen's kappa coefficient(#) and reported as a point estimate with a 95% confidence interval (CI). Interobserver agreement of appendiceal diameter was calculated using the intraaclass correlation coefficient. In each case, the kappa coefficient values were interpreted as follows: < 0.20 indicates poor agreement; 0.21-0.40 indicates fair agreement; 0.41-0.60 indicates moderate agreement; 0.61-0.80 indicates good agreement and 0.81-1 indicates very good agreement, respectively. A P-value of less than 0.05 was considered to indicate a statistically significant difference. All analyses were performed using proprietary software (Medcalc®, version 12.1.4; MedCalc Software, Mariakerke, Belgium).
Figure 1. Patients flow diagram.

- 158 initially eligible
- 25 lost to follow up
  - 9 US before CT
  - 5 time interval between US and CT over 1 week
  - 4 transfer to another hospital
- 115 finally included
- 34 underwent surgery
- 81 did not undergo surgery

*Underwent CT and US for suspected acute appendicitis and the initial CT reports were equivocal appendix.

**Fig. 1:** Figure 1. Patients flow diagram. Eligible criteria: underwent CT and US for suspected acute appendicitis and the initial CT reports were equivocal appendix.

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Appendix figure 1. Diagnostic flow chart for patient with suspected acute appendicitis in our institution
Fig. 7: Appendix figure1. Diagnostic flow chart for patient with suspected acute appendicitis in our institution

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Table 1. US diagnostic criteria for acute appendicitis of our institution

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<td></td>
<td>Increased periappendiceal fat echogenicity</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
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<td>Non-visible appendix without any periappendiceal inflammatory changes</td>
</tr>
<tr>
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</tr>
<tr>
<td>Normal appendix</td>
<td>Normal appendix, diameter &lt;6mm</td>
</tr>
</tbody>
</table>

* visible compressible tubular structure with a blind end without wall thickening, localized tenderness or other periappendiceal inflammatory changes

Table 1: Table 1. US diagnostic criteria for acute appendicitis of our institution Normal appendix is visible compressible tubular structure with a blind end without wall thickening, localized tenderness or other periappendiceal inflammatory changes.

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Results

Definite diagnosis

Among 115 patients, 34 patients were diagnosed as acute appendicitis after US reevaluation. Twenty-seven patients confirmed acute appendicitis pathologically. In one case who did not undergo surgery despite US report was mild appendicitis, and the follow up CT after 1 week later show normal appendix. Six patients were pathologically confirmed as negative appendicitis and the pathologic reports were fecalith impaction (n=1), congestion (n=3), fecalith impaction with serosal congestion(n=1) and fecalith impaction with lymphoid hyperplasia and congestion(n=1). The other 81 patients who diagnosed as normal appendix or low possibility of appendicitis on US reevaluation successfully treated conservatively. Sixty-six patients were treated with antibiotics and the other 15 patients improved after observation.

CT reassessment result

Figure 2 shows the CT reassessment result of two reviewers and definite diagnosis of each group. Table 2 shows interobserver agreement and frequency of each CT findings and diagnose appendicitis. Appendiceal diameter, intraluminal air in the appendix, other inflammatory lesions, and mesenteric lymphadenopathy demonstrated good interobserver agreement. Appendiceal wall enhancement and periappendiceal fat infiltration show poor interobserver agreement. Interobserver agreement of diagnosing appendicitis was moderate.
Fig. 2: CT reassessment result of two reviewers.

References: Radiology, Daejin medical center, Bundang Jesaeng hospital - Seongnam-si/KR

Table 2. Frequency of individual CT findings, diagnosis of acute appendicitis and interobserver agreement.

<table>
<thead>
<tr>
<th></th>
<th>Reviewer 1</th>
<th>Reviewer 2</th>
<th>Interobserver agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendiceal diameter</td>
<td>6.4mm (SD:1.2mm)</td>
<td>7.2mm (SD:1.3mm)</td>
<td>0.704 (0.5725 ~ 0.7956)</td>
</tr>
<tr>
<td>Appendiceal wall enhancement</td>
<td>63 (54.8%)</td>
<td>14 (12.2%)</td>
<td>0.076 (-0.0323 ~ 0.183)</td>
</tr>
<tr>
<td>Appendiceal wall thickening</td>
<td>64 (55.7%)</td>
<td>61 (53.0%)</td>
<td>0.317 (0.143 ~ 0.491)</td>
</tr>
<tr>
<td>Intraluminal air in appendix</td>
<td>54 (47.0%)</td>
<td>56 (48.7%)</td>
<td>0.686 (0.554 ~ 0.819)</td>
</tr>
<tr>
<td>Periappendiceal fat infiltration</td>
<td>24 (20.9%)</td>
<td>30 (26.1%)</td>
<td>0.180 (-0.0161 ~ 0.377)</td>
</tr>
<tr>
<td>Cecal apical change</td>
<td>24 (20.9%)</td>
<td>26 (22.6%)</td>
<td>0.540 (0.353 ~ 0.727)</td>
</tr>
<tr>
<td>Mesenteric lymphadenopathy</td>
<td>35 (30.4%)</td>
<td>35 (30.4%)</td>
<td>0.630 (0.475 ~ 0.785)</td>
</tr>
<tr>
<td>Diagnose acute appendicitis</td>
<td>25 (21.7%)</td>
<td>31 (27.0%)</td>
<td>0.436 (0.247 ~ 0.624)</td>
</tr>
</tbody>
</table>

Note - SD : standard deviation
Table 2: Table 2. Frequency of individual CT findings, diagnosis of acute appendicitis and interobserver agreement. Note - SD : standard deviation

References: Radiology, Daejin medical center, Bundang Jeaeng hospital - Seongnam-si/KR

Table 3 shows the alternative diagnosis at CT reassessment of two reviewers. Enterocolitis and pelvic inflammation disease were most common alternative diagnosis.

Table 3. The alternative diagnosis at CT reassessment.

<table>
<thead>
<tr>
<th></th>
<th>Reviewer 1</th>
<th>Reviewer 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLA</td>
<td>6 (10.3%)</td>
<td>6 (10.0%)</td>
</tr>
<tr>
<td>Enterocolitis</td>
<td>32 (55.1%)</td>
<td>21 (35.0%)</td>
</tr>
<tr>
<td>PID</td>
<td>12 (20.7%)</td>
<td>21 (35.0%)</td>
</tr>
<tr>
<td>Diverticulitis</td>
<td>6 (10.3%)</td>
<td>9 (15.5%)</td>
</tr>
<tr>
<td>APN</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Epiploic appendagitis</td>
<td>1 (1.7%)</td>
<td>0</td>
</tr>
<tr>
<td>Omental infarction</td>
<td>0</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Salpingitis</td>
<td>0</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>58</td>
<td>60</td>
</tr>
</tbody>
</table>

Table 3: Table 3. The alternative diagnosis at CT reassessment.

References: Radiology, Daejin medical center, Bundang Jeaeng hospital - Seongnam-si/KR

Diagnostic performances of CT reassessment and US reevaluation

The diagnostic performance of each reviewers CT reassessment and US reevaluation for acute appendicitis is summarized in Table 4. The sensitivity and specificity of two reviewers' CT reassessment were 51.9%, 87.5% in reviewer 1 and 66.7%, 85.2% in reviewer 2, respectively. It was slightly lower than previously reported rate [8]. The sensitivity and specificity of US reevaluation was higher than CT reassessment, which were 100% and 92.1%, respectively.
<table>
<thead>
<tr>
<th>Outcome Results</th>
<th>CT (Reviewer 1)</th>
<th>CT (Reviewer 2)</th>
<th>CT + US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>25 (21.7%)</td>
<td>31 (27.0%)</td>
<td>34 (29.6%)</td>
</tr>
<tr>
<td>Negative</td>
<td>90 (78.3%)</td>
<td>84 (73.0%)</td>
<td>81 (70.4%)</td>
</tr>
<tr>
<td>True-positive</td>
<td>14 (12.1%)</td>
<td>18 (15.7%)</td>
<td>27 (23.5%)</td>
</tr>
<tr>
<td>True-negative</td>
<td>77 (66.9%)</td>
<td>75 (65.2%)</td>
<td>81 (70.4%)</td>
</tr>
<tr>
<td>False-positive</td>
<td>11 (9.6%)</td>
<td>13 (11.3%)</td>
<td>7 (6.1%)</td>
</tr>
<tr>
<td>False-negative</td>
<td>13 (11.3%)</td>
<td>9 (7.8%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Performance</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>51.9 [31.9 ~ 71.3]</td>
<td>66.7 [46.0 ~ 83.5]</td>
<td>92.1 [84.3 ~ 96.7]</td>
<td>79.5 [61.9 ~ 91.5]</td>
<td>0.697 (p = 0.0002)</td>
</tr>
<tr>
<td></td>
<td>87.5 [78.7 ~ 93.6]</td>
<td>85.2 [76.1 ~ 91.9]</td>
<td>89.3 [80.6 ~ 95.0]</td>
<td>89.3 [80.6 ~ 95.0]</td>
<td>0.759 (p&lt;0.0001)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>95.6 [89.4 ~ 99.5]</td>
<td>95.6 [89.4 ~ 99.5]</td>
<td>0.960 (p&lt;0.0001)</td>
</tr>
</tbody>
</table>

Note — PPV = positive predictive value, NPV = negative predictive value.

Table 4: Table 4. Diagnostic performance of CT reassessment and CT plus US. Note
# PPV = positive predictive value, NPV = negative predictive value.

References: Radiology, Daejin medical center, Bundang Jesaeng hospital - Seongnam-si/KR

Figure 3 shows the comparison of ROC curves of two reviewers CT reassessment and US reevaluation. The differences between the areas under ROC curves were statistically significant different (P<0.0001).
Figure 3. Comparison of area under the ROC between CT reassessment and US reevaluation.

**Fig. 3:** Figure 3. Comparison of area under the ROC between CT reassessment and US reevaluation.

**References:** Radiology, Daejin medical center, Bundang Jesaeng hospital - Seongnam-si/KR

**Coexistent inflammation group**

Reviewer 1 categorized 62 patients and reviewer 2 categorized 56 patients as coexistent inflammation group. The diagnostic performance of CT reassessment and US reevaluation in coexistent inflammation group were on the *table 5*. US reevaluation shows higher diagnostic performance than CT reassessment.
Table 5. Diagnostic performance of CT reassessment and US reevaluation in coexistent inflammation group and no other inflammation group

<table>
<thead>
<tr>
<th></th>
<th>Coexistent inflammation</th>
<th>Appendicitis proper</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CT reassessment</td>
<td>US reevaluation</td>
</tr>
<tr>
<td>Reviewer 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>27.3 [6.0 - 61.0]</td>
<td>100 [71.5 − 100]</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>94.1 [83.8 − 98.8]</td>
<td>98.0 [89.6 − 100]</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>49.9 [11.8 − 88.1]</td>
<td>91.5 [59.5 − 99.8]</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>85.8 [73.7 − 93.7]</td>
<td>100 [92.9 − 100]</td>
</tr>
<tr>
<td>AUC</td>
<td>0.607 (p=0.1394)</td>
<td>0.990 (p&lt;0.0001)</td>
</tr>
<tr>
<td>Reviewer 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>14.3 [9.4 − 57.9]</td>
<td>100 [59.0 − 100]</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>98.0 [89.1 − 99.9]</td>
<td>98.0 [89.1 − 99.9]</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>58.5 [0.04 − 100]</td>
<td>87.7 [44.2 − 99.8]</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>88.9 [77.3 − 95.8]</td>
<td>100 [92.6 − 100]</td>
</tr>
<tr>
<td>AUC</td>
<td>0.561 (p=0.3961)</td>
<td>0.990 (p&lt;0.0001)</td>
</tr>
</tbody>
</table>

Note — PPV : positive predictive value, NPV : negative predictive value.

Table 5: Table 5. Diagnostic performance of CT reassessment and US reevaluation in coexistent inflammation group and no other inflammation group Note # PPV : positive predictive value, NPV : negative predictive value.

References: Radiology, Daejin medical center, Bundang Jesaeng hospital - Seongnam-si/KR

Obesity result based on CT

There was only one case (sagittal abdominal diameter on CT : 27.7 cm in 16 year-old boy) of the sagittal abdominal diameter greater than 25cm which indicated obesity. And there was no women patient with sagittal abdominal diameter greater than 25cm. The average of sagittal abdominal diameter was 18.2cm(range : 11.6 - 27.7cm).

Case 1.
**Fig. 4:** Figure 4. A 35-year-old men diagnosed as normal appendix on CT reassessment. (A, B) Contrast-enhanced CT images show appendiceal dilatation without other findings of acute appendicitis. (C) Greyscale US showing increased appendix diameter (7.6 mm) and mild appendiceal wall thickening. (D) Color Doppler US showing mild mural hyperemia. The US diagnosis was acute appendicitis. The patient underwent appendectomy, and acute appendicitis was histopathologically confirmed.

**References:** Radiology, Daejin medical center, Bundang Jesaeng hospital - Seongnam-si/KR

**Case 2.**
**Fig. 5:** Figure 5. A 36-year-old women diagnosed as PID with secondary periappendicitis on CT reassessment. (A-C) Contrast-enhanced CT images show appendiceal dilatation with diffuse fat infiltration in pelvic peritoneum. (D) Greyscale US showing increased appendix diameter (6.2 mm) and mild appendiceal wall thickening. (E) Color Doppler US showing mild mural hyperemia. The US diagnosis was acute appendicitis. The patient underwent appendectomy, and acute appendicitis was histopathologically confirmed.

**References:** Radiology, Daejin medical center, Bundang Jesaeng hospital - Seongnam-si/KR

**Case 3.**
**Fig. 6:** Figure 6. A 13-year-old boy diagnosed as normal appendix and mesenteric lymphadenopathy on CT reassessment. (A, B) Contrast-enhanced CT images show appendiceal dilatation without other findings of acute appendicitis. (C, D) Greyscale US showing increased appendix diameter (6.3 mm diameter) and mild appendiceal wall thickening. The US diagnosis was acute appendicitis. The pathological report noted fecalith impaction with serosal congestion.

**References:** Radiology, Daejin medical center, Bundang Jesaeng hospital - Seongnam-si/KR
**Figure 2.** CT reassessment result of two reviewers.

**Observer 1**
- Coexistent inflammation (n=62)
  - Secondary periappendicitis (n=56)
  - Acute appendicitis (n=6)
- Appendicitis proper (n=53)
  - Normal appendix (n=34)
  - Acute appendicitis (n=19)

**Observer 2**
- Coexistent inflammation (n=56)
  - Secondary periappendicitis (n=54)
  - Acute appendicitis (n=2)
- Appendicitis proper (n=59)
  - Normal appendix (n=30)
  - Acute appendicitis (n=29)

**Definite diagnosis**
- Not appendicitis (n=48)
- Acute appendicitis (n=8)
- Not appendicitis (n=3)
- Acute appendicitis (n=3)
- Not appendicitis (n=29)
- Acute appendicitis (n=5)
- Not appendicitis (n=8)
- Acute appendicitis (n=11)
- Not appendicitis (n=48)
- Acute appendicitis (n=6)
- Not appendicitis (n=1)
- Acute appendicitis (n=1)
- Not appendicitis (n=27)
- Acute appendicitis (n=3)
- Not appendicitis (n=12)
- Acute appendicitis (n=17)

**Fig. 2:** Figure 2. CT reassessment result of two reviewers.

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Table 2. Frequency of individual CT findings, diagnosis of acute appendicitis and interobserver agreement.

<table>
<thead>
<tr>
<th>Findings</th>
<th>Reviewer 1</th>
<th>Reviewer 2</th>
<th>Interobserver agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendiceal diameter</td>
<td>6.4mm (SD: 1.2mm)</td>
<td>7.2mm (SD: 1.3mm)</td>
<td>0.704 (0.5725 – 0.7956)</td>
</tr>
<tr>
<td>Appendiceal wall enhancement</td>
<td>63 (54.8%)</td>
<td>14 (12.2%)</td>
<td>0.076 (-0.0323 – 0.183)</td>
</tr>
<tr>
<td>Appendiceal wall thickening</td>
<td>64 (55.7%)</td>
<td>61 (53.0%)</td>
<td>0.317 (0.143 – 0.491)</td>
</tr>
<tr>
<td>Intraluminal air in appendix</td>
<td>54 (47.0%)</td>
<td>56 (48.7%)</td>
<td>0.686 (0.554 – 0.819)</td>
</tr>
<tr>
<td>Periappendiceal fat infiltration</td>
<td>24 (20.9%)</td>
<td>30 (26.1%)</td>
<td>0.180 (-0.0161 – 0.377)</td>
</tr>
<tr>
<td>Cecal apical change</td>
<td>24 (20.9%)</td>
<td>26 (22.6%)</td>
<td>0.540 (0.353 – 0.727)</td>
</tr>
<tr>
<td>Mesentere lymphadenopathy</td>
<td>35 (30.4%)</td>
<td>35 (30.4%)</td>
<td>0.630 (0.475 – 0.785)</td>
</tr>
<tr>
<td>Diagnose acute appendicitis</td>
<td>25 (21.7%)</td>
<td>31 (27.0%)</td>
<td>0.436 (0.247 – 0.624)</td>
</tr>
</tbody>
</table>

Note - SD : standard deviation

Table 2: Table 2. Frequency of individual CT findings, diagnosis of acute appendicitis and interobserver agreement. Note - SD : standard deviation

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Table 3. The alternative diagnosis at CT reassessment.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Reviewer 1</th>
<th>Reviewer 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>MLA</td>
<td>6 (10.3%)</td>
<td>6 (10.0%)</td>
</tr>
<tr>
<td>Enterocolitis</td>
<td>32 (55.1%)</td>
<td>21 (35.0%)</td>
</tr>
<tr>
<td>PID</td>
<td>12 (20.7%)</td>
<td>21 (35.0%)</td>
</tr>
<tr>
<td>Diverticulitis</td>
<td>6 (10.3%)</td>
<td>9 (15.5%)</td>
</tr>
<tr>
<td>APN</td>
<td>1 (1.7%)</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Epiploic appendagitis</td>
<td>1 (1.7%)</td>
<td>0</td>
</tr>
<tr>
<td>Omental infarction</td>
<td>0</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Salpingitis</td>
<td>0</td>
<td>1 (1.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>58</td>
<td>60</td>
</tr>
</tbody>
</table>

Table 3: Table 3. The alternative diagnosis at CT reassessment.

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Table 4. Diagnostic performance of CT reassessment and CT plus US.

<table>
<thead>
<tr>
<th>Outcome Results</th>
<th>CT (Reviewer 1)</th>
<th>CT (Reviewer 2)</th>
<th>CT + US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>25 (21.7%)</td>
<td>31 (27.0%)</td>
<td>34 (29.6%)</td>
</tr>
<tr>
<td>Negative</td>
<td>90 (78.3%)</td>
<td>84 (73.0%)</td>
<td>81 (70.4%)</td>
</tr>
<tr>
<td>True-positive</td>
<td>14 (12.1%)</td>
<td>18 (15.7%)</td>
<td>27 (23.5%)</td>
</tr>
<tr>
<td>True-negative</td>
<td>77 (66.9%)</td>
<td>75 (65.2%)</td>
<td>81 (70.4%)</td>
</tr>
<tr>
<td>False-positive</td>
<td>11 (9.6%)</td>
<td>13 (11.3%)</td>
<td>7 (6.1%)</td>
</tr>
<tr>
<td>False-negative</td>
<td>13 (11.3%)</td>
<td>9 (7.8%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Performance

<table>
<thead>
<tr>
<th></th>
<th>CT (Reviewer 1)</th>
<th>CT (Reviewer 2)</th>
<th>CT + US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>51.9 [31.9 - 71.3]</td>
<td>66.7 [46.0 - 83.5]</td>
<td>100 [87.2 - 100]</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>87.5 [78.7 - 93.6]</td>
<td>85.2 [76.1 - 91.9]</td>
<td>92.1 [84.3 - 96.7]</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>56.1 [35.0 - 75.6]</td>
<td>58.1 [39.1 - 75.5]</td>
<td>79.5 [61.9 - 91.5]</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>85.6 [76.5 - 92.1]</td>
<td>89.3 [80.6 - 95.0]</td>
<td>100 [95.6 - 100]</td>
</tr>
<tr>
<td>AUC</td>
<td>0.697 (p=0.0002)</td>
<td>0.759 (p&lt;0.0001)</td>
<td>0.960 (p&lt;0.0001)</td>
</tr>
</tbody>
</table>

Note — PPV = positive predictive value, NPV = negative predictive value.

Table 5. Diagnostic performance of CT reassessment and US reevaluation in coexistent inflammation group and no other inflammation group

<table>
<thead>
<tr>
<th>Coexistent inflammation</th>
<th>Appendicitis proper</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT reassessment</td>
<td>US reevaluation</td>
</tr>
<tr>
<td>Reviewer 1</td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>27.3 [6.0 - 61.0]</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>94.1 [83.8 - 98.8]</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>49.9 [11.8 - 88.1]</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>85.8 [73.7 - 93.7]</td>
</tr>
<tr>
<td>AUC</td>
<td>0.607 (p=0.1394)</td>
</tr>
<tr>
<td>Reviewer 2</td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>14.3 [9.4 - 57.9]</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>98.0 [89.1 - 99.9]</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>50.5 [0.4 - 100]</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>88.9 [77.3 - 95.8]</td>
</tr>
<tr>
<td>AUC</td>
<td>0.561 (p=0.3961)</td>
</tr>
</tbody>
</table>

Note — PPV : positive predictive value, NPV : negative predictive value.
Table 5: Table 5. Diagnostic performance of CT reassessment and US reevaluation in coexistent inflammation group and no other inflammation group Note # PPV : positive predictive value, NPV : negative predictive value.

Figure 3. Comparison of area under the ROC between CT reassessment and US reevaluation.

Fig. 3: Figure 3. Comparison of area under the ROC between CT reassessment and US reevaluation.

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**Fig. 4:** Figure 4. A 35-year-old men diagnosed as normal appendix on CT reassessment. (A, B) Contrast-enhanced CT images show appendiceal dilatation without other findings of acute appendicitis. (C) Greyscale US showing increased appendix diameter (7.6 mm) and mild appendiceal wall thickening. (D) Color Doppler US showing mild mural hyperemia. The US diagnosis was acute appendicitis. The patient underwent appendectomy, and acute appendicitis was histopathologically confirmed.

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**Fig. 5:** Figure 5. A 36-year-old women diagnosed as PID with secondary periappendicitis on CT reassessment. (A-C) Contrast-enhanced CT images show appendiceal dilatation with diffuse fat infiltration in pelvic peritoneum. (D) Greyscale US showing increased appendix diameter (6.2 mm) and mild appendiceal wall thickening. (E) Color Doppler US showing mild mural hyperemia. The US diagnosis was acute appendicitis. The patient underwent appendectomy, and acute appendicitis was histopathologically confirmed.

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Fig. 6: Figure 6. A 13-year-old boy diagnosed as normal appendix and mesenteric lymphadenopathy on CT reassessment. (A, B) Contrast-enhanced CT images show appendiceal dilatation without other findings of acute appendicitis. (C, D) Greyscale US showing increased appendix diameter (6.3 mm diameter) and mild appendiceal wall thickening. The US diagnosis was acute appendicitis. The pathological report noted fecalith impaction with serosal congestion.

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Conclusion

When patient have equivocal CT findings of appendicitis, US reevaluation shows better diagnostic performance than CT reassessment. The sensitivity, specificity, PPV, NPV, accuracy and AUC of US reevaluation were higher than those of CT reassessment. We think that US reevaluation can increased diagnostic accuracy and prevent delayed complicated appendicitis. Also previous study report that US reevaluation can decrease negative appendectomy rate [9]. The US has many advantages. The graded compression ultrasound technique was helpful for distinguishing acute appendicitis from dilatation due to fluid or feces. The spatial resolution of bowel wall in high-frequency ultrasound image is greater than that of CT. In addition, ultrasound probe-induced tenderness over the appendix was also an important finding to improve the accuracy of diagnosis of acute appendicitis.

We also compared the diagnostic performance in coexistent inflammation group and appendicitis proper group. The sensitivity and specificity of US reevaluation (reviewer 1: 100% and 98.0%, reviewer 2: 100% and 98.0%, respectively) were also higher than CT reassessment (reviewer 1: 27.3% and 94.1%, reviewer 2: 14.3% and 98.0%, respectively). Especially, the sensitivity of US reevaluation was far higher than CT reassessment when coexistent with other inflammation. Presence of coexistent inflammatory lesion indicate negative appendicitis [8], but primary appendicitis may coexist with other inflammatory lesions [12]. Although the CT findings of secondary periappendicitis was reported that diffuse or focal wall thickening without severe distension [12], it is difficult to differentiate between primary appendicitis and secondary periappendicitis on CT. For these reasons, CT specificity was high enough but CT sensitivity was low in case of coexistent other inflammatory lesion. We think US may have complement to the CT's low sensitivity because real-time probe-induced tenderness provide information of most tender point is over the appendix or other inflammatory lesion. Also, evaluation of compressibility of appendix may help to differentiate primary appendicitis from secondary periappendicitis. Patient-related factors such as age, body habitus and location of appendix are important influencing factors of US. Operator dependence and lack of reproducibility are also major limitation of US.

There was no false negative case on US reevaluation. But there were seven false positive cases on US re-evaluation. All of these cases show appendiceal diameter less than 8mm on both of initial CT and US. And there were intraluminal air except one case on initial CT. All of these cases show normal proximal appendix and mild distention only at distal portion of appendix on US reevaluation. But there were probe-induced tenderness and some of cases show appendiceal wall thickening. The evaluation of the appendix tip is challenging part on US exam, because in most patients the appendix tip is located in the pelvis. Paying close attention to the evaluation of the appendix tip, can improve diagnostic accuracy. And correlate with clinical information and laboratory data also needed.
Among each CT findings for diagnosing acute appendicitis, periappendiceal fat infiltration and appendiceal wall enhancement show poor interobserver agreement. As the increased use of CT in patients with acute appendicitis, patients undergo CT examination earlier. Consequently, periappendiceal fat stranding is found less frequently [13]. If fat stranding was positive, initial CT report might not be equivocal, as Kim et. al mentioned before [8]. Additionally, fat infiltration can occur with many other inflammatory disorders, so its specificity was relatively low. We decided wall enhancement subjectively compared with other normal bowel loops. But Kim et al. [8] analyzed appendiceal wall enhancement using maximal attenuation in a region of interest, and it was statistically significant finding. In daily practice, it is hard to evaluate wall enhancement quantitatively, but in equivocal cases it may help accurate diagnosis. And this quantitative analysis of wall enhancement could improve interobserver agreement.

The mean appendiceal diameter were 6.4mm (±1.2) in reviewer 1 and 7.2mm (±1.34) in reviewer 2. And there was no significant different between appendicitis group and non-appendicitis group. Increased appendiceal diameter was most common finding in patients with equivocal CT findings of appendicitis. [9] US may help for differentiate between feces and obstructive fluid with graded compression technique. Kim et. al [12] report that the pathognomonic CT #ndings of secondary periappendicitis are diffuse or focal wall thickening without severe distension or target-like enhancement. But our result shows no statistically significant of appendiceal wall thickening nor appendiceal diameter difference between coexistent inflammation group and appendicitis proper group. We think it was because we included only equivocal cases.

**Limitations**

There are important limitations of this study that should be addressed. Firstly, this study is a retrospective study. There was a selection bias because we excluded the patients who have equivocal CT findings of appendicitis without US reevaluation. Some of these patients with clinically highly suspected appendicitis underwent surgery without US. The others with clinically low suspicion of appendicitis were observed without US. Secondly, the final diagnosis of patients who did not undergo surgery was made on the basis of chart review. Spontaneously resolving appendicitis could be included in these group. Thirdly, we didn't evaluate correlation between US accuracy and patient obesity because there was only one obese patient who has sagittal abdominal diameter over 25cm. The accuracy of US is lower in obese patients than non-obese patient. But if the patient has sufficient intraabdominal fat, the CT diagnostic accuracy will be higher and the rate of equivocal CT finding may also lower [14]. Fourthly, the time interval between performance of CT and US varied. But, we excluded patients with the interval US between CT over 1 week, 86.1%(99/115) of patients underwent US within 24 hours after the CT. Fifthly, the study period was relatively short, and the study population was also small. A further large, prospective randomized controlled study for equivocal case of appendicitis is required.
to confirm our result. Lastly, we used two CT systems (16-MDCT and 64-MDCT) but did not divide these subgroups because most of the CT examinations were performed in the emergency room with 16-MDCT and previous studies reported similar diagnostic performances of CT for diagnosing acute appendicitis with using both 16- and 64-MDCT.

**Conclusion**

In conclusion, for patients with equivocal CT findings of acute appendicitis, US re-evaluation have a better diagnostic performance than CT reassessment. US is also helpful for differentiate secondary periappendicitis and acute appendicitis.
Personal information

Hyuk Jung Kim
Department of Radiology, Daejin Medical Center Bundang Jesaeng General Hospital, Sungnam-si, Republic of Korea.
Email: hyukjungk@naver.com

Ji Ye Sim
Department of Radiology, Daejin Medical Center Bundang Jesaeng General Hospital, Sungnam-si, Republic of Korea.

Jae Woo Yeon
Department of Radiology, Daejin Medical Center Bundang Jesaeng General Hospital, Sungnam-si, Republic of Korea.

Suk Ki Jang, M.D
Department of Radiology, Daejin Medical Center Bundang Jesaeng General Hospital, Sungnam-si, Republic of Korea.
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