INTRODUCTION

In an adult population, CT is a primary imaging modality for the evaluation of patients with suspected appendicitis (1, 2). Multidetector CT (MDCT) with thin-section (section thickness, ≤ 5 mm) imaging has proven to be a highly effective and accurate means of diagnosing acute appendicitis, with reported sensitivities of 90–100%, specificities of 91–99%, and accuracies of 94–98% (2, 3). Typical CT findings in acute appendicitis include enlargement of the appendix (outer diameter > 6 mm), appendiceal wall thickening (≥ 3 mm), appendiceal wall hyperenhancement, and periappendiceal fat stranding (4-7). Periappendiceal abscess usually indicates perforated appendicitis and is associated with extraluminal air, ileocecal inflammation, and localized peritonitis in the right lower quadrant (8). However, challenges still remain in the evaluation of appendicitis. Characteristic
CT findings are mostly observed in advanced stages of inflammation and may not be found in patients having early-stage appendicitis (2, 4, 9). Appendiceal enlargement determined by the maximum outer-to-outer diameter, one of the primary criteria for diagnosing acute appendicitis, has high sensitivity but low specificity (10). Also, the diameters of the normal and inflamed appendices vary (11, 12) and there is yet no consensus regarding the single cutoff value to define abnormal appendiceal enlargement on CT. Furthermore, controversies have persisted regarding the presence of air within the appendix, which have been described as having contradictory implications during the diagnosis. Several investigators described that air in the appendix was indicative of a normal appendix (13) or helped exclude acute appendicitis (10). Other authors have described that intra-appendiceal air was a marker of gangrenous change or perforation in the setting of acute appendicitis (14). During our daily interpretation of CT imaging, we have more frequently observed air within a normal appendix than within an inflamed appendix. To our knowledge, the diagnostic implications of intra-appendiceal air at CT in the evaluation of acute appendicitis, have not been clearly established till date. Therefore, the purpose of the present study was to investigate the significance of intra-appendiceal air at CT, in the evaluation of patients with suspected acute appendicitis.

MATERIALS AND METHODS

This retrospective study was approved by the Institutional Review Board of our hospital, and the requirement for informed patient consent was waived.

Patients

From March 2010 to September 2010, we searched the database of our radiology department and collected patients who presented to the emergency department with acute abdominal pain and subsequently had CT scans of the abdomen and pelvis. Eligibility criteria included clinical suspicion of acute appendicitis and visualization of the appendix on intravenous (IV) contrast material-enhanced CT. We initially identified CT scans of 472 patients. Of the patients, 6 were transferred to another institution for further care, and 8 were lost to clinical follow-up. After an exclusion of the 14 patients, the remaining 458 patients (216 men and 242 women; mean age, 42 years; age range, 18–91 years) constituted the final study population.

Acute appendicitis was surgically confirmed in 102 patients. The range of time interval between CT and surgery was from the day of CT examination to 6 days (mean, a half day). Of the 102 patients, 72 underwent surgery on the day of CT scan and 27 on the following day in less than 24 hours. In 3 patients, surgery was performed 2, 4, and 6 days after the CT, respectively. The reasons for the time gap in the 3 patients were delay of hospital arrangement in 2 patients (2 and 4 days later) and for preoperative staging of cecal cancer, which was the underlying cause of acute appendicitis in 1 patient (6 days later). The remaining 356 patients were considered negative for appendicitis by means of surgical pathology in 5 patients, and via alternative diagnoses in 351 patients (133 right urinary stones, 124 no specific diagnoses, 29 non-appendiceal gastrointestinal inflammation, 27 gynecologic diseases, 11 intestinal perforation, 9 cecal diverticulitis, 6 acute cholecystitis, 4 small bowel obstruction, 4 acute pyelonephritis, 2 acute pancreatitis, 1 liver abscess, and 1 spontaneous hemorrhage of the rectus muscle). The alternative diagnoses were made by means of all available clinical, laboratory, and imaging data, including medical chart review, results of clinical follow-up, and typical imaging findings.

CT Technique

All CT examinations were performed with a 64-row multidetector scanner (Somatom Sensation 64; Siemens Medical Solutions, Forchheim, Germany). Patients were placed in the supine position and scanned from the diaphragm to the symphysis pubis. All patients underwent CT examinations following a single identical protocol that had been prepared for patients referred from the emergency department having a complaint of acute abdominal pain. Non-contrast images were routinely incorporated in the given protocol in order to make an alternative diagnosis of urinary stone. The scanning parameters were 120 kVp, reference effective 160 mAs with automatic dose modulation (CARE Dose4D, Siemens Healthcare), detector collimation of 64 x 0.6 mm, a rotation time of 0.5 seconds, and a pitch of 1.2. CT images were reconstructed with 5-mm slice thickness in the transverse plane and 4-mm in the coronal plane, and with no overlap. In all the patients, a single-phase contrast-enhanced scan was performed and was acquired 65 seconds after starting the administration of IV contrast agent. Using a power injector (Dual Shot; Nemoto-kyorindo, Tokyo, Japan), 100–120 mL (2 mL/kg of body weight) of nonionic iodinated contrast agent (iohexol,
Omnipaque 350; Nycomed Amersham, Princeton, NJ, USA) was injected into the antecubital vein through an 18 gauge needle, at a rate of 3 mL/sec, followed by a 20 mL saline flush. Oral or rectal contrast material was not administered.

Image Analysis
CT images were retrospectively and independently reviewed by two radiologists (with 16 and 13 years of experience in abdominal CT interpretation, respectively) who were blinded to the original CT reports and final patient outcomes. The images were evaluated with a soft-tissue window setting (window width, 400 Hounsfield unit [HU]; window level, 40 HU; and with some minor modifications at the discretion of the readers) on a picture archiving and communication system workstation (PiView; Infinitt Healthcare, Seoul, Korea). Both transverse and coronal reformatted images were analyzed together in the cine or stack mode. Additional review with multiplanar reconstruction or thinner-section images was not used.

On each CT scan, the readers evaluated the presence or absence of air within the appendix. When intraluminal air was present, the amount of air was classified as one of the three categories: less than one third of the observed appendiceal length, between one third and two thirds, or greater than two thirds. The appearance of intraluminal air was divided into localized air column, scattered air bubbles and columns, stool-like, punctiform, and air-fluid level.

The readers determined the overall likelihood of acute appendicitis according to the CT findings indicative of appendicitis, using a 5-point Likert scale: 1, normal appendix; 2, probably not appendicitis; 3, indeterminate; 4, probably appendicitis; and 5, definitely appendicitis (15). CT findings indicative of appendicitis included enlargement of the appendix (measured by outer-to-outer diameter > 6 mm), appendiceal wall thickening (≥ 3 mm), appendiceal wall hyperenhancement, and periappendiceal fat stranding, fluid, or abscess according to the established criteria for diagnosing acute appendicitis (4-7). During the aforementioned image interpretation, the presence or absence of intra-appendiceal air was considered neither suggestive of, nor excluding acute appendicitis.

To investigate if intra-appendiceal air may influence the diagnosis of acute appendicitis (particularly in interpreting the indeterminate cases [category 3]), performance of CT diagnosis was evaluated in two reading strategies. In the first reading strategy (strategy 1), cases with rating scores 5, 4, and 3 were considered as positive for appendicitis, and the remaining were classified as negative. In the second reading strategy (strategy 2), any indeterminate case (cases with a diagnostic rating score of 3) that showed intra-appendiceal air were considered negative for appendicitis.

Statistical Analysis
The prevalence, amount, and appearance of intra-appendiceal air were compared between patients with and without appendicitis, and the significant differences were determined using the Fisher’s exact test. A separate sub-analysis was performed for the indeterminate cases, and the prevalence of air was compared between cases with and without appendicitis.

Performances of the two reading strategies were estimated and were compared using receiver operating characteristic (ROC) analysis with pairwise comparison of the ROC curves. Significant differences in statistical measures of the performance were determined between the two strategies by observing the overlap or separation of confidence intervals (CIs).

Inter-reader agreement was calculated using the unweighted kappa statistic for evaluating the prevalence and appearance of intra-appendiceal air. Agreement between the readers for assessing the amount of air was calculated using the weighted kappa with linear weights. For the amount and appearance of intra-appendiceal air, cases were only included in the analysis if air was observed by both readers. Inter-reader agreement for each reading strategy was estimated using the weighted kappa with linear weights. The agreement was determined using the following scale: 0 to 0.2, slight agreement; 0.21 to 0.4, fair agreement; 0.41 to 0.6, moderate agreement; 0.61 to 0.8, substantial agreement; and 0.81 to 1, almost perfect agreement (16, 17). A two-tailed p value less than 0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics for Windows (version 21.0; IBM Corp., Armonk, NY, USA) and MedCalc (version 11.5; MedCalc Software, Mariakerke, Belgium).

RESULTS
Prevalence, Amount, and Appearance of Intra-Appendiceal Air
The prevalence of intra-appendiceal air was significantly higher in patients without appendicitis than in patients with appendicitis, as evaluated by both the readers: reader 1 (289/356 [81.2%] vs. 14/102 [13.7%], p < 0.001) and
The amount and appearance of intra-appendiceal air were significantly different between patients with and without appendicitis (Table 1). For reader 1, the proportion of cases with appendicitis which showed intraluminal air less than one third of the appendix was significantly higher than that of cases without appendicitis (13/14 [92.9%] vs. 171/289 [59.2%], \( p = 0.011 \)). Proportions of the amount less than one third were significantly different for reader 2, between cases with appendicitis (13/13, 100%) and without appendicitis (162/274 [59.1%]) \( ( p = 0.002 \)). In the normal appendices, the appearance of scattered air bubbles and columns were predominantly seen, compared with the inflamed appendices for both reader 1 (213/289 [73.7%] vs. 4/14 [28.6%], \( p = 0.001 \)) and reader 2 (202/274 [73.7%] vs. 2/13 [15.4%], \( p < 0.001 \)) (Fig. 1). Stool-like appearance and an air-fluid level were more frequently observed in patients with appendicitis compared with patients without appendicitis for both reader 1 (2/14 [14.3%] vs. 5/289 [1.7%], \( p = 0.037 \); 1/14 [7.1%] vs. 0/289 [0%], \( p = 0.046 \)) and reader 2 (1/13 [7.7%] vs. 0/274 [0%], \( p = 0.045 \); 8/13 [61.5%] vs. 1/274 [0.4%], \( p < 0.001 \)) (Fig. 2).

**Table 1. Amount and Appearance of Intra-Appendiceal Air in Patients with and without Acute Appendicitis**

| Amount of intra-appendiceal air | Appendicitis | No Appendicitis | \( P \)  |
|---------------------------------|--------------|-----------------|--------|
| **Reader 1**                    |              |                 |        |
| < 1/3                           | 13/14 (92.9)| 171/289 (59.2) | 0.011* |
| 1/3–2/3                         | 1/14 (7.1)  | 73/289 (25.3)  | 0.201  |
| > 2/3                           | 0/14 (0)    | 45/289 (15.6)  | 0.238  |
| **Reader 2**                    |              |                 |        |
| < 1/3                           | 13/13 (100) | 162/274 (59.1) | 0.002* |
| 1/3–2/3                         | 0/13 (0)    | 53/274 (19.3)  | 0.135  |
| > 2/3                           | 0/13 (0)    | 59/274 (21.5)  | 0.077  |

| Appearance of intra-appendiceal air | Appendicitis | No Appendicitis | \( P \)  |
|------------------------------------|--------------|-----------------|--------|
| **Reader 1**                       |              |                 |        |
| Localized                          | 4/14 (28.6)  | 20/289 (6.9)    | 0.018  |
| Scattered                          | 4/14 (28.6)  | 213/289 (73.7)  | 0.001  |
| Stool-like                         | 2/14 (14.3)  | 5/289 (1.7)     | 0.037  |
| Punctiform                         | 3/14 (21.4)  | 51/289 (17.6)   | 0.721  |
| Air-fluid level                    | 1/14 (7.1)   | 0/289 (0)       | 0.046  |
| **Reader 2**                       |              |                 |        |
| Localized                          | 1/13 (7.7)   | 15/274 (5.5)    | 0.533  |
| Scattered                          | 2/13 (15.4)  | 202/274 (73.7)  | < 0.001 |
| Stool-like                         | 1/13 (7.7)   | 0/274 (0)       | 0.045  |
| Punctiform                         | 1/13 (7.7)   | 56/274 (20.4)   | 0.001  |
| Air-fluid level                    | 8/13 (61.5)  | 1/274 (0.4)     | < 0.001 |

Data are numerators and denominators with percentages in parentheses. *Difference in proportion of “< 1/3” vs. “1/3–2/3” combined with “> 2/3” between patients with and without appendicitis.
the two reading strategies for the evaluation of acute appendicitis. Similar trends in performance were shown for the two readers. For both readers, sensitivities and negative predictive values (NPVs) were slightly decreased in strategy 2 compared with strategy 1, but with no statistical significance (i.e., the CIs largely overlapped). Similarly, specificities and positive predictive values (PPVs) were slightly higher with reading strategy 2 compared with those of strategy 1, with a large overlap in their CIs. Overall, use of reading strategy 2, as compared with strategy 1, caused a marginal improvement in the value of area under the ROC curve (AUC) for reader 1: 0.985 (95% CI, 0.969–0.994) for strategy 2 vs. 0.971 (95% CI, 0.951–0.985) for strategy 1, \( p = 0.056 \). However, there was a small significant increase in AUC for reader 2: 0.986 (95% CI, 0.970–0.995) for strategy 2 vs. 0.969 (95% CI, 0.949–0.983) for strategy 1, \( p = 0.042 \).

**Inter-Reader Agreement**

Inter-reader agreement was almost perfect for assessing the presence or absence of intra-appendiceal air (kappa =

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**Fig. 1.** 53-year-old female patient presented to emergency department with right-sided abdominal pain.

A, B. Hemorrhagic cyst was found in right adnexa (not shown). Contrast-enhanced transverse (A) and coronal (B) CT images demonstrate normal appendix (arrows in A and B) containing intraluminal air, with appearance of scattered air bubbles and columns.

**Fig. 2.** 49-year-old male patient diagnosed as acute appendicitis by surgery.

A, B. Contrast-enhanced transverse (A) and coronal (B) CT images show characteristic findings of acute appendicitis, including appendiceal enlargement, appendiceal wall thickening and enhancement, and periappendiceal fat stranding. Appendix (arrows in A and B) is abnormally enlarged and dilated with air-fluid level in lumen (arrowhead in A).
In 285 patients with intra-appendiceal air observed by both readers, substantial agreements were seen for evaluating the amount of air (weighted kappa = 0.746 [95% CI, 0.684–0.809]) and the appearance of air (kappa = 0.624, p < 0.001). Agreements for reading strategies for the CT diagnosis of appendicitis were almost perfect with weighted kappa values of 0.971 (95% CI, 0.961–0.981) for reading strategy 1 and 0.902 (95% CI, 0.874–0.929) for reading strategy 2.

DISCUSSION

In the results of our study, air was more frequently seen within the normal appendix (79.8%, mean of the two observations) than within the inflamed appendix (13.2%), with a significant difference. According to literature, the appendix normally contains air (2, 11, 18). Normal intra-appendiceal air is thought to be a regurgitation from the cecum, and subsequent expelling of air to the colon may occur. When acute appendicitis develops with luminal obstruction, the retained intra-appendiceal air is gradually absorbed (10), and ultimately disappears. Therefore, we think air is usually present within the normal appendix. However, the absence of air cannot be a specific marker for appendicitis, due to the substantial prevalence of air within the inflamed appendix.

Intra-appendiceal air has been a longstanding controversy in the diagnosis of appendicitis (14). Earlier investigators reported that air is a sign of appendicitis (19, 20), whereas some reports provided usefulness of the presence of intraluminal air as an indicator of the normal appendix or a sign of excluding appendicitis (10, 13). Recently, Azok et al. (14) reported that intraluminal air in the setting of acute appendicitis is a marker of perforated or necroticappendicitis. Their study demonstrated intraluminal air had a significant association with perforation or necrosis. Thus, an apparent contradiction is seen between their and our results. However, we think the two results should be considered to have different implications in acute appendicitis, as Azok et al. described in their discussion. Intraluminal air appeared in the setting of acute appendicitis and was suggestive of signs of serious complications in the previous series. There have been several explanations for intraluminal air in acute appendicitis (10, 14). Since air resorption takes time following appendiceal obstruction, some intraluminal air can be seen in the inflamed appendixes. There is retention of nonpathogenic air, which is normally regurgitated from the colon. The other source of intra-appendiceal air may be pathogenic, which is produced by the presence of gas-forming microorganisms in the inflamed appendix. In a few cases of distal appendicitis, air can be retained in the proximal normal portion of the appendix when the inflammatory process is confined to the distal portion (21). In contrast to the aforementioned investigation, we studied the absorption of nonpathogenic air, and our results indicated that in the normal appendix, intra-appendiceal air was a typical finding, and more frequently seen than in the inflamed appendix. We think these two different implications of a single radiographic feature, i.e., intra-appendiceal air, should be clearly understood during the evaluation of appendicitis.

So far, intra-appendiceal air has not been included as a diagnostic criterion in the evaluation of appendicitis, while extra-appendiceal air was generally considered as an indicator of appendiceal perforation (8). It may be explained...
by the fact that intra-appendiceal air can be seen in both normal and inflamed appendices with a substantial overlap in the prevalence, which leads to lower the diagnostic sensitivity and specificity. Previously published data and our results show that the prevalence of intraluminal air in acute appendicitis was relatively high, and ranged from 8.3% to 27% (13, 14, 18, 22), including 13.2% as seen in our results. Also, absence of intra-appendiceal air for evaluating indeterminate CT interpretations did not show particular influence on the diagnostic performance, although the analysis was inherently limited by its small sample size (18–25 cases). The sensitivity and NPV did not change significantly, and the improved specificity and PPV were compromised by overlap in CI. Significances in the results of AUC were discrepant between the readers. Although the prevalence of intra-appendiceal air was also significantly different between cases with and without appendicitis for indeterminate cases, the use of intra-appendiceal air may have a limited value in the evaluation of appendicitis. In the substantial number of cases evaluated in our study as well as in the previous reports (11, 18), the presence or absence of intraluminal air alone cannot accurately exclude or diagnose appendicitis.

There were significant differences in the amount and appearance of intra-appendiceal air between patients with and without appendicitis. In acute appendicitis, the amount of intraluminal air was relatively small compared with the normal appendix. The inflamed appendices showed significantly different features of intraluminal air as a stool-like appearance or an air-fluid level compared with the normal appendices in which scattered air bubbles and columns was most commonly seen. A few, earlier case series described “bubbly” or “dirty” air as indicative of appendicitis, and a tubular shaped air collection as a normal appendix with a patent lumen (23, 24). The previous and our observations pose an assumption that the imaging features of intraluminal air may have a potential role in the diagnosis of acute appendicitis. However, we have only showed significant differences in the morphologic features of air between appendicitis and normal appendix, and further studies are needed to confirm the diagnostic role of the air morphology.

Our study showed high levels of inter-reader agreements in the image analysis. It was possibly due to the fact that the two readers had similar levels of expertise regarding the CT diagnosis of appendicitis. Also, the small number of indeterminate cases might be attributed to the experience for substantial periods of daily practice in diagnosing appendicitis. However, we admit there might have been recall bias or leaning toward more confident rating in the image analysis because the readers were the same attending radiologists who carried out daily practice.

Our study has some limitations. First, the rate of appendectomy in our study cohort (107 of 458, 22.4%) was relatively low compared with the data from previous investigations (15, 25). This may imply that the clinical presentation in some of the patients in our study cohort may not have been typical suspected acute appendicitis. Given the retrospective data collection based largely on the information already available in the medical records, further clarification was not possible. The suspicion of acute appendicitis was primarily made by referring physicians in the emergency department at our institution. Nevertheless, there is no single definition of suspicion of appendicitis and, in fact, the suspicion is up to the expertise and discretion of individual attending physicians. Second, to investigate the influence of intra-appendiceal air on the diagnosis of appendicitis, we analyzed indeterminate cases incorporated in the total study population. Due to the small number of the indeterminate cases, the analysis might have lacked statistical power in the comparison. Third, we only analyzed cases with a visualized appendix. If acute appendicitis had developed in cases without a visualized appendix, it would have been missed during the patient collection. In a study by Ganguli et al. (26), the frequency of non-visualization of the appendix is relatively common and was found in 15% of the scans, even with MDCT. However, according to their study, the chance of developing acute appendicitis in the non-visualized appendix was very low. Lastly, only post-contrast CT images were evaluated in our study, and precontrast images or images with oral contrast were not included in the analysis. This might have affected the accuracy in the diagnosis.

In conclusion, air was more frequently seen within a normal appendix than within an inflamed appendix. In acute appendicitis compared with the normal appendix, intraluminal air was relatively lesser in amount, and more frequently showed stool-like or air-fluid level appearances. Despite the differences, intra-appendiceal air had a limited incremental value for the diagnosis of acute appendicitis.

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