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Original Article

Determination of acute appendicitis histologic subtypes by MDCT findings

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Abstract

Aim: Our aim was to investigate if histological subtypes of acute appendicitis (AA) can be predicted by multidetector computed tomography (MDCT) and laboratory findings.

Material and Methods: A retrospective search of the hospital database to identify patients who underwent appendectomy and had an abdominal MDCT scan and laboratory tests including white blood cell (WBC) count and c-reactive protein (CRP) available before the operation revealed 123 patients (mean age: 25.69 ± 17.23 years). Histopathological results were classified as mucosal, gangrenous and suppurative AA. MDCT scans of the patients were evaluated for appendix diameter, appendix wall thickness, presence of pericecal fluid and extraluminal air. The relationship between MDCT and laboratory findings and histological subtypes of AA were assessed.

Results: There were 24 (19.5%) mucosal, 47 (38.2%) suppurative and 52 (42.3%) gangrenous AA. WBC count, CRP level, appendix wall thickness and appendix diameter was significantly different between mucosal and gangrenous AA ($p < 0.05$) and between suppurative and gangrenous AA ($p < 0.05$). However, there was no significant difference between mucosal and suppurative AA in terms of all variables ($p = 0.752$, 0.551, 0.756, 0.250 and 0.051, respectively). Presence of pericecal fluid was 92.2% sensitive and 93.1% specific for gangrenous AA. Presence of extraluminal air was 94.7% sensitive and 97.3% specific for gangrenous AA.

Conclusion: AA histologic subtypes can be predicted by especially MDCT findings.

Keywords: Appendicitis; diameter; wall thickness; multidetector computed tomography; subtype

INTRODUCTION

Acute appendicitis (AA) is the most common cause of surgical acute abdomen (1). For many years, the treatment of AA was emergency surgical intervention (2). However, recent studies have shown that conservative management with antibiotics is equally safe and effective to appendectomy in uncomplicated AA cases (3, 4). In complicated AA cases, the risk of complications such as perforation and intraabdominal abscesses is high, therefore early diagnosis is very important to prevent related morbidity. The different management of these two AA types indicates that accurate diagnosis of AA is very important in order to plan appropriate treatment.

Imaging prior to AA surgery has largely prevented negative appendectomies, complications and general health expenditures (5). The American College of Radiology (ACR) recommends the use of intravenous contrast-enhanced multidetector computed tomography (MDCT) in the evaluation of adults and adolescents with suspected AA, and ultrasound (US) in pregnant women and children under 14 years of age (6). However, US is highly operator dependent and shows variable sensitivity and specificity for the diagnosis of AA. On the other hand, MDCT is not operator dependent and it has higher sensitivity (94 %) and specificity (95 %) than US (7). Main disadvantage of MDCT is the exposure to ionizing radiation. However recent advancements in detector technology and the routine use of radiation dose reduction strategies like iterative reconstruction techniques reduces the radiation dose of a MDCT examination.

In the current literature, there are studies investigating the role of inflammatory blood markers in the differentiation of complicated and uncomplicated AA (8, 9, 10). In addition, recently, studies evaluating clinical and MDCT - based radiological predictors of complicated AAs are being conducted. Imaoka et al. reported that a body temperature over 37.4 °C, C – reactive protein (CRP) level over 4.7 mg/dl, and presence of pericecal fluid collection on MDCT had almost 100% accuracy in the diagnosis complicated AA

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(11). Atema et al. proposed a scoring system including eight combined clinical and radiological parameters in the differentiation of complicated and uncomplicated AA cases (12).

Our aim in this study is to develop a MDCT - based system that can accurately predict the histopathological results of AA cases. In addition, it was investigated whether the laboratory parameters white blood cell (WBC), CRP and neutrophil levels differed between histopathological results.

MATERIAL and METHODS

This research was conducted in accordance with the 1964 Helsinki Declaration and the requirement for informed consent was waived as this was a retrospective study.

Study Population

A retrospective search of our hospital database for the period between April 2018 and September 2019 was queried to identify patients who underwent surgical operation for the diagnosis of AA. Among those, a total of 234 patients were identified who had pre-operation MDCT examinations available. We excluded patients whose MDCT examination were performed more than 48 hours earlier than the surgery (n= 75), patients whose MDCT examination were performed without admission of intravenous contrast agent (n = 21), patients with poor image quality (n = 12) and patients whose laboratory examinations were not available or were belonged to more than 24 hours before the surgery (n = 3). As a result, 123 patients (75 men vs. 48 women) were enrolled in the study. The mean age of the study population was 25.69 ± 17.23 years, ranging from 9 to 84 with a median of 19 years.

Laboratory findings of the patients were reviewed for WBC count and CRP levels. The results of each blood tests were noted and then classified as normal or elevated according to the determined cut off values (WBC > 12.000 /uL, CRP > 0.5 mg/dl). If the patient had more than one laboratory results available, the maximum values were taken for statistical analysis. The time interval between CT and laboratory evaluation was 253 ± 75 minutes (min. 100, max. 397). Histopathological results were reviewed for the final pathological diagnosis whether it was a mucosal appendicitis, suppurative appendicitis or gangrenous appendicitis.

MDCT Acquisitions and Image Interpretation

MDCT examinations of the patients were acquired by using a 64 - slice CT scanner (Discovery CT750 HD, GE Healthcare, Milwaukee, WI). A 100 ml of intravenous iodine-based contrast agent followed by a 20 ml of saline flush was administered with a flow rate of 3 ml/sec. The imaging started 70 s after the start of contrast agent injection. Field of view (FOV) included the area between the diaphragms to the pubic symphysis. Axial and coronal reconstructions in 1.5 mm thickness were created.

MDCT examinations of the patients were reviewed in consensus by a board - certified radiologist (SA, 7 th years of experience) and a senior radiology resident (MO, 5th year radiology resident) using a PACS workstation. The interpreters were aware of the diagnosis of acute appendicitis of the patients, but blinded to the laboratory and the histopathological results. Appendix diameter was measured as the maximum outer of the appendix. Appendix wall thickness was measured as the maximum wall thickness of the appendix. Presence of pericecal fluid and presence of extraluminal air were assessed and noted.

Surgical and Histopathological Diagnosis

All patients were operated within 48 hours after MDCT. Some patients underwent open appendectomy and some patients underwent laparoscopic appendectomy. All surgical specimens were analyzed by pathologist with > 7 years of experience. The pathologist was blinded to the CT results of each individual case. he histopathological diagnosis was based on changes and density of neutrophil infiltration in the appendiceal wall. The severity of appendiceal inflammation was grouped in three histopathological conditions: mucosal AA (neutrophilic infiltration involving the mucosa/submucosa), suppurative AA (mucosa, submucosa and the muscularis propria) and gangrenous AA (transmural necrosis of the appendiceal wall).

Statistical Analysis

Statistical analysis was conducted with Statistical Package for Social Sciences 15.0 (SPSS Inc., Chicago, IL, USA) for windows software program. A p value less than 0.05 was indicative of statistical significance. Categorical variables were expressed as frequencies and compared with chi-square test. Normal distribution of the continuous data was assessed using Shapiro-Wilk test and presented as median and range or mean and standard deviation as appropriate. Kruskal wallis test was used to compare age, WBC count, neutrophil count, appendix wall thickness and appendix diameter among histopathological subcategories. Mann Whitney U test with Benforini correction was used to perform pairwise comparison of the appendicitis subgroups. Receiver operating characteristics (ROC) curve analysis was performed to determine the diagnostic performance of appendix wall thickness and appendix diameter in determining the histopathological subcategories. Each ROC curve was reconstructed as the examined histopathological category vs. other (gangrenous appendicitis vs. mucosal appendicitis; gangrenous appendicitis vs. suppurative appendicitis). Optimal cut off values were obtained by maximizing the youden index (Youden index = sensitivity + specificity – 1).

RESULTS

Demographic data, laboratory results and MDCT findings and the comparison of the variables between appendicitis subgroups are displayed in Table 1. All 123 patients underwent open (n = 90) or laparoscopic (n =33) appendectomy. Twenty four (19.5%) patients were diagnosed with mucosal appendicitis (Figure 1), 47 (38.2%) patients were diagnosed with suppurative appendicitis (Figure 2) and 52 (42.3%) patients were diagnosed with gangrenous appendicitis (Figure 3).

Figure 1. A 25-years-old male patient with mucosal appendicitis. The appendix diameter (arrow) is 5.8 mm. The appendix wall thickness is approximate 1.2 mm

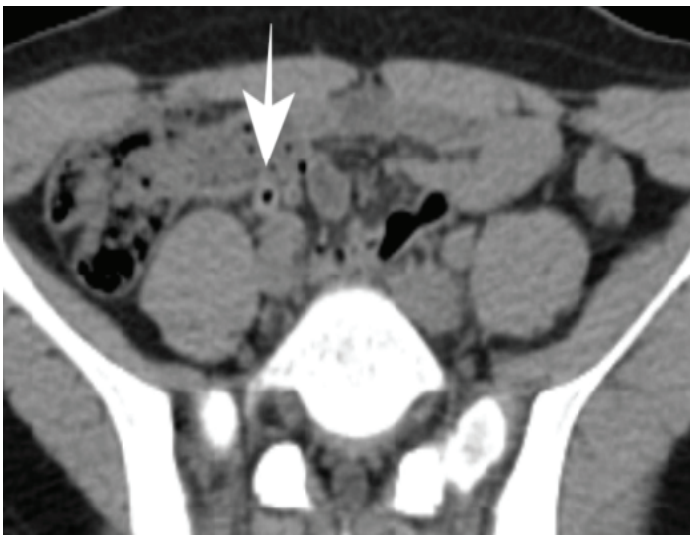

Figure 2. A 22-years-old female patient with suppurative appendicitis. The appendix diameter (arrow) is 6.5 mm. The appendix wall thickness is 1.7 mm

Table 1. Demograhic data, laboratory results and MDCT interpretations of the study population

Variable	Total number n = 123	Mucosal Appendicitis n = 24 (19.5%)	Suppurative Appendicitis n = 47 (38.2%)	Gangrenous Appendicitis n = 52 (42.3%)	p value
Age (years) [a]	19 (3 – 84)	17.5 (5 – 63)	19 (3 – 49)	23 (6 – 84)	0.037
Gender					0.315
Male	75 (61%)	17 (22.7%)	25 (33.3%)	33 (44%)	
Female	48 (39%)	7 (14.6%)	22 (45.8%)	19 (39.6%)	
WBC (/uL) [a]	10760 (4560 – 23431)	8605 (4560 – 20561)	8200 (4820 – 22600)	13335 (5390 – 23431)	< 0.001
WBC					< 0.001
Normal	71 (57.7%)	19 (26.8%)	35 (49.3%)	17 (23.9)	
Elevated	52 (42.3%)	5 (9.6%)	12 (23.1%)	35 (67.3%)	
Neutrophile (/uL) [a]	6600 (1302 – 20491)	4970 (1990 – 15000)	5130 (1302 – 18690)	10190 (2510 – 20491)	< 0.001
CRP [a]	0.39 (0.11 – 10.75)	0.23 (0.14 – 5.45)	1.03 (0.12 – 10.29)	2.33 (0.11 – 10.75)	0.008
CRP					
Normal	69 (56.1%)	17 (24.6%)	30 (43.5%)	22 (31.9%)	
Elevated	54 (43.9%)	7 (13.0%)	17 (31.5%)	30 (55.6%)	
Appendix wall thickness (mm) [a]	2 (0.90 – 4.50)	1.3 (0.9 – 3)	1.6 (0.9 – 3.4)	3.1 (1 – 4.5)	< 0.001
Appendix diameter (mm) [a]	7.5 (4.50 – 14)	6.25 (4.5 – 8.7)	6.5 (5.5 – 10)	9.75 (6.1 – 14)	< 0.001
Pericecal fluid					< 0.001
Present	51 (41.5%)	0 (0%)	4 (7.8%)	47 (92.2%)	
Absent	72 (58.5%)	24 (33.3%)	43 (59.7%)	5 (6.9%)	
Extraluminal Air					
Present	19 (15.4%)	0 (0%)	1 (5.3%)	18 (94.7%)	
Absent	104 (84.6%)	24 (23.1%)	46 (44.2%)	34 (32.7%)	

n: numbers and percentages in paranthesis, a: median and range in paranthesis

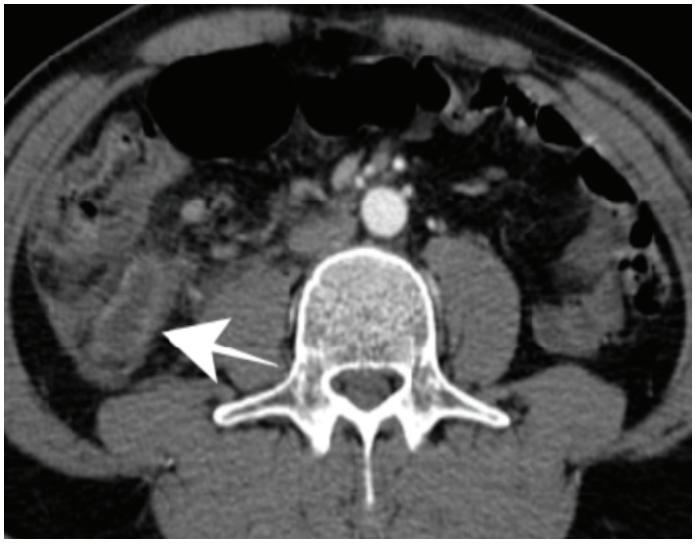

Figure 3. A 36-years-old man male patient with gangrenous appendicitis. The appendix diameter (arrow) is 9.8 mm. The appendix wall thickness is 3.2 mm

Figure 4 . A 14-years-old female patient with gangrenous appendicitis. The appendix diameter (white arrow) is 9.7 mm. The appendix wall thickness is 3 mm. Extensive fluid is observed at pericecal area

WBC count, neutrophil count, CRP level, appendix wall thickness and appendix diameter were statistically different between appendicitis subgroups. Results of the pairwise comparison of the variables between mucosal, suppurative and gangrenous appendicitis are displayed in Table 2. Age was not significantly different between appendicitis subgroups. WBC count, neutrophil count, CRP level, appendix wall thickness and appendix diameter were significantly different between mucosal and gangrenous appendicitis ($p < 0.05$) and between suppurative and gangrenous AA ($p < 0.05$). However, there was no significant difference between mucosal and suppurative AA in terms of all variables ($p = 0.752$, 0.551, 0.756, 0.250 and 0.051, respectively). Presence of pericecal fluid was 92.2% sensitive and 93.1% specific for gangrenous appendicitis (Figure 4). Presence of extraluminal air was 94.7% sensitive and 97.3% specific for gangrenous appendicitis.

Table 2. Pairwise comparison of WBC count, neutrophile count, CRP level, appendix wall thickness and appendix diameter

	Mucosal vs. suppurative	Suppurative vs. gangrenous	Mucosal vs. gangrenous
Age	0.559	0.038	0.030
WBC	0.752	< 0.001	< 0.001
Neutrophile	0.551	< 0.001	< 0.001
CRP	0.756	0.008	0.013
Appendix wall thickness	0.250	< 0.001	<0.001
Appendix diameter	0.051	< 0.001	<0.001

Diagnostic performances of appendix wall thickness and appendix diameter for appendicitis subgroups are shown in Figure 5. A cut-off appendix wall thickness value of equal or greater than 2.55 mm to differentiate gangrenous appendicitis from mucosal appendicitis led to 76.9% sensitivity and 87.5% specificity (AUC: 0.905, CI: 0.837 -0.972). A cut-off appendix diameter of equal or greater than 7.05 mm to differentiate gangrenous appendicitis from mucosal appendicitis led to 90.4% sensitivity and 83.3% specificity (AUC: 0.935, CI: 0.882 -0.987). A cut-off appendix wall thickness of equal or greater than 2.35 mm to differentiate gangrenous appendicitis from suppurative appendicitis led to 82.7% sensitivity and 83.0% specificity. (AUC: 0.875, CI: 0.805 – 0.945). A cut-off appendix diameter of equal or greater than 7.55 mm to differentiate gangrenous appendicitis from suppurative appendicitis led to 84.6% sensitivity and 78.7% specificity. (AUC: 0.891, CI: 0.828 – 0.954).

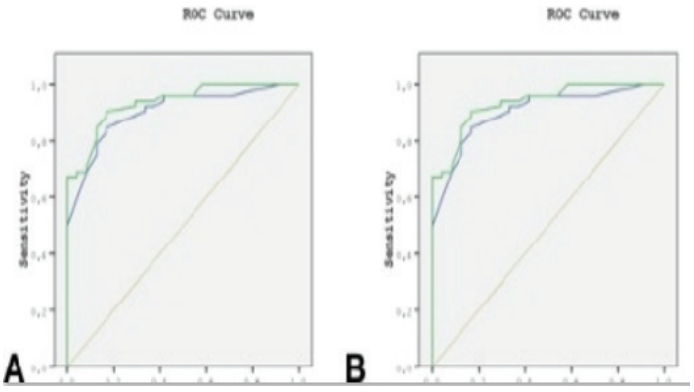

Figure 5 . ROC curves of gangrenous vs. mucosal appendicitis (A) and gangrenous vs. suppurative appendicitis (B)

Table 3. Cut off, sensitivity, specificity, PPV and NPV values for differentiating gangrenous appendicitis from mucosal appendicitis and gangrenous appendicitis from suppurative appendicitis

	Appendix wall thickness		Appendix diameter	
	Gangrenous vs. mucosal appendicitis	Gangrenous vs. suppurative appendicitis	Gangrenous vs. mucosal appendicitis	Gangrenous vs. suppurative appendicitis
Cut-off value (mm)	2.55	2.35	7.05	7.55
Sensitivity	76.9%	82.7%	90.4%	84.6%
Specificity	87.5%	83.0%	83.3%	78.7%
PPV	93%	84.3%	92.1%	81.5%
NPV	63.6%	81.3%	80%	82.2%
P value	< 0.001	< 0.001	< 0.001	< 0.001

DISCUSSION

Our study showed that the appendix wall thickness and appendix diameter, and MDCT detection of pericecal fluid and extraluminal air, are high effective in the differentiation of mucosal and gangrenous appendicitis. Thus, a model for predicting histological status and determination of cut-off values in suspected AA patients with a MDCT scan may provide significant benefit in guiding treatment, especially in patients with clinically uncertain findings.

There are some studies in the literature which suggest that conservative antibiotic treatment is as reliable as surgery in uncomplicated mucosal appendicitis cases (13,14). By this way, unnecessary surgery and related complications as a result of surgery, and health expenditures can be prevented. WBC and neutrophil count, and CRP levels which are the most commonly used laboratory parameters to determine histological status of AA were reported to have different sensitivity and specificity (10, 15, 16). In our study, WBC levels were not significantly different between mucosal and suppurative appendicitis cases ($p = 0.752$). However, the WBC level was significantly different between mucosal and gangrenous appendicitis ($p < 0.001$) and suppurative - gangrenous appendicitis ($p < 0.001$). Similar to WBC, neutrophil levels did not differ significantly between mucosal and suppurative appendicitis cases ($p = 0.551$); but there was significant difference between mucosal and gangrenous appendicitis ($p < 0.001$), and between suppurative and gangrenous appendicitis ($p < 0.001$). In terms of CRP levels, there was no difference between mucosal and suppurative appendicitis cases ($p = 0.756$); but there was a significant difference between mucosal and gangrenous appendicitis ($p = 0.008$), and between suppurative and gangrenous appendicitis ($p = 0.013$).

In patients with positive MDCT scan for AA, a model by determining cut off values of appendix wall thickness and appendix diameter can predict histological status of AA and thereby can guide for appropriate treatment option. In the presence of radiologic findings that can predict gangrenous AA, patients can be operated immediately and complications because of the delay in the diagnosis can be prevented. Avanesov et al. (17) proposed an appendix severity index including 3 clinical and 4 radiological findings and reported 87% accuracy, 92% positive predictive value (PPV) and 83% negative predictive value (NPV) for complicated appendicitis in cases with a score above 3. To the best of our knowledge, there are no studies in the literature investigating the histological discrimination of AA on MDCT - scan based. However, our study had similar results with the studies conducted to distinguish between uncomplicated and complicated AA cases.

There are studies in the literature reporting that conservative treatment is very effective in patients with mucosal appendicitis or with uncomplicated suppurative appendicitis (18,19). By this way, unnecessary appendectomy and therefore complications and unnecessary health expenses may be avoided. Hansen et al. described radiologic factors that strongly correlate with the histologic diagnosis of complicated AA, as follows: (i) extraluminal air (ii) the appendix diameter, (iii) periappendiceal fat staining, (iv) appendicoliths, (v) dependent fluid (20). Despite the defined these results, appendicolitis can also be seen in normal appendix. Periappendiceal fat staining also occurs in a wide range of inflammatory events that are not specific for AA. Choi et al. reported that the detection of thickening of the appendiceal wall of over 1 mm has a sensitivity, specificity, and accuracy of 66%, 96%, and 87% for the diagnosis of AA (21). We focused on appendix diameter, wall thickness, extraluminal air and presence of pericecal fluid. In our study, selecting an appendix diameter cut-off value of 7.05 mm for differentiating gangrenous and mucosal appendicitis revealed 90.4% sensitivity, 83.3% specificity, 92.1% PPV and 80% NPV. Selecting a cut-off appendix wall thickness of 2.55 mm for differentiating gangrenous and mucosal appendicitis revealed 76.9% sensitivity, 87.5% specificity, 93% PPV and 63.6% NPV. For the differentiation of gangrenous and suppurative AA, a cut-off value of 7.55 mm for appendix diameter revealed 84.6% sensitivity, 78.7% specificity, 81.5% PPV and 82.2% NPV. Selecting an appendix wall thickness cut-off value of 2.35 mm for differentiating gangrenous and suppurative AA revealed 82.7% sensitivity, 83% specificity, 84.3% PPV and 81.3% NPV. Furthermore, presence of pericecal fluid

and extraluminal air had high sensitivity, specificity, PPV and NPV (92.2%, 93.1% and 94.7%, 97.3% respectively). Our results were similar to the literature.

Our study had several limitations. Firstly, it was limited by the retrospective study design and the missing external prospective validation of MDCT findings on larger cohorts. Secondly, MDCT images were evaluated by consensus by two radiologists. Interobserver consistency was not evaluated. Thirdly, the most specific parameters determined by the observers on MDCT images were evaluated. Evaluation of other parameters may contribute to more specific results.

CONCLUSION

As a result, when evaluating the AA, the four factors of appendix diameter, wall thickness, extraluminal air and presence of pericecal fluid on MDCT are simple to obtain and useful for predicting the current pathological severity of patients. Therefore, we think that, MDCT findings can be used to predict the current pathological status and severity of AA. These preoperative data are extremely useful for selecting the treatment strategy for AA.

Competing interests: The authors declare that they have no competing interest.

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Ethical approval: This research was conducted in accordance with the 1964 Helsinki Declaration and the requirement for informed consent was waived as this was a retrospective study.

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