

Impact of the Use of Contrast-Enhanced Multidetector CT for Acute Appendicitis: A Prospective Comparison with the Alvarado Score¹

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Purpose: To determine the diagnostic performance of contrast-enhanced multidetector CT (MDCT) and the Alvarado score for acute appendicitis.

Materials and Methods: MDCT and determination of the Alvarado score were prospectively performed in 282 patients with 146 pathologically proven cases of acute appendicitis and 136 pathologically proven or clinically diagnosed cases of non-acute appendicitis. To compare the diagnostic performance of MDCT and the Alvarado score, the patients were subdivided according to age and sex, and receiver operating characteristics (ROC) analysis and Spearman rank correlation were performed.

Results: ROC analysis revealed that the optimal cut off value of the CT appendicitis grades was 2 in all patients, resulting in a sensitivity of 96.6% and a specificity of 94.9%. The optimal cut off values of the Alvarado score was different according to age and sex, resulting in a sensitivity of 85.6% and a specificity of 48.5%. There was a significant correlation between the CT appendicitis grades and the surgical-pathological grades ($r=0.496$, $p<.0001$). However, no significant correlation was observed between the Alvarado score and the surgical-pathological grades.

Conclusion: Contrast-enhanced MDCT has a higher diagnostic accuracy and significant correlation with pathological findings than those of the Alvarado score in patients with acute appendicitis.

Index words : Appendicitis
Tomography
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Acute disease
Prospective studies

Acute appendicitis is one of the most common causes of surgical emergencies. Methods advocated to assist in the diagnosis of acute appendicitis include clinical scor-

ing systems, ultrasonography, computed tomography (CT), and magnetic resonance imaging.

Clinical scoring systems have been advocated as a means of identifying patients that should undergo imaging. The Alvarado score is a 10-point scoring system based on the signs, symptoms, and laboratory assessments associated with acute appendicitis (1). In the original study, Alvarado recommended an appendectomy for patients with a score of 7 or more, observation for patients with scores of 5 or 6, and discharge from hospital for patients with score of 4 or below (1). Subsequent

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studies (2 - 4) revealed the Alvarado score to be a simple, complementary aid to support the diagnosis of acute appendicitis. However, a lower diagnostic accuracy was observed when the scores were applied to women because of the potential presence of several, gynecological diseases (5, 6).

Several studies (7, 8) have demonstrated the high accuracy of the use of MDCT for detecting acute appendicitis. Raptopoulos *et al.* (9) also reported that CT findings are significantly correlated with the histopathological severity in acute appendicitis and that they therefore influence treatment methods.

In our clinical practice, we observed that the Alvarado score is inaccurate for diagnosing acute appendicitis, especially in women and in older individuals, and that the Alvarado score cannot predict the histopathologic severity. To the best of our knowledge, there are no literature reports comparing the diagnostic performance of the Alvarado score and the CT results according to age and sex; there are also no reports correlating the Alvarado score and CT findings with histopathology for acute appendicitis.

Therefore, the purpose of this study is to determine prospectively the diagnostic performance of both contrast-enhanced MDCT and the Alvarado score according to patient age and sex, and to determine whether the use of contrast-enhanced MDCT and the Alvarado score correlate with the histopathology for acute appendicitis.

Materials and Methods

Patient population

The institutional review board of our institution approved this research protocol, and written informed consent was obtained from all patients. A total of 295 patients with right lower quadrant abdominal pain who visited the emergency room between May 2005 and March 2006, were recommended to undergo contrast-enhanced MDCT by the emergency room physician for an evaluation of acute appendicitis. Thirteen patients

were excluded from the study due to a contraindication of undergoing contrast-enhanced CT, such as pregnancy, compromised renal function or a prior adverse contrast reaction. The remaining 282 patients (131 females and 151 males, mean age 43.2 years) were enrolled in this study.

Alvarado Score

Prior to undergoing contrast-enhanced MDCT, the senior general surgery residents gave all patients specific scores in accordance to the variables of the Alvarado scoring system. Alvarado scores are composed of a total of 10 points (1). There is one point for each item as follows; migration of pain from the epigastrium to the right lower quadrant; anorexia; nausea with vomiting; rebound tenderness in the right lower quadrant; and an elevated body temperature $> 37.5^{\circ}\text{C}$; increased neutrophils $> 75\%$. There are two points for each of the following two items: tenderness in the right lower quadrant, and leukocytosis $> 10,000/\text{mm}^3$ ($10 \times 10^9/\text{L}$).

Contrast-Enhanced MDCT Protocol

CT examinations were performed on a four-detector row CT scanner (Somatom Plus Volume Zoom; Siemens Medical Systems, Forchheim, Germany). A frontal, 52-cm scout view was obtained at 120 kVp and 50 mA, followed by acquisition of two phases of enhanced scans. First, focused arterial-phase scans were acquired from the lower pole of the right kidney to the symphysis pubis, with a scanning delay of 45 seconds for focusing the appendix. Non-focused, portal phase scans were then acquired from the diaphragm to the symphysis pubis, with a scanning delay of 70 seconds.

The protocol parameters were as follows: 120 kVp; 160 mAs; 2.5 mm collimation; pitch, 1.25:1; rotation speed, 0.5 mm; slice thickness, 3 mm/5 mm (arterial/portal); and reconstruction interval, 1.5 mm/2.5 mm (arterial/portal). Approximately 100 - 120 mL of iodinated contrast material (Ultravist 370; Schering, Berlin, Germany) was injected intravenously with a mechani-

Table 1. Surgery-pathological Grades and CT Appendicitis Grades

Grade	Surgery and Pathology Definition	CT Definition
0	Normal	Normal
1	Probable appendicitis	Fluid-filled appendix larger than 6 mm in diameter or gas-filled appendix larger than 8 mm in diameter
2	Simple appendicitis	Fluid-filled appendix larger than 6 mm in diameter with enhancing wall thickening
3	Appendicitis with localized peritonitis	Grade 2 definition plus localized periappendiceal strands
4	Gangrenous appendicitis	Grade 2 definition plus generalized mesenteric strands or periappendiceal gas
5	Appendiceal abscess	Appendiceal abscess

cal injector at 2 - 3 mL/sec. No oral or transrectal contrast materials were administered to the patients.

Image Analysis

Axial images without coronal reformatted reconstruction were displayed on a picture archiving and communications system (Infinit; Piview star, Seoul, Korea) for interpretation. Two radiologists (with 6 and 9 years, respectively, of abdominal imaging experience) evaluated the images by consensus. The radiologists interpreted the images with knowledge that a CT examination for suspected acute appendicitis was performed, but were blinded to the Alvarado score of the patients. The diagnosis of acute appendicitis on the CT scan was assessed based on a different six-grade scale from 0 (normal) to 5

(appendiceal abscess), as defined in Table 1 and shown in Figures 1 - 5.

Reference Standard

Of the 282 patients with clinically suspected acute appendicitis, 146 had acute appendicitis and 136 did not have acute appendicitis. The diagnosis in 146 patients with acute appendicitis was confirmed at surgery and by a histological examination. In the 136 patients without acute appendicitis, the diagnosis was confirmed at surgery and by a histological examination in 21 patients and at clinical follow-up for 115 patients.

The time interval from the CT examination to appendectomy was not more than 24 hours. As we had modified the six-grade, surgical-pathologic scale of acute ap-

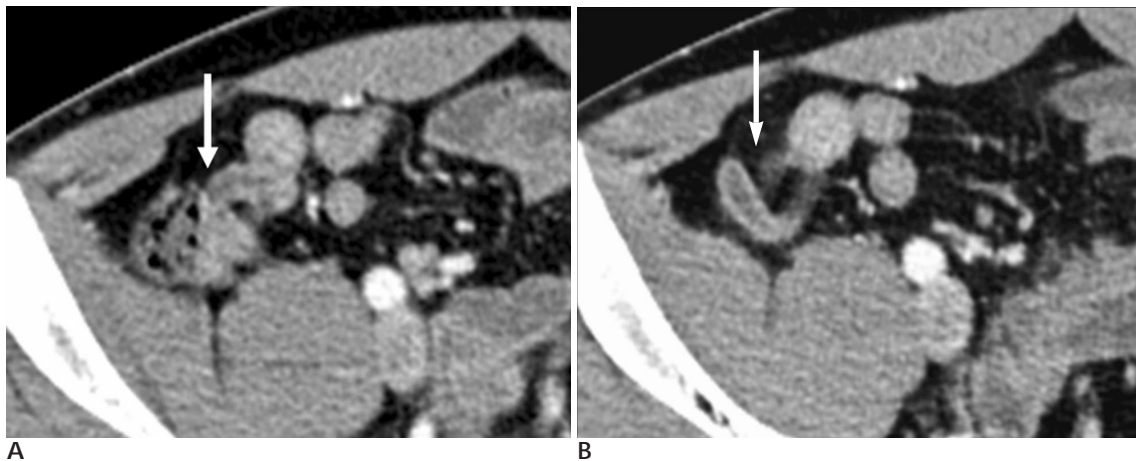


Fig. 1. CT appendicitis grade 1-probable appendicitis.

A. A transverse CT image shows the fluid-filled appendix (arrow) arising from the cecum.

B. A CT image obtained just inferiorly shows that the fluid-filled appendix (arrow) is 7 mm in diameter and that the wall is not enhancing.

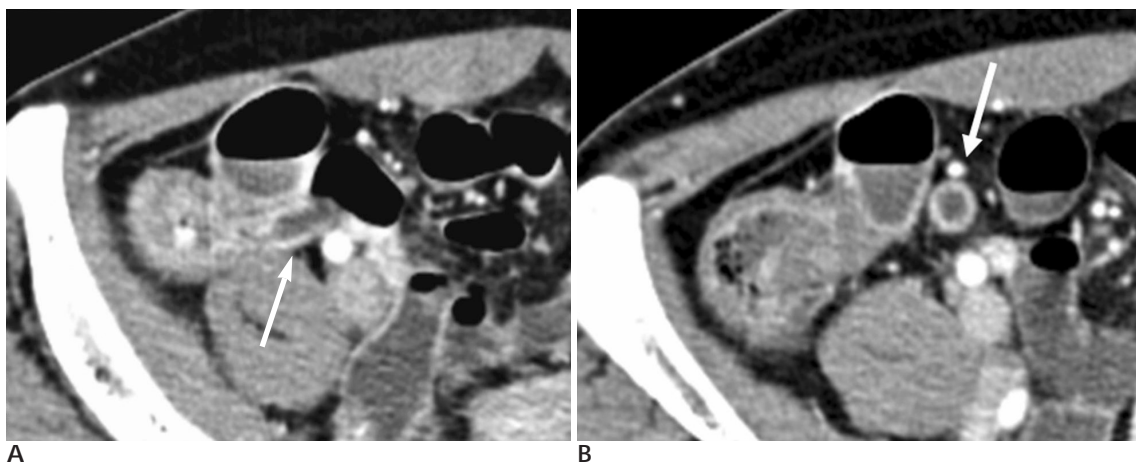


Fig. 2. CT appendicitis grade 2-simple appendicitis.

A. A transverse CT image shows the fluid-filled appendix (arrow) arising from the cecum.

B. A CT image obtained just superiorly shows the fluid-filled appendix (arrow) is 10 mm in diameter and that the wall is enhanced with intravenously administered contrast material. There is no periappendiceal stranding.

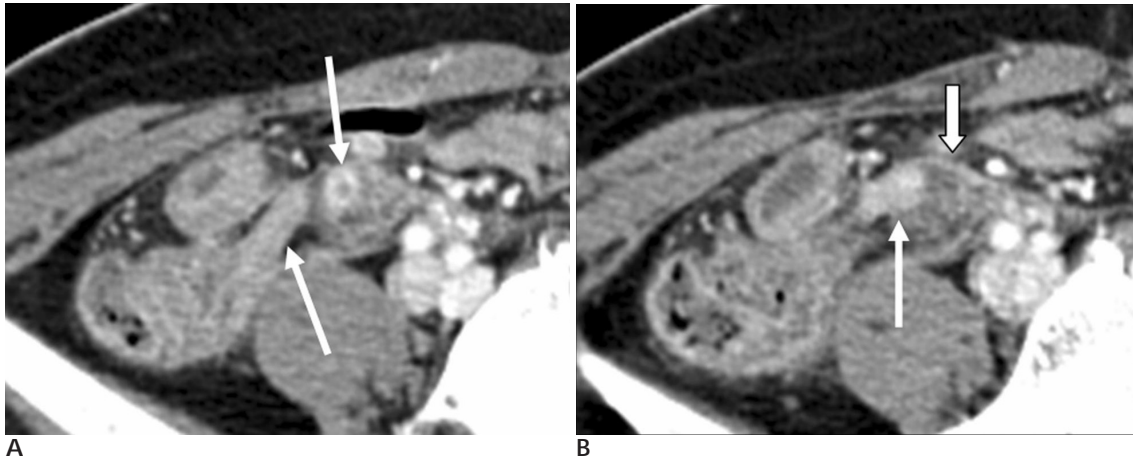


Fig. 3. CT appendicitis grade 3-appendicitis with localized peritonitis.

A. A transverse CT image shows the fluid-filled appendix (arrows) arising from the cecum.

B. A CT image obtained just superiorly shows that the fluid-filled appendix (arrow) is 7 mm in diameter and that it has an enhancing wall. Localized periappendiceal stranding (open arrow) is present.



Fig. 4. CT appendicitis grade 4-appendicitis with generalized peritonitis or perforation.

A. A transverse CT image shows an appendicolith (open arrow) with the nearly disrupted appendix wall (arrows).

B. A CT image obtained just superiorly shows mesenteric stranding (arrow) and extraluminal gas (short arrow).

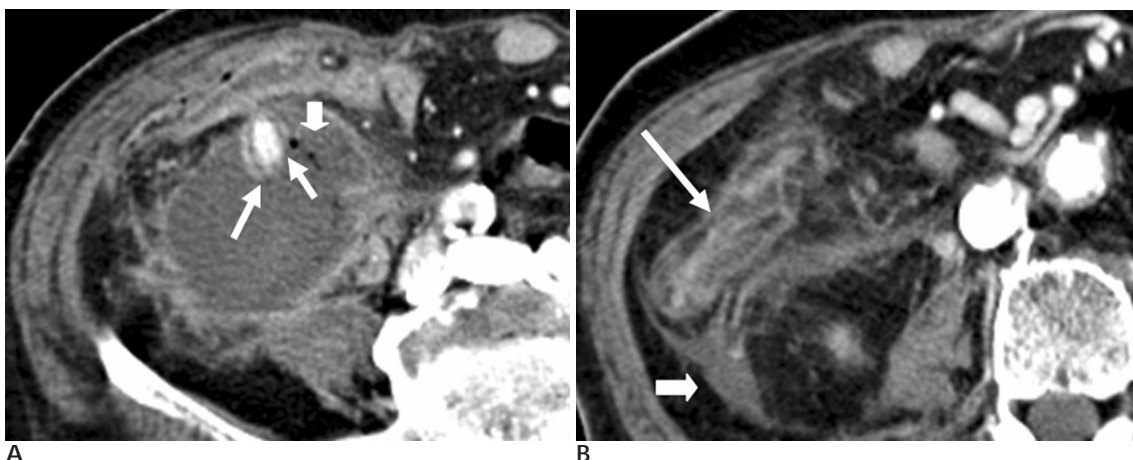


Fig. 5. CT appendicitis grade 5-periappendiceal abscess.

A. A transverse CT image shows an appendicolith in the fluid-filled appendix with a break in the enhancing wall (arrows). Extraluminal gas is present (short arrow).

B. A CT image obtained just superiorly shows edematous cecal wall thickening (arrow) and fluid collection (short arrow).

pendicitis based on a previously published study (9), we reviewed the surgical and pathological reports, and a combined assessment was made based on the six-grade scale from 0 (normal) to 5 (appendiceal abscess), as shown in Table 1 (9).

In 115 non-appendicitis patients that did not undergo surgery, clinical follow-up consisted of symptom resolution during the hospital stay and its confirmation per a telephone call at least eight weeks after hospitalization.

Statistical Analysis

To compare the diagnostic performance of contrast-enhanced MDCT and the Alvarado score according to patient age and sex, the study patients were subdivided according to sex and also subdivided according to age into groups under 60 years and over 60 years. Receiver operating characteristics (ROC) analysis was evaluated respectively for both categories.

The area under the ROC curves and the 95% confidence intervals were calculated. The cutoff values, that provided a balance between sensitivity and specificity for the diagnosis of acute appendicitis, i.e. the values less than or equal to the cutoff values used to indicate positivity for acute appendicitis, were determined by selecting the coordinate nearest to the left upper corner (0, 1) on each ROC curve.

The Spearman rank correlation was used to estimate the correlation between the Alvarado score and the surgical-pathological appendicitis grade and to estimate the correlation between the CT appendicitis grades and the surgical-pathological grades.

Table 2. Surgical-pathological Grades in Patients with Appendicitis

Grade	Surgical-pathologic grades	No. of Patients (<i>n</i> = 146)
1	Probable appendicitis	3
2	Simple appendicitis	16
3	Appendicitis with localized peritonitis	43
4	Gangrenous appendicitis	68
5	Appendiceal abscess	11

All statistical tests were performed using two, commercially available software programs (SPSS 11.5 for Windows, SPSS, Chicago, IL USA and MedCalc 7.4, MedCalc Software, Mariakerke, Belgium). For all tests, a *p* value less than 0.05 was considered statistically significant.

Results

Demographics

Of the 282 patients with clinically suspected acute appendicitis, 146 had acute appendicitis and 136 did not have acute appendicitis. Of the 282 patients, there were 131 men and 151 women; 218 patients were under 60 years and 64 patients were over 60 years. Table 2 shows the surgical-pathological grades for 146 patients with appendicitis. The final diagnoses in 136 patients without appendicitis included non-specific pain (*n* = 62), enterocolitis (*n* = 16), diverticulitis (*n* = 14), pelvic inflammatory disease (*n* = 14), a hemorrhagic ovarian cyst (*n* = 9), a right ureteral stone (*n* = 7), right acute pyelonephritis (*n* = 3), fecal impaction (*n* = 3), Crohn's disease (*n* = 2), an appendiceal mucocele (*n* = 1), pancreatitis (*n* = 1), acute cholecystitis (*n* = 1), epiploic appendagitis (*n* = 1), ovarian cyst torsion (*n* = 1) and colon cancer perforation (*n* = 1).

Diagnostic Performance and Optimal Cutoff

The optimal cutoff level for differentiating appendicitis from non-appendicitis was 6 for the Alvarado score, including all patients. Sensitivity was 85.6%, specificity was 48.5%, and the diagnostic accuracy was 67.7%; the area under the curve was 0.731, and the 95% confidence interval was 0.676 - 0.782 (Table 3). The optimal cutoff level for differentiating appendicitis from non-appendicitis was 7 for the Alvarado score in men and in patients under 60 years of age. However, the optimal cutoff level was 6 in women and 5 in patients over 60 years of age, respectively.

The optimal cutoff level for differentiating appendici-

Table 3. Diagnostic Performance and Optimal Cutoff Values of the Alvarado Score

	All	Male	Female	Younger than 60 years	Older than 60 years
AUC	0.731 (0.676 - 0.782)	0.747 (0.664 - 0.819)	0.722 (0.643 - 0.792)	0.756 (0.694 - 0.812)	0.648 (0.519 - 0.763)
Optimal Cutoff	6 or higher	7 or higher	6 or higher	7 or higher	5 or higher
Sensitivity	85.6 (78.9 - 90.9)	58.7 (46.7 - 69.9)	84.5 (74.0 - 92.0)	63.6 (53.7 - 72.6)	89.7 (75.8 - 97.1)
Specificity	48.5 (39.9 - 57.2)	80.4 (67.6 - 89.8)	47.5 (36.2 - 59.0)	75.7 (66.6 - 83.3)	32.0 (15.0 - 53.5)
Accuracy	67.7 (60.1 - 74.6)	68.0 (55.6 - 78.4)	64.9 (54.0 - 74.5)	69.8 (60.3 - 78.0)	67.2 (52.1 - 80.1)

Note - Numbers in parentheses with 95% confidence interval

Abbreviation: AUC = area under curve

Table 4. Diagnostic Performance and Optimal Cutoff Values of Contrast-Enhanced MDCT

	All	Male	Female	Younger than 60 years	Older than 60 years
AUC	0.973 (0.947 - 0.989)	0.963 (0.915 - 0.988)	0.982 (0.946 - 0.996)	0.965 (0.931 - 0.985)	0.998 (0.939 - 1.000)
Optimal Cutoff	2 or higher	2 or higher	2 or higher	2 or higher	2 or higher
Sensitivity	96.6 (92.2 - 98.9)	97.3 (90.7 - 99.6)	98.6 (92.4 - 99.8)	97.2 (92.0 - 99.4)	100.0 (90.9 - 100.0)
Specificity	94.9 (89.7 - 97.9)	92.9 (82.7 - 98.0)	95.0 (87.7 - 98.6)	92.8 (86.3 - 96.8)	96.0 (79.6 - 99.3)
Accuracy	95.8 (91.0 - 98.4)	95.4 (87.3 - 98.9)	96.7 (89.9 - 99.2)	95.0 (89.1 - 98.1)	98.4 (86.5 - 99.7)

Note - Numbers in parentheses with 95% confidence interval

Abbreviations: AUC = area under curve, CE-MDCT = contrast-enhanced MDCT

Table 5. Results of Spearman Rank Correlation Coefficients

	Alvarado score		CT appendicitis grade	
	r Value	p Value	r Value	p Value
Surgical-pathological appendicitis grade	- 0.104	0.2151	0.496	<0.0001

tis from non-appendicitis was 2 for the CT appendicitis grade, including all patients. For this grade, the sensitivity was 96.6%, the specificity was 94.9% and the diagnostic accuracy was 95.8%; the area under the curve was 0.973, and the 95% confidence interval was 0.947 - 0.989 (Table 4). The optimal cutoff level for differentiating appendicitis from non-appendicitis was 2 for the CT appendicitis grade, regardless of patient age or sex. Therefore, the use of contrast-enhanced MDCT has a significantly higher accuracy than the use of the Alvarado score for diagnosing appendicitis regardless of patient age or sex ($p < 0.0001$).

Correlation between the Alvarado Score and the Surgical Pathology and CT Appendicitis Grades

The correlation between the CT appendicitis grade and the surgical-pathological appendicitis grade was statistically significant. The Spearman rank correlation coefficient was 0.496 ($p < 0.0001$) (Table 5). The Alvarado score did not have a significant correlation with the surgical-pathological appendicitis grade (Table 5).

Discussion

The advent of MDCT is expected to improve the diagnostic accuracy of CT owing to its use of thinner sections, faster imaging, and improved spatial resolution capabilities. Recent studies (7, 8) have shown that the sensitivities and specificities of MDCT for the diagnosis of acute appendicitis ranged between 95 - 100% and 94 - 96%, respectively. Our results showed a 96.6% sensitivity and a 94.9% specificity that agreed with values in prior studies. Our study showed that the optimal cut-

off and high diagnostic accuracy of contrast-enhanced MDCT were not associated with age or sex in adults. Therefore, contrast-enhanced MDCT might be a valuable diagnostic modality for adults, especially for clinically equivocal females and older patients of both sexes, except if contraindicated because of the use of an iodine contrast agent.

As reported by Johnson *et al.* (13), MDCT scanning with IV and oral contrast material is the widely used MDCT protocol for diagnosing suspected appendicitis. Our results showed that only IV contrast-enhanced MDCT with thin sectioning had a high sensitivity and specificity similar to those of previous studies using both oral and IV contrast-enhanced MDCT. In addition, a recent study by Mun *et al.* (14) reported that using IV contrast alone is highly sensitive and specific for the confirmation or exclusion of acute appendicitis and by eliminating the time required to administer oral contrast, a diagnosis could be made more quickly.

Rao *et al.* (15) first described a focused appendiceal CT that involves contiguous thin-collimation helical scanning limited to the right lower quadrant following administration of both oral and rectal contrast material. This focused CT approach revealed high sensitivity and specificity similar to those of non-focused CT approaches for the confirmation or exclusion of appendicitis and had the advantage of minimizing the time required for diagnosis and the amount of radiation exposure (15 - 18). However, a limited evaluation of the intraabdominal pathological conditions resulting from a limited scanning field of view is the major reason that this approach is only rarely used (13, 16, 17). Our contrast-enhanced MDCT protocol included a focused arterial phase composed of thin sectioning slices of 3 mm around the appendix and the non-focused portal phase was composed of conventional sectioning slices of 5 mm over the entire abdomen in order to reach an alternative diagnosis without the use of any internal contrast material. Our results showed that this MDCT protocol was

simple to perform as it did not use an oral contrast agent, was accurate, and had an acceptable amount of radiation exposure.

As previously reported by Raptopoulos et al. (9), we also observed a significant correlation between the surgical-pathological appendicitis grade and the CT appendicitis grade. These results suggest that contrast-enhanced MDCT may be used to guide treatment by aiding in the identification of patients with different types of advanced appendicitis, such as perforation and abscess.

In 1988, Alvarado first described the Alvarado score, which was a simple scoring system composed of three signs, three symptoms, and two laboratory assessments for the diagnosis of acute appendicitis (1). Subsequent studies (2 - 4) revealed that the Alvarado score was a useful triage tool for providing a guideline of further studies and for the reduction of negative appendectomy rates. However several studies (5, 6) showed that a limitation of the Alvarado score is its low diagnostic accuracy in female patients. This limitation occurs as many gynecological diseases, such as pelvic inflammatory disease, a ruptured ovarian follicle, and an ectopic pregnancy causing non-specific, diffuse lower abdominal pain, can mimic acute appendicitis and can therefore interfere with making a correct diagnosis in female patients.

To the best of our knowledge, this is the first study to determine prospectively the optimal cutoff of the Alvarado score according to age and sex. Males and patients under 60 years of age had a cutoff value of 7, in accordance with previous Alvarado-score-related studies. However, females and patients older than 60 years had cutoff values of 6 and 5, respectively. These findings indicate that a lower cutoff value for the Alvarado score is needed for female patients and for older patients. The need for the lower optimal cutoff value in females might be due to the ineffectiveness of the Alvarado scores for female patients. Therefore, further prospective research studies with larger patient populations will be needed in order to understand fully the lower optimal cutoff value for female subjects.

Our results indicate that older patients had a lower optimal cutoff value, and this finding has not been reported in previous Alvarado-score-related studies. However, several studies of appendicitis in older patients (19, 20) showed that because symptoms are often inconspicuous in the elderly and the inflammatory parameters are often not present as in younger patients, a diagnosis is sometimes delayed. Our results suggest that older patients have a lower optimal cutoff value because of the

indistinct and atypical nature of the symptoms, signs, and inflammatory laboratory findings.

A number of limitations of this study must be considered. First, the same physician did not measure the described Alvarado scores for all of the patients. However, this bias probably did not dramatically influence the Alvarado scoring, as these parameters were composed primarily of objective laboratory findings and the symptoms were checked against the oral statements of the patient. Although tenderness in the right lower quadrant and rebound tenderness in the right lower quadrant were somewhat affected by the skill of the physician, the general surgeons fully experienced them on the physical examinations. Second, patients who were given analgesics or refrigerant medicine before scoring in their homes or in other hospitals were not excluded from the study.

In conclusion, this prospective study has showed that the use of contrast-enhanced MDCT has a significantly higher diagnostic accuracy than the use of the Alvarado score regardless of patient age or sex. This study also revealed a significant correlation between the contrast-enhanced MDCT findings and histopathology.

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