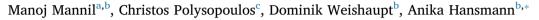
Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Research article

Clinical-radiological scoring system for enhanced diagnosis of acute appendicitis



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ARTICLE INFO

Keywords: Ultrasound Appendicitis Modified alvarado score Clinical-radiological scoring system Appendix diameter Vermix

ABSTRACT

Introduction: Acute appendicitis is the most common surgical condition in industrialized countries. However, diagnosis in borderline cases is often cumbersome and requires follow-up examinations, and/or a Computed Tomography examination. Therefore, our aim was to develop a combined clinical and sonographic score to enhance prediction of acute appendicitis.

Patients and methods: The modified Alvarado score and various established sonographic criteria were investigated in 132 patients with suspected acute appendicitis. Two models were computed accounting for missing values. After analysis of sensitivity and specificity for the modified Alvarado score, logistic regression analysis was performed to identify significantly contributing sonographic features.

Results: The threshold of the logistic regression analysis of the two models resulted in the formula: modified Alvarado score + axial Appendix diameter [mm]. When the Appendix diameter is > 8 mm, 1 point/mm is added, while for a diameter < 8 mm, 1 point/mm is subtracted. The cut-off value is \geq 13 for acute appendicitis with a sensitivity 91.4% and a specificity of 100%, compared to a sensitivity of 90% and a specificity of 84.4% for the modified Alvarado score in our cohort.

Conclusion: The established modified Alvarado score for diagnosis of acute Appendicitis can be improved by adding the axial diameter of the Appendix in a sonographic examination.

1. Introduction

Acute appendicitis is the most common surgical condition in industrialized countries. It is the second most common cause of right lower quadrant pain of patients presenting to the emergency department after non-specific abdominal pain and constipation [1,2]. The lifetime incidence is reported to be in the range of 7-14% [3]. According to the American College of Radiology (ACR) appropriateness guidelines, computed tomography (CT) with intravenous contrast material is recommended for evaluation of adults and adolescents suspected of suffering from acute Appendicitis, while abdominal ultrasonography (US) is recommended for use in pregnant patients and children younger than the age of 14 years [4,5]. Since the introduction of pre-surgical imaging, negative appendectomies, treatment-associated complications, as well as overall healthcare costs have been significantly reduced [6]. While the use of abdominal CT is proven to be of higher sensitivity compared to abdominal ultrasound (sensitivity and specificity for US diagnosis of Appendicitis in adults are 83% (95% CI: 78%, 87%) and 93% (95% CI: 90%, 96%), compared to CT sensitivity and specificity of 94% (95% CI: 92%, 95%) and 94% (95% CI: 94%, 96%), respectively), the use of potentially harmful ionizing radiation needs to be taken into consideration [7,8]. Abdominal US utilizes no ionizing radiation and shows a similar specificity for the diagnosis of acute Appendicitis compared to CT [9,10]. First line abdominal US could reduce radiation exposure by 57% and imaging costs by 45% compared to initial contrast enhanced CT [11]. Furthermore, data from large retrospective trials show radiation of repeated CT scans may triple the risk of brain cancer and leukaemia in younger populations [9,12,13].

There is a plethora of scores available for cases of suspected acute Appendicitis, including but not limited to the Adult Appendicitis Score [14], Appendicitis Inflammatory Response Score [15], Pediatric Appendicitis Score [16], and RIPASA score for Asian individuals [17]. However, the most frequently used measure to clinically evaluate acute Appendicitis is the Alvarado Score in its modified version consisting of 7 parameters (Table 1) [18,19]. Scores range from 0 to 9 points and the absolute score positively correlates with the likelihood of acute Appendicitis.

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https://doi.org/10.1016/j.ejrad.2017.11.020





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Received 20 July 2017; Received in revised form 23 October 2017; Accepted 27 November 2017 0720-048X/ © 2017 Elsevier B.V. All rights reserved.

Table 1

Modified Alvarado Score [7;8].

Variables	Clinical features	Score
Symptoms	Migratory right iliac fossa (RIF) pain	1
	Anorexia	1
	Nausea and vomiting	1
Signs	Tenderness (RIF)	2
	Rebound tenderness	1
	Elevated temperature	1
Laboratory	Leukocytosis	2
Total Score	-	9

In light of the artificial separation between clinical and imageguided diagnosis of acute Appendicitis with potentially inconclusive or contradicting outcomes, a clinical-pathological-radiological scoring system was recently proposed [10,20]. In this context, Álvarez et al. recently evaluated the Alvarado score in its full form and a range of sonographic features [21] with promising results.

The purpose of this study was to develop a combined clinical-radiological scoring system using the modified Alvarado score and only significantly contributing sonographic findings in order to enhance the prediction of histo-pathologically proven acute Appendicitis and provide guidance to examiners in case the Appendex cannot be visualized in abdominal ultrasound. The hypothesis was that a clinical-radiological scoring system can enhance sensitivity and specificity compared to the commonly used Alvarado score alone.

2. Subjects and methods

2.1. Patients and study design

Ethical approval of the local Ethic's commission (blinded for review) was obtained for the retrospective analysis of pre-surgical imaging studies in patients with suspected acute Appendicitis. Between 2012 and 2014 492 patients with clinically suspected diagnosis of acute Appendicitis presented to the local emergency department and received an initial abdominal ultrasound. Patients without following surgical intervention, without histo-pathologically confirmed diagnosis, or with a first-line CT/MRI examination were excluded (n = 298). 62 patients were excluded as the imaging studies and/or clinical reports were incomplete. 132 patients were consecutively enrolled into the study. 100 patients had a histo-pathologically confirmed case of acute Appendicitis. The remaining 32 cases with negative surgical-pathological evaluation were used as a control group. The mean age was 31.3 (6;87) years for the Appendicitis group and 26.4 (8;80) years for the control group. The Appendicitis group had 54% female and 46% male patients. The control group had 78.1% female patients and 21.9% male patients (Table 2).

The clinical outcome measure, Alvarado Score in its modified version, was performed on all study participants [18,19]. The necessary clinical information was obtained via the local clinical information system. The clinical components of the modified Alvarado score had to be explicitly mentioned in the clinical history (positive or negative).

The ultrasound examination of the abdomen was standardized to internal guidelines. All images and reports were retrospectively reanalyzed according following criteria: Appendix found, axial Appendix diameter, Appendix compressible, Appendix stone, abscess formation, perforation, primary gynecological/urological findings, large bowel inflammation, small bowel inflammation, inflamed mesenteric fatty tissue, free fluid. All endpoints were classified according to an internal consensus and evaluated by two radiologists with 4 and 10 years of experience in gastrointestinal ultrasound. The axial Appendix diameter was measured perpendicular to the longitudinal axis at its widest diameter from outer wall to outer wall. Inflammation of the mesenteric tissue was defined as a hyperechogenic, well-defined fatty structure in

European Journ	al of Radiology	98 (2018)	174-178
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Table 2	
Descriptive	Statistics.

Parameter	Cohort	Mean	Median
Age [years]	Appendicitis Group Control Group	31.3 26.4	22 (6;87) 21 (8;80)
Gender [%]	Gender	Appendicitis Group	Control Group
	female male	54 46	78.1 21.9
Modified Alvarado score	Cohort	Mean	Median
	Appendicitis Group Control Group	6.5 2.8	6.5 (4;9) 2 (0;7)
Appendix diameter [mm]	Cohort	Mean	Median
	Appendicitis Group Control Group	10.2 6.2	10 (5;17) 7 (3;9)

the root of the mesentery with displacement of bowel loops and hyperemia. Mesenteric lymphadenopathy was defined as ≥ 3 oval/round lymph nodes with a diameter of ≥ 10 mm and diminished fatty hilum. The diagnosis of perforation had to be confirmed by CT imaging or surgery with histo-pathology results.

2.2. Ultrasound technique

All examinations were performed using the latest generation of GE Logiq E9 ultrasound machines (General Electric Healthcare, Little Chalfont, UK). A complete abdominal Ultrasound examination using a 4 Hz (C1-5) convex transducer was followed by a focused examination of the bowels using a 9 Hz (9L) linear transducer. Color duplex sonography was regularly used to visualize parenchymal organ perfusion and hyperemia. The abdominal ultrasound was internally standardized and performed by board certified radiologists or supervised residents. The above mentioned ultrasound criteria were routinely examined and explicitly mentioned in the final report.

2.3. Statistical analysis

For statistical analysis R software by R Core Team (URL http:// www.R-project.org/) was used. Two models were computed depending on the visualization of the Appendix (Table 3). To impute for missing values of Appendix diameter, compressibility and Appendix stone, imputation was performed using the random forest method (missForest R package) [22].

Logistic regression analysis was performed to identify significantly contributing sonographic criteria for score generation. Threshold analysis of the new score evaluated cut-off values to determine the diagnosis of acute Appendicitis in accordance with the histo-pathological gold standard.

Model selection was conducted using bestglm R package, with Morgan and Tatar's method of complete enumeration [23]. Results were based on Bayesian Information Criterion. A ROC-analysis was performed computing sensitivity and specificity. After cross validation using the R package cvAUC, the two regression equations were combined to find the optimal threshold for the Appendicitis group and control group.

3. Results

100 patients had a histo-pathologically confirmed case of acute Appendicitis. The remaining 32 patients with a confirmed alternative diagnosis served as a control group. Descriptive statistical analysis is depicted in Table 2. The mean modified Alvarado score was 6.5 (4–9) points for the Appendicitis group and 2.8 (0–7) points for the control

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