Accuracy in Diagnosis of Acute Appendicitis by Comparing Serum C-Reactive Protein Measurements, Alvarado Score and Clinical Impression of Surgeons

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Abstract

Objective : To compare the accuracy of a surgeon's clinical diagnosis of acute appendicitis with Alvarado's predictive model and C-reactive protein (CRP) measurements.

Method : The records of 231 adult patients between 14-75 years admitted to the hospital with suspected appendicitis from August 1999 to November 2001 were studied prospectively. Serum CRP measurements (217 patients) and Alvarado scores (231 patients) were performed before operations but were not taken into account prior to the decision to perform a laparotomy to compare the surgeon's clinical diagnosis.

Results : Based on the surgeon's clinical diagnosis, 193 patients underwent surgery, and 38 patients were observed. Histopathologic findings found acute appendicitis, confirming the surgeon's clinical impression, in 178 patients (positive predictive value = 92%) and normal appendix in 15 patients. Of the observed patients, 8 subsequently underwent operation for appendicitis (negative predictive value = 79%). Compared with the surgeon's clinical diagnosis (sensitivity 96% and specificity 67%), diagnosis based on an Alvarado score of ≥ 7 had a lower sensitivity (79%) and that based on CRP of > 10 mg/l a much lower sensitivity (62%) and lower specificity (56%). Overall accuracy of these three diagnostic modalities were 90 per cent, 72 per cent and 61 per cent, respectively. However, median serum CRP value increased from 5 mg/l (range 3-188 mg/l) in patients with normal appendix, to 14 mg/l (range 3-222 mg/l) in patients with non-perforated appendicitis and 65 mg/l (range 3-213 mg/l) in patients with perforated or gangrenous appendicitis.

Conclusion : The clinical assessment in diagnosing appendicitis by an experienced surgeon remains reliable and superior to either Alvarado score or CRP measurement. Nevertheless, Alvarado

score and serum CRP measurements may be of value to the inexperienced surgeon, and a high Alvarado score and serum CRP should not be ignored.

Key word : Appendicitis, C-Reactive Protein, Alvarado Score

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Acute appendicitis is the most common cause of acute abdominal pain and surgery for appendectomy is the most frequent abdominal operation. The disease occurs at all ages but infrequently in very young children and elderly persons, with the highest incidence between 20 and 30 years of age[1,2]. The goal of surgical treatment is removal of the inflamed appendix prior to perforation, with a minimal number of negative appendectomies. Pre-operative diagnosis of acute appendicitis remains challenging despite improvement in history taking and clinical examination, clinical diagnosis scoring and new imaging techniques such as ultrosonography[3] and computed tomography[4,5].

Diagnosis scores are useful and easy methods that help a surgical decision to be reached. Ohmann et al[6]. evaluated the performance of 10 different diagnosis scoring systems for acute appendicitis using the following criteria : 1) an initial negative appendectomy rate of 15 per cent or less, 2) a potential perforation rate of 35 per cent or less, 3) an initial missed perforation rate of 15 per cent or less, and 4) a missed appendicitis rate of 5 per cent or less. The scoring system described by Alvarado[7] was the only scoring system that fulfilled all four of these criteria. A high score was found to be an easy and satisfactory aid to early diagnosis of acute appendicitis.

C-reactive protein (CRP) is an adjunctive laboratory study useful in the diagnosis of acute appendicitis. A very high level of CRP may indicated severe infection such as perforated or gangrenous appendices. It is easily obtainable and inexpensive with rapid results. CRP is not disease-specific because of the synthesis by hepatocytes during the acute-phase response to inflammation, but offers valuable diagnostic information.

The aim of this study was to compare the diagnostic accuracy of serum CRP level, Alvarado score and surgeon's clinical evaluation in the diagnosis of acute appendicitis.

PATIENTS AND METHOD

This was a prospective data collection study, performed on 231 adult patients between 14 and 75 years of age who were admitted with suspected appendicitis to Songklanagarind Hospital, southern Thailand, from August 1999 to November 2001. The exclusion criteria were : 1) patients under 14 years or over 75 years of age, 2) patients who were HIV-positive, 3) patients under treatment with steroids, chemotherapy or radiation, and 4) patients presenting with abdominal pain and palpable right lower quadrant mass because they were under another investigation.

Patients admitted to the hospital between 8.30 a.m. and 11.00 p.m. with suspected appendicitis were examined by a staff surgeon followed by some routine laboratory tests (white blood cell count, urinalysis). There were 173 patients (74.9%). From 11.00 p.m. - 8.30 a.m. patients were evaluated by senior general surgery residents. There were 58 patients

(25.1%). On initial evaluation, the patients were placed into two categories: I, acute appendicitis unequivocally; II, equivocal for appendicitis. Patients in category II were admitted to the general surgery service for observation without surgery except if they showed worsening signs such as fever or progression of abdominal pain, in which case they underwent laparotomy. Patients in category I and category II answered a questionnaire about their disease history. For each patient the symptoms, signs and laboratory results were recorded and graded with the Alvarado score (Table 1). Serum CRP concentrations were measured before the operation by Behring Nephelometer 100, and analyzed using Nephelometer N. Latex CRP monokit. A CRP concentration above the detection level of 10 mg/l was taken to be çraisedé. Patients with a surgeon's clinical diagnosis of appendicitis were taken to surgery regardless of the Alvarado score or serum CRP concentrations (Fig. 1). Specimens were evaluated histologically for acute process. The diagnosis was based on operative findings and the histologic presence of neutrophilic infiltration through the wall and within the muscularis of the appendix. Patients in category II who did not undergo surgery were considered as not having appendicitis. According to operative and histopathologic findings or the lack of a requirement for surgery, true and false surgeon's clinical diagnosis, true and false positive or negative Alvarado scores and serum CRP results were determined. Sensitivity, specificity, positive and negative predictive values, accuracy and receiver operating characteristics (ROC) curve of Alvarado scores and serum CRP concentrations were calculated.

Table 1. Alvarado score based on symptoms, signs and laboratory findings.

Variable	Alvarado score Score
Symptoms	
Migration of pain	1
Anorexia	1
Nausea, vomiting	1
Signs	
Tenderness in right lower quadrant	2
Rebound pain	1
Laboratory	
Fever (BT ≥ 37.8°C)	1
WBC > 10,000/mm^3)	2
Shift to the left (PMN > 75%)	1
Total scores	10

Cut-off point: ≤ 4 = exclusion; 5-6 = monitoring; ≥ 7 = operation

RESULTS

Of the 231 patients who presented with suspected appendicitis, there were 134 women and 97 men, median age 27 years (range 14-75 years). Most of the patients (46%) were aged between 14 and 25 years (Fig. 2). Following history taking and physical

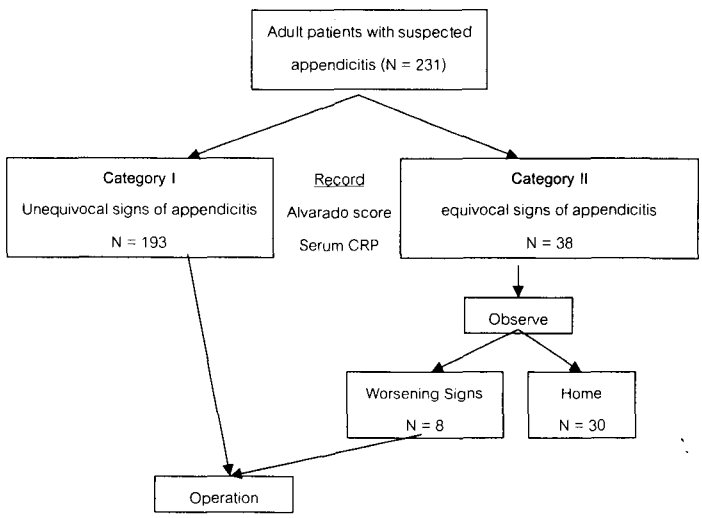

Fig. 1. Algorithm for management of suspected appendicitis.

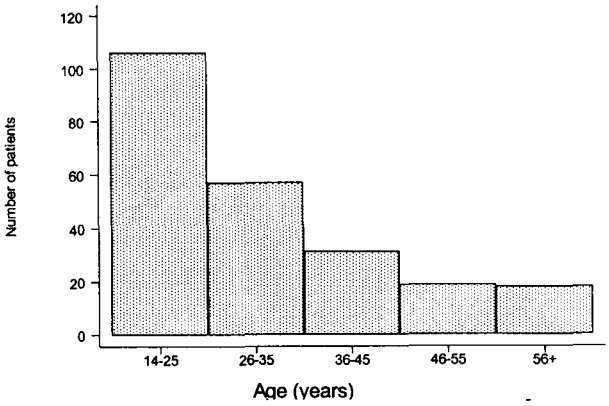

Fig. 2. The age distribution of acute appendicitis, August 1999 to November 2001.

examination, 193 patients underwent surgery with a clinical diagnosis of acute appendicitis (Category I) and 38 patients were kept for further observation (Category II). Based on the final pathologic examination, the diagnosis of acute appendicitis was confirmed in 178 patients, 5 with gangrenous appendix, 20 with perforated appendix and 153 with non-perforated appendix, while 15 patients were normal. Thus, the clinical impression of the surgeons was true in 178 patients, giving a positive predictive value (PPV) of 92.2 per cent, and false in the remaining 7.8 per cent. The PPV of the staff surgeon was slightly, but not significantly, higher than that of the senior resident. There was no statistically significant difference in histopathologic findings between the sexes ($p = 0.84$). Thirty-eight patients with equivocal signs of appendicitis were observed and given a repeat examination by the staff surgeon. Because of worsening signs, 8 patients were taken to surgery, 7 with non-ruptured acute appendicitis and 1 with ruptured appendix, while 30 did not undergo an operation (Table 2). Thus the negative predictive value of the surgeons' clinical examination was 79 per cent, and overall accuracy 90 per cent.

Alvarado scores were recorded for all 231 patients. Using a cut-point of ≥ 7 to indicate a positive result, the sensitivity (79%), negative predictive value (44%) and overall accuracy (72%) were lower than these parameters based on the surgeon's decision-making (Table 3).

Pre-operative serum CRP measurements were made on a subset of 217 patients, 182 of the 193 who underwent surgery initially and 35 of the 38 who were initially observed. Using a cut-point of > 10 mg/l to indicate a positive result, all parameters were lower than the corresponding parameters using the Alvarado

Table 2. Results and histopathologic findings among the 231 patients.

Surgeon's initial decision	Gangrene	%	Perforated	%	Non-perforated	%	Not appendicitis*	%	Total	%
Surgery	5		20		153		15		193	84
Observation	0		1		7		30		38	16
Total	5	2	21	9	160	69	45	19	231	100

* Found at surgery to have healthy appendix or observed and not subsequently sent for surgery.
Percentages may not add to 100 because of rounding.
Sensitivity 96%, Specificity 67%, PPV 92%, NPV 79%, Accuracy 90%.

Table 3. Alvarado scores according to histopathologic findings.

Alvarado score	Gangrene	%	Perforated	%	Non-perforated	%	Not appendicitis	%	Total	%
7-10	2		19		126		14		161	70
1-6	3		2		34		31		70	30
Total	5	2	21	9	160	69	45	19	231	100

Percentages may not add to 100 because of rounding.
Sensitivity 79%, Specificity 69%, PPV 91%, NPV 44%, Accuracy 72%.

score and much poorer than those based on the surgeon's decision-making (Table 4). However, the levels of CRP increased progressively from patients with normal or non-operated appendix (median 4.8 mg/l, range 3-188 mg/l) to non-perforated (median 13.8 mg/l, range 3-222 mg/l) and perforated or gangrenous appendices (median 65.3 mg/l, range 3-213 mg/l). Almost two-thirds of patients (16/25) with perforated or gangrenous appendices had CRP levels in excess of 50 mg/l.

The correspondence between the surgeon's decision-making and the Alvarado score and serum CRP levels is shown in Table 5. Among the patients initially observed, only one of the 14 patients with negative results on both Alvarado score and CRP level had appendicitis, compared with 7 of the 22 with at least one positive result.

DISCUSSION

In the present study, the clinical impression of the experienced surgeons was more accurate than both CRP and the Alvarado score in diagnosis of appendicitis in adults. The authors found that a normal CRP level (0-10 mg/l) did not effectively rule out the diagnosis of appendicitis (Table 4: 67 false negatives out of 90 patients) and at levels above 10 mg/l the predictive ability was only modest (Table 5: 18 false positives out of 127 patients). The CRP is synthesised by hepatocytes and is normally present as a trace constituent of the plasma, but mostly less than 10 mg/l in healthy adults[8,9]. The rate of CRP synthesis and secretion increases after inflammation, myocardial infarction and surgical trauma within 8 hours and peaks in 24 to 48 hours. When symptoms of appendicitis proceed rapidly, a patient's level of CRP may be normal on admission, so CRP values may not be valuable for diagnosing early appendicitis. However, serial measurement of CRP has been found to be useful[10,11].

Application of the Alvarado's predictive model for the diagnosis of acute appendicitis in adults is non-invasive and requires no special equipment. According to the analysis of Alfredo Alvarado on 305 patients, a score of 5 to 6 was compatible with appen-

Table 4. Serum C-reactive protein (CRP) levels according to histopathologic findings.

CRP level (mg/l)	Gangrene	%	Perforated	%	Non-perforated	%	Not appendicitis	%	Total	%
> 10	4		20		85		18		127	59
0-10	0		1		66		23		90	41
Total	4	2	21	10	151	70	41	19	217	100

Percentages may not add to 100 because of rounding.
Sensitivity 62%, Specificity 56%, PPV 86%, NPV 34%, Accuracy 61%.

Table 5. Cross-classification of patients by surgeon's initial decision, Alvarado score and serum C-reactive protein level.

Alvarado score	C-reactive protein (mg/l)	Surgeon's initial decision-making				Total
		Surgery		Observation		
		Appendicitis	Not appendicitis	Appendicitis	Not appendicitis	
≥ 7	> 10	83	3	3	2	91
≥ 7	≤ 10	50	3	2	4	59
≥ 7	ND	9	1	-	1	11
< 7	> 10	21	5	2	8	36
< 7	≤ 10	14	3	1	13	31
< 7	ND	1	-	-	2	3
Total		178	15	8	30	231

ND = not determined

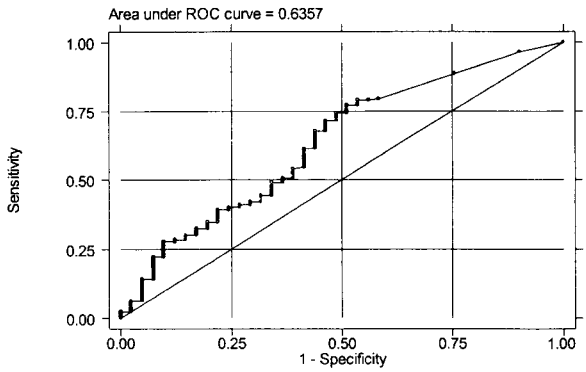

Fig. 3. **Receiver operating characteristic curve evaluation of CRP in the diagnosis of appendicitis. AUC = 0.64.**

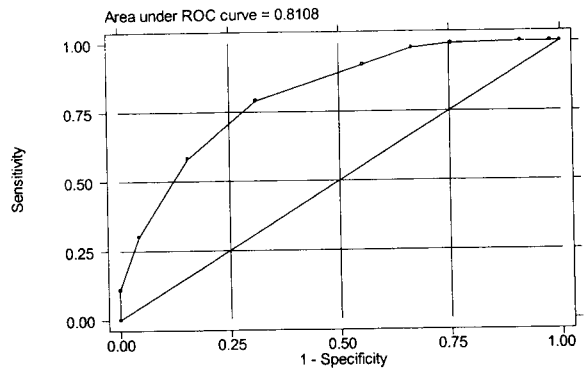

Fig. 4. **Receiver operating characteristic curve evaluation of the Alvarado score, AUC = 0.81.**

dicitis, a score of 7 to 8 indicated probable appendicitis and a score of 9 to 10 indicated a very probable appendicitis[4]. Wade et al[12] found that 76 per cent of patients with appendicitis had an Alvarado score higher than 6, whereas only 38 per cent of those who did not have appendicitis had a score higher than 6. They believed a score higher than 6 could clearly distinguish those who needed urgent surgery from those who could be observed[13,14]. The proportions in the presented patients were closely similar to those of Wade, 79 per cent among those with appendicitis and 31 per cent among those without.

Gwynn[14] used the Alvarado score as a diagnostic test and to assess the effectiveness of a computed tomography scan as a supplemental tool in the evaluation of acute appendicitis. They found that in a positive diagnosis of acute appendicitis, 91.6 per cent scored 5 or greater, and the oldest (60-80 years) and youngest (0-10 years) age groups were more likely to be falsely diagnosed. Some studies had a high false-positive rate in women[15]. Among the presented patients, 98 per cent of those with appendicitis had an Alvarado score of 5 or higher.

The results of scoring and CRP level obviously depend on the selection of the cut-off point. The receiver operating characteristic (ROC) curve displays the sensitivity of a test as a function of specificity. The area under the curve indicates the ability to discriminate between patients who do and do not have appendicitis. An optimal test result gives a value of 1, and a useless test result gives a value of 0.5. In the present study the area under the ROC curve was 0.64 for CRP (Fig. 3) and 0.81 for Alvarado score (Fig. 4), which confirms that the Alvarado score yielded better discrimination than CRP.

The equivocal cases are interesting because the Alvarado score and, to a lesser degree, CRP level show some ability to distinguish appendicitis from normal. However, the 38 observation cases are too few to draw a firm conclusion and this issue needs to be studied further.

In a study evaluating clinical assessment alone in diagnosing appendicitis, accuracy ranged from 83 per cent to 97 per cent with values correlating with the surgeon's experience[16]. Despite recent advances in new technology such as the computed tomography (CT) scan, ultrasonography or laparoscopy in the diagnosis of acute appendicitis, improvement in outcome has not been shown with routine use of these new technologies[16-19] and all of them should be acquired for reasonable cost, especially in a developing country. New tests have to be carefully evaluated because they are intended to assist and not replace a surgeon's judgement. A prospective study of 118 children found that current clinical practice was more accurate than the modified Alvarado score in the diagnosis of acute appendicitis[20]. Routine history and physical examination remain the most effective and practical diagnostic modalities[21]. Patients in this study were chosen between ages 14 - 75 years because

in the extreme age groups, an accurate history and physical examination is more difficult to obtain, leading to a higher probability of erroneous diagnosis.

On the basis of the present results, the authors conclude that clinical assessment by experienced surgeons and routine laboratory tests (CBC, urine exam) remain the most reliable diagnostic asset for evaluating a patient with suspected acute appendicitis. Overall, clinical assessment yielded an accuracy of 90 per cent. Alvarado score and serum CRP measurement had accuracies of 72 per cent and 61 per cent respectively, neither one as accurate as an experienced surgeon's clinical impression. They should be reserved for non-surgeons or inexperienced surgeons. However, a high diagnostic score or high serum CRP level should not be ignored. Alvarado score and serum CRP may be useful for excluding appendicitis in equivocal cases.

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การศึกษาความแม่นยำในการวินิจฉัยโรคไส้ติ่งอักเสบ โดยการเปรียบเทียบค่า C-reactive protein ในกระแสโลหิต, Alvarado score และการตรวจร่างกายโดยศัลยแพทย์

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วัตถุประสงค์ : เพื่อศึกษาวิธีที่จะช่วยในการวินิจฉัยโรคไส้ติ่งอักเสบได้อย่างถูกต้องรวดเร็ว ประหยัดและปลอดภัย โดยการเปรียบเทียบค่า C-reactive protein (CRP) ในกระแสเลือด, Alvarado score และการตรวจวินิจฉัยโรคโดยศัลยแพทย์

วิธีการศึกษา : ได้ทำการศึกษาผู้ป่วยที่อายุระหว่าง 14-75 ปี ที่รับเข้ารักษาในหอผู้ป่วยศัลยกรรมด้วยอาการปวดท้องฉับพลันและแพทย์ให้การวินิจฉัยว่าเป็นหรือน่าจะเป็นโรคไส้ติ่งอักเสบ ระยะเวลาศึกษาตั้งแต่ 1 สิงหาคม 2542 - 30 พฤศจิกายน 2544 พบผู้ป่วยจำนวน 231 ราย โดยผู้ป่วยทุกรายจะถูกบันทึก Alvarado score และมีอยู่ 217 ราย ที่อนุญาตให้แพทย์ตรวจเลือดเพื่อหาค่า CRP, ศัลยแพทย์จะให้การรักษา และนำผู้ป่วยไปผ่าตัดโดยไม่สนใจค่า Alvarado score และ CRP จะถือว่าผู้ป่วยเป็นไส้ติ่งอักเสบโดยดูจากผลการตรวจพยาธิวิทยาของไส้ติ่ง

ผลการศึกษา : จากผู้ป่วยทั้งหมด 231 ราย วินิจฉัยจากการตรวจร่างกายโดยศัลยแพทย์ว่าเป็นไส้ติ่งอักเสบและนำไปผ่าตัดจำนวน 193 ราย อีก 38 รายรับไว้สังเกตดูอาการเนื่องจากไม่แน่ใจว่าเป็นไส้ติ่งอับเสบหรือไม่ ในจำนวน 193 รายที่ผ่าตัด ผลการตรวจทางพยาธิพบว่าเป็นไส้ติ่งอักเสบจริง 178 ราย (positive predictive value 92%) และเป็นไส้ติ่งปกติ 15 ราย ผู้ป่วย 38 รายที่สังเกตอาการพบว่ามีอยู่ 8 รายที่มีอาการชัดเจนในเวลาต่อมาต้องนำไปผ่าตัดไส้ติ่งอักเสบ และผลการตรวจทางพยาธิวิทยาพบว่าเป็นไส้ติ่งอักเสบจริงทั้งแปดราย (negative predictive value 79%)

เมื่อเปรียบเทียบการวินิจฉัยโรคไส้ติ่งอักเสบทั้งสามวิธีพบว่าการวินิจฉัยโดยศัลยแพทย์จะมี sensitivity 96%, specificity 67% ถ้าวินิจฉัยโดยอาศัยข้อมูล Alvarado score $\geq$ 7 จะมี sensitivity 79% และวินิจฉัยโดยอาศัยค่า CRP > 10 mg/l จะมี sensitivity 62% และ specificity 56% เมื่อคำนวณหาความแม่นยำในการวินิจฉัยโรคไส้ติ่งอักเสบในทางสถิติจะพบว่าเมื่อวินิจฉัยโดยศัลยแพทย์ที่มีประสบการณ์จะมีความแม่นยำ 90%, ขณะที่ Alvarado score และ CRP ให้ความแม่นยำ 72% และ 61% ตามลำดับ

ค่า CRP โดยเฉลี่ยของผู้ป่วยไส้ติ่งปกติจะอยู่ที่ 5 mg/l, ผู้ป่วยไส้ติ่งอักเสบมีค่าเฉลี่ย 14 mg/l และผู้ป่วยที่ไส้ติ่งแตกหรือเน่าจะมีค่าเฉลี่ย CRP สูงที่สุดคือ 65 mg/l

สรุป : การวินิจฉัยโรคไส้ติ่งอักเสบโดยศัลยแพทย์ที่มีประสบการณ์ยังคงมีความถูกต้องมากกว่า การใช้ Alvarado score หรือการหาค่า CRP ในกระแสโลหิต อย่างไรก็ตามค่า Alvarado score และ CRP ก็ยังมีประโยชน์เนื่องจากทำได้เร็ว ราคาไม่แพง อาจเหมาะสำหรับแพทย์เวชปฏิบัติทั่วไป หรือศัลยแพทย์ที่มีประสบการณ์ไม่มาก กรณีที่คะแนน Alvarado score หรือค่า CRP ที่สูง อย่าละเลยผู้ป่วยเนื่องจากมีโอกาสเป็นไส้ติ่งอักเสบสูง

คำสำคัญ : ซี-รีแอ็คทีฟโปรตีน, อาว์วาราโด้ สกอร์, ไส้ติ่งอักเสบ

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