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# Correlation of alvarado scoring system with C - Reactive protein and leukocytes in the diagnosis of acute appendicitis

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**Abstract**

In this study, we aimed to investigate the correlation of Alvarado scoring with C-reactive protein and leukocytes and the reliability of Alvarado scoring, and to guide clinicians for patient management. This study was planned as a prospective study. Data of the patients who presented to the emergency department with abdominal pain and diagnosed with acute appendicitis, and the control group were examined by the researchers. After a detailed physical examination, patients' Alvarado scoring parameters and laboratory outcomes were recorded. Pathologic outcomes of the patients who were considered to have acute appendicitis and operated were studied. A different pathology other than appendicitis was found in 13 (15.1%) of 86 patients who were considered to have acute appendicitis and operated (negative appendectomy). According to the pathologic outcomes of the patient group, the most common cause of acute appendicitis was found to be fecalloids by 84.9%. Whereas simple appendicitis was observed in 85% of the patients, perforation was found in 8.2%. The most common finding of physical examination was right iliac fossa (95.8%), while the most common symptom was nausea / vomiting (67.1%) the in the cases of acute appendicitis. Among the Alvarado scoring parameters, fever was the least common symptom by 12.4%. In our study, we found a significant correlation between Alvarado scoring and leukocytes both in patients and control groups. Whereas there was no correlation between Alvarado scoring and C-reactive protein in the patient group, there was a correlation between these two parameters in the control group. There was a weak negative correlation between Alvarado scoring and acute appendicitis. Although Alvarado scoring has been reported to be a guiding scoring system in management of patients considered to have acute appendicitis, in our study this scoring was found to be statistically insignificant. Alvarado scoring alone is not sufficient in establishing a diagnosis, and the diagnosis should be supported by laboratory tests or imaging methods.

**Keywords:** Alvarado, appendicitis, CRP, leukocyte

## Introduction

Acute appendicitis (AA) is one of the conditions that are seen as acute abdominal manifestation in all age groups, and require emergency surgery. Especially in young population, AA is more common between 10 and 30 years of age. Approximately 7% of general population is diagnosed with acute appendicitis in a certain period of life, and operated [1]. With early diagnosis, the rates of morbidity and mortality are low in AA [2]. AA may be encountered with different complaints, clinical findings, and laboratory outcomes. Complaints and finding may be confused with other diseases than can cause abdominal pain, causing difficulty in the diagnosis. This in turn may lead to delay in the diagnosis of AA or unnecessary negative appendectomy. Studies have shown various complications developing due to negative appendectomy [3]. Delayed diagnosis of AA increases possibility of perforation. Morbidity and mortality are more likely in the case of perforation. Therefore, many patients with suspected AA are taken to the operation without delaying. It has been reported that normal appendix vermiformis is encountered between 13% and 36% following appendectomy [4,5]. The most important cause of AA is lumen obstruction. Stool stones known as fecalith are the most common of lumen obstruction. The other causes may include tumors, vegetable and fruit stones, intestinal parasites, obstruction of the lumen by barium after barium imaging, and lymphoid tissue hypertrophy [6,7]. Fecaliths are responsible for the etiology in simple appendicitis by 40%, in non-perforated gangrenous appendicitis by 65%, and in perforated gangrenous appendicitis by 90% [7,8]. Easy to use, rapid and inexpensive methods are needed in order to establish the diagnosis, and reduce

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the rate of negative laparotomy, thus preventing the possible complications. In addition to the clinical findings and laboratory outcomes of the patient; scoring systems, ultrasonography (USG), computed tomography (CT), magnetic resonance imaging (MRI) and diagnostic laparoscopy are among the diagnostic methods [9]. Among the scoring systems, Alvarado scoring (AS) was described in 1986. AS is a clinical scoring system consisting of medical history, physical examination findings, and laboratory outcomes [9,10]. Patients with a total score ≤ 4 points are considered to have a low risk, patients with a score between 5 – 6 points are suggested to be followed-up and undergo further investigations, and those with a score ≥ 7 point should be evaluated for operation [11]. Some studies have reported the AS alone is an insufficient test to establish a diagnosis, but it may be a guiding scoring tests which can be used in clinical practice if AS is supported with imaging methods and other possible potential laboratory tests. Leukocyte and C-reactive protein (CRP) are the most used tests in the diagnosis of AA. Studies have been conducted to investigate leukocyte and CRP levels in the diagnosis of AA in emergency departments [12,13]. These parameters rapidly raise in the cases of acute inflammation. Leukocyte count is usually elevated in the patients diagnosed with AA, but leukocyte elevation may be found also in other inflammatory diseases imitating AA. Leukocyte is not helpful enough for the diagnosis despite its high sensitivity, because its specificity is low [14,15]. CRP is another test helpful for the diagnosis and is an acute phase reactant [3,16]. Elevation of serum CRP level is manifested 6-12 hours after initiation of the inflammatory process [17]. There are AA cases with normal CRP levels due to late elevation of this parameters, and there have been misdiagnosed patients with high level of CRP which may be raised also in the disease groups progressing with inflammatory process [12,18]. There are publications in the literature reporting 98% sensitivity for a combination of increased leukocyte and CRP, and appendicitis is less likely in case of both parameters being within normal limits [19]. There are different opinions in the literature about whether the AS alone is sufficient in AA or should be supported by alternative methods. In this study, we studied reliability of AS in patients with suspected AA and we reviewed the correlation of AS, CRP and leukocyte for the diagnosis in patients who presented to emergency department with abdominal pain, and aimed to guide clinicians for emergency patient management.

## Material and Methods

The study was started after receiving the necessary approval from the Gaziosmanpasa University Medical School, Clinical Research Ethics Committee (14-KAEK-023). The study was designed as a prospective study. The stud y included a total of 150 patients including 130 patients who presented to the Gaziosmanpasa University Medical Faculty Hospital, Emergency Department (ED) with abdominal pain, and 20 patients who presented to Tokat Public Hospital with the same complaint and pathologically diagnosed with acute appendicitis between 15/08/2013 and 26/01/2016. Data of 73 patients with pathologic diagnosis of AA, and of the control group of 77 patients who were considered to not have AA after observation in the general surgery clinic were examined. All patients gave informed consent. Patients <18 years old and > 65 years, and pregnant were excluded from the study. After receiving informed consent from all patients, a detailed physical examination was performed from the time of admission to the ED. Patients' age, gender, vital findings, AS parameters, microbiological and biochemical laboratory parameters were recorded. Examination findings, symptoms, and laboratory outcomes in the scoring were evaluated and recorded. AS parameters are shown in Table-1. Patients' outcomes in the ED were also recorded. Pathologic outcomes of the patients operated with the presumed diagnosis of AA were recorded. Patients whom pathologic outcome was not AA, and those considered to have appendicitis, hospitalized by the general surgery clinic, but not operated and discharged after follow-up were included in the control group. Patients in the control group who presented to the ED with abdominal pain, and were discharged upon the outcome was not AA, and those discharged by the general surgery clinic after follow-up were called by phone, and questioned about whether they have been diagnosed in a different center or the hospitals where this study was conducted in the following period. For complete blood count, among the microbiological parameters white blood cell (WBC) and neutrophil were recorded. Among the biochemical parameters CRP values were recorded. Complete blood count parameters were analyzed using sysmex Xn 1000, and CRP was measured using Cobase-501 devices.

Statistical analysis of the data was performed using SPSS for Windows version 18.0. The correlations between AS and CRP, AS and WBC, AA and AS were tested using Chi-square independence test. $p<0.5$ values considered statistically significant.

**Table 1.** Alvarado Scoring Parameters

| | Parameters | Points |
|---|---|---|
| Symptoms | Migratory pain | 1 |
| | Anorexia | 1 |
| | Nausea/Vomiting | 1 |
| Signs | Right lower quadrant tenderness | 2 |
| | Rebaund | 1 |
| | Fever (>37.3$^0$) | 1 |
| Laboratory | Leukocytosis (>10000/mm3) | 2 |
| | Shift to the left of neutrophils (>%75 neutrophil) | 1 |
| **Total point** | | **10** |

## Results

Epidemiological data of the 150 patients evaluated within the scope of this study are given in Table 2.

**Table 2.** Epidemiological Distribution of the Patients

| Gender (Total=150) | Number | % |
|---|---|---|
| Female | 77 | 51.3 |
| Male | 73 | 48.7 |
| **Age** | Mean | Min.-Max. |
| | 30.73+12.25 | 18-65 |

Of the 150 patients, 73 (48.6%) were diagnosed with AA, while 77 (51.4%) were considered as the controls. Of the 73 patients evaluated in the AA group, 37 (50.6%) were female and 36 (49.4%) were male (F/M: 1.02 / 1). The mean age was found as 30.6 in general, 30.5 in male and 30.8 in female patients.

Of patients in the AA group, 33 aged between 18-25, 23 aged between 26-40, and 17 aged 41 and over. Majority (45.2%) of

the patients aged between 18-25 years. Evaluating AS scores of the AA group; 10.9% of the patients received 0-4 points, 35.6% received 5-6 points, and 53.5% received 7-10 points. Scoring points are given in Table 3.

**Table 3.** Acute Appendicitis Group Alvarado Scores

| Points | Number of Patients |
|---|---|
| 0-4 | 8 |
| 5-6 | 26 |
| 7-10 | 39 |
| **Total** | **73** |

When among AS parameters, clinical symptoms and vital signs of the AA group were examined; nausea was found in 67.1%, anorexia in 54.8%, and migration in 54.8% of the patients. Fever was observed in 12.4% and evaluated as the parameter with the lowest sensitivity. When among AS parameters, physical examination finding and laboratory parameters were analyzed; elevated leukocyte level was found in 79.4%, elevated neutrophil level in 75.3%, tenderness in the right iliac fossa in 95.8%, and rebound in 69.8% of the patients. Alvarado scoring outcomes of the AA group are given in Table 4.

**Table 4.** Alvarado Scoring Outcomes of the Acute Appendicitis Group

| Parameter | Number (73) | % |
|---|---|---|
| **WBC** | | |
| High | 58 | 79.4 |
| Normal | 15 | 20.6 |
| **Elevated neutrophil** | | |
| High | 55 | 75.3 |
| Normal | 18 | 24.7 |
| **Tenderness in the right iliac fossa** | | |
| Yes | 70 | 95.8 |
| No | 3 | 4.2 |
| **Rebound** | | |
| Yes | 51 | 69.8 |
| No | 22 | 30.2 |
| **Nausea** | | |
| Yes | 49 | 67.1 |
| No | 24 | 32.9 |
| **Anorexia** | | |
| Yes | 40 | 54.8 |
| No | 33 | 45.2 |
| **Migration** | | |
| Yes | 40 | 54.8 |
| No | 33 | 45.2 |
| **Fever** | | |
| Yes | 9 | 12.4 |
| No | 64 | 87.6 |

Appendicitis was found as a result of the pathological examination in 8 (23.5%) of 34 patients in AS 0-4 range, 26 (53%) of 49 patients in AS 5-6 range, and 39 (58.2) of 67 patients in AS 7-10 range. The correlation between AS and AA was studied with Chi-square test, and a weak and negative correlation was found between these two parameters ($p<0.05$). The results are given in Table 5.

**Table 5.** Correlation between Acute Appendicitis and Alvarado Scoring

| | OUTCOME | |
|---|---|---|
| | **Acute appendicitis** | **No appendicitis** |
| **Low (0-4)** | 8 | 26 |
| **Moderate (5-6)** | 26 | 23 |
| **High (7-10)** | 39 | 28 |
| **TOTAL** | 73 | 77 |

In contrary to what was expected, AS was not considered as significant in evaluation of patients who presented with abdominal pain for AA. When we examined AS points of 5 patients who we called by phone and learned that they have been diagnosed with AA in the following period; three of them were in the low risk group with 0-4 points, and two were in the high risk group with 7-10 points.

When among AS parameters, clinical symptoms and vital signs of the control group were examined; nausea was found in 75.3%, anorexia in 44.1%, migration in 29.8%, and fever in 20.8% of the patients. When among AS parameters, physical examination finding and laboratory parameters were analyzed in the control group; elevated leukocyte level was found in 58.4%, elevated neutrophil level in 53.2%, tenderness in the right iliac fossa in 87%, and rebound in 36.3% of the patients. Alvarado scoring outcomes of the AA group are given in Table 6.

**Table 6.** Alvarado Scoring Outcomes of the Control Group

| Parameter | Number (77) | % |
|---|---|---|
| **WBC** | | |
| High | 45 | 58.4 |
| Normal | 32 | 41.6 |
| **Elevated neutrophil** | | |
| High | 41 | 53.2 |
| Normal | 36 | 46.8 |
| **Tenderness in the right iliac fossa** | | |
| Yes | 67 | 87 |
| No | 10 | 13 |
| **Rebound** | | |
| Yes | 28 | 36.3 |
| No | 49 | 63.7 |
| **Nausea** | | |
| Yes | 58 | 75.3 |
| No | 19 | 24.7 |
| **Anorexia** | | |
| Yes | 34 | 44.1 |
| No | 43 | 55.9 |
| **Migration** | | |
| Yes | 23 | 29.8 |
| No | 54 | 70.2 |
| **Fever** | | |
| Yes | 16 | 20.8 |
| No | 61 | 79.2 |

Considering the parameters in the AA and control groups; nausea which was the most common symptom in both groups was not statistically significant in the diagnosis of AA ($p>0.05$). Again,

tenderness in the right iliac fossa which was the most common sign in both groups, was significantly higher in the AA group ($p<0.05$).

When AS-CRP correlation was examined in the AA group; CRP values were high in 50%, and normal in 50% of 8 patients with AS 0-4 points, high in 73.1% and normal in 26.9% of 26 patients with AS 5-6 points, and high in 58.9% and normal in 41.1% of 39 patients with AS 7-10 points. There was no statistically significant correlation between AS scores and CRP values of the AA group ($p>0.05$). When AS-CRP correlation was examined in the control group; CRP values were high in 34.6%, and normal in 65.4% of 26 patients with AS 0-4 points, high in 47.8% and normal in 52.2% of 23 patients with AS 5-6 points, and high in 85.7% and normal in 14.3% of 28 patients with AS 7-10 points. There was a statistically significant correlation between Alvarado scores and CRP values in the control group ($p<0.001$).

When AS-WBC correlation was examined in the AA group; WBC values were high in 37.5%, and normal in 62.5% of 8 patients with AS 0-4 points, high in 61.5% and normal in 38.5% of 26 patients with AS 5-6 points, and high in 100% 39 patients with AS 7-10 points. There was a statistically significant correlation between Alvarado scores and leukocyte values in the AA group ($p<0.001$). When AS-WBC correlation was examined in the control group; WBC values were high in 11.5%, and normal in 88.5% of 26 patients with AS 0-4 points, high in 65.2% and normal in 34.8% of 23 patients with AS 5-6 points, and high in 96.4% and normal in 3.6% of 28 patients with AS 7-10 points. There was a statistically significant correlation between Alvarado scores and leukocyte values in the group ($p<0.001$). Of all patients, 86 (57%) were considered to have AA and operated, 64 (43%) were not scheduled for operation, and discharged after follow up or because they were considered to not have AA. Operation status of the patients is given in Table 7.

**Table 7.** Evaluation of Patients' Operation Status

| | **Number** |
|---|---|
| Operated | 86 |
| Non-operated | 64 |
| **Total** | **150** |

Pathological examination of the 86 operated patients was reported as AA in 73 (84.9%) patients, while there was a different pathology other than appendicitis in 13 (15.1%) patients (negative appendectomy). Of these 13 patients, pathological examination was reported as follicular lymphoid hyperplasia in 4 (30.7%), appendix vermiformis showing luminal obliteration in 4 (30.7%) patients. The other outcomes included duodenal perforation, inflammatory bowel disease, acute salpingitis, acute cholecystitis and fibro inflammation in the appendix in each one patient. These 13 patients were assigned to the control group.

When pathology results of the AA group were examined; simple appendicitis was found in 62 (85%), and appendix perforation in 6 (8.2%) of the 73 patients. Whereas pathology result was necrotizing appendicitis in 5 (6.8%) patients. The cause of appendicitis was fecaloid in 62 (84.9%) of the 73 patients. Looking to the pathology outcomes, the most common cause of AA was fecaloid by 84.9%, while simple appendicitis was found in 85%, perforation in 8.2%, and necrotizing appendicitis in 6.8% of the patients.

A total of 64 patients in the control group who were considered to not have AA after emergency department evaluation or follow up in the general surgery clinic were called by phone and asked if they have been operated due to AA after discharge. Of these, five (7.8%) patients verbally reported that they had been operated in outer center with the presumed diagnosis of AA and their pathological reports were compatible with acute appendicitis.

When AS scores of these patients were examined; three patients were in the lower risk group with AS 0-4 points, and two patients were in the high risk group with 7-10 points.

## Discussion

AA is a pathology that may be encountered in all age groups as an acute abdominal manifestation, and require emergency surgery. Early diagnosis is crucial to prevent the possible postoperative complications and patients' comfort. Well received history and detailed physical examination are of paramount importance for the diagnosis of AA. Several studies have shown that AS alone is not sufficient for the diagnosis of AA and should be supported by various laboratory assays if available and with imaging methods if deemed necessary especially in patients with low and moderate risk [6,30,41]. Of the 73 patients in the AA group, 37 (50.6%) were female and 36 (49.4%) were male. It has been stated in the literature that AA is more common among women (F/M 1.2-1.3/1) [7]. We found F/M ratio as. While the mean age is 31.3 years in AA patients, the most common peak age has been reported as 22 years [16,26,29]. Studies by Shafi SM et al. and Bröker Me et al. reported the mean age of patients who underwent appendectomy due to AA between 20.3 and 27.1 years [20,21]. Sand M et al. found the mean age as 33.8 years [22], while Anielski R et al. reported the mean age as 36 years [23]. In the present study, the mean age was found as 30.6 years in study population, 30.5 years in male patients, and 30.8 years in female patients. We think the difference from the other studies might be resulted from the exclusion of patients < 18, and > 65 years old.

Looking to our negative laparotomy data, a different pathology other than appendicitis was observed in 13 (15.1%) of 86 operated patients. Studies by Inan et al. and Lee SL et al. reported this rate between 13% and 36% [4,5]. In their two separate studies, Flum et al. found the rate of negative appendectomy as 15.5% and 23.2%, respectively [24,25]. Ma et al. reported this rate as 18.2% [26], and Mohebbi et al. as 18.2% [27]. In our study, this rate was lower than reported in the literature. One of the most common complications encountered due to the delays in diagnosis and treatment of AA is appendix perforation which progresses with high rate of morbidity and mortality. Studies by Körner et al. and Flum DR et al. reported the incidence of appendix perforation as 25.8% [24,28]. In their meta-analysis evaluating 24 studies, Andersson et al. reported the rate of appendix perforation as 17.4% [29]. In their prospective study, M Inan et al. reported this rate as 3.7% [4]. We found the rate of perforation as 8.2%. The major mechanism leading to AA is development of obstruction in the appendix lumen due to various reasons. The most common cause of this obstruction are fecaliths that are also known as stool stones. Turhan et al. and Birnbaum et al. reported the incidence of fecaliths between 15% and 30% [30, 31]. In the present study, we found the rate of fecaliths as 84.9% with histopathological studies. In their study, Wagner et al.

reported two parameters with the highest sensitivity as tenderness in the right iliac fossa and vomiting after pain [32]. We found the rate of tenderness in the right iliac fossa as 95.8% and this was the highest-sensitivity parameter. In physical examinations, rebound was seen by 69.8%. Whereas nausea/vomiting was the most commonly observed symptom among the AS parameters in the AA group by 67.1%. Andersson et al. reviewed 24 study in 2004 and created a meta-analysis about clinical findings and laboratory outcomes in acute appendicitis [29]. In this analysis, two parameters with the highest diagnostic value were reported as rigidity in the right lower quadrant (involuntary defense) and migration. In our study, migration was the second most common symptom by 54.8% following nausea / vomiting. Fever (>37.3oC) was found only in 12.4% of our patients. Fever was more common in the control group (20.8%). We thought that this was resulted from the other inflammatory diseases leading to abdominal pain or various infectious reasons. We believe that, fever may be a leading sing rather in the complicated appendicitis cases.

Turhan et al. stated that anorexia is one of the most important clinical findings, and the presumed diagnosis should be revised in the lack of anorexia in a case of suspected appendicitis [31]. Old et al. reported the most commonly observed signs during the diagnosis of AA as abdominal pain and anorexia [33]. We found the rate of anorexia as 54.8%, same with the migration. Lau et al. found the sensitivity of leukocytosis as 81% in 1032 patients who underwent appendectomy [34]. Peltola et al. investigate the place of leukocyte count in the diagnosis of AA in 162 patients, and found the sensitivity of leukocytosis as 58% in the uncomplicated patients, and 76% in the complicated patients [35]. Looking to these rates, Peltola emphasized the importance of serial leukocyte count in patients with suspected AA. In their study on the importance of laboratory tests in the diagnosis of AA, Marchand et al. reported the sensitivity as 84% in the patients with leukocyte count ≥ 10.000/mm3 [36]. In their study on 212 AA patients, Kafetzis et al. accepted a leukocyte count ≥ 10.000/mm3 as significant for leukocytosis, and found the sensitivity of leukocytosis as 87.5% [37]. In our study, we found the leukocyte count ≥ 10.000/mm3 in 58 of the 73 patients in the study group and the sensitivity was 79.4%, consistently with the literature. As seen in these analyses, we believe that despite it has a high sensitivity in the diagnosis of AA, leukocyte alone is not sufficient alone because of its low specificity, although it may be a guiding parameter.

CRP which is among the reliable laboratory parameter in distinguishing acute bacterial inflammations from the other types has a non-specific and variable reliability [38,39]. CRP may be elevated due to infections and inflammatory diseases as well as because of several reasons including malignancies, trauma, autoimmune diseases, sepsis, burn, and ageing. It has a high sensitivity, but a low specificity [40]. Blood levels of CRP begin to raise 6 to 12 hours after the initiation of inflammatory process in AA, and further elevation of the control values with leukocyte count in the following hours supports the diagnosis of AA. In our study, we found no correlation between CRP values and AS scores of the 73 patients. We thought that this was resulted from the late elevation of CRP values during the inflammatory process of AA. Whereas, CRP was correlated with AS scores in 77 patients in the control group. Peltola et al. found significantly high CRP values 72% at least 12 hours after onset of the complaints in 162 patients with AA. This rate was reported as 83% in the complicated cases. Both or one of CRP and leukocyte levels have been found to be high in 88% of all AA cases. This rate was reported as 96% in the complicated cases [35]. In their study with 212 AA patients, Kafetzis et al. reported CRP sensitivity as 46% and specificity as 90% in appendicitis cases [37]. In our study, we found elevated CRP by 60.2% in our patients with AA.

## Conclusion

AA remains a condition with problems that maybe encountered in patients presenting to emergency departments with abdominal pain. AS may guide the diagnosis of AA. However, as seen in our study, there are patients with a high AS score (AS 7-10 points) but without appendicitis, as well as patients with a low score of AS (AS 0-4 points), but resulted in appendicitis. No statistically significant correlation was found between AS and CRP in the AA group. We found that tenderness in the right iliac fossa in the physical examination and in laboratory tests, leukocyte elevation is seen as the most guiding factor in AA evaluation findings from the AS parameters. According to our study results, AS is not a direct-acting scale for the diagnosis of AA but it is more appropriate to use it for guidance and diagnosis. Our results indicate that AS should be supported both with various laboratory tests and imaging methods in patients with suspected AA. Despite all these approach, if no any outcome could be achieved and suspicion of AA continues, the patient should be taken under observation and surgical consultation should be ordered.

**Competing interests**
*The authors declare that they have no competing interest*

**Financial Disclosure**
*The financial support for this study was provided by the investigators themselves.*

**Ethical approval**
*The study was started after receiving the necessary approval from the Gaziosmanpasa University Medical School, Clinical Research Ethics Committee (14-KAEK-023).*

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