ORIGINAL ARTICLE

An investigation into the factors predicting acute appendicitis and perforated appendicitis

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ABSTRACT

BACKGROUND: To investigate the factors predicting acute appendicitis (AAp) and perforated AAp in patients who underwent surgery with a preliminary diagnosis of AAp.

METHODS: Between May 2009 and December 2018, 1316 patients underwent appendectomy with a presumed diagnosis of AAp. To investigate the factors predicting AAp, patients were divided into two groups considering the histopathological presence of inflammatory changes in the appendix: AAp positive (AAp group; n=1043) and AAp negative (Non-AAp group; n=273). Also, to investigate the factors predicting appendiceal perforation, patients with AAp were divided into two groups considering the presence of perforation: non-perforated AAp (n=850) and perforated AAp (n=193). ROC curve analysis was used to identify optimum cut-off values of quantitative variables. The groups were compared using univariate analysis methods and parameters with a p≤ 0.20 were taken into a multivariate logistic regression model.

RESULTS: Multivariate analysis method related to factors predicting AAp showed that gender (male; p=0.034; OR=1.4), WBC (≥10.900; p=0.022; OR=1.5), MPV (≥29.1; p=0.006; OR=1.6), TBil (≥0.61; p=0.034; OR=1.4), CRP (≥0.725; p=0.002; OR=1.7), NLR (≥5.13; p=0.034; OR=1.5), PNR (<24.04; p=0.001; OR=1.9) and US findings (AAp+; p<0.001; OR=2.9) were independent factors for predicting AAp. Multivariate analysis method related to factors predicting appendiceal perforation showed that age (≥32 years; p<0.001; OR=2.5), TBil (≥0.67; p=0.046; OR=1.5), CRP (≥3.75; p<0.001; OR=3.0) and NLR (≥5.69; p=0.006; OR=1.8) were independent factors for predicting perforated AAp.

CONCLUSION: We believe that predicting both AAp and perforation will help the clinician evaluate patients who applied to the emergency unit with presumed diagnosis AAp. This approach will also contribute to reducing the negative appendectomy and perforation rates.

Keywords: Acute appendicitis; appendix vermiformis; negative appendectomy; perforated acute appendicitis; predicting factors.

INTRODUCTION

Acute appendicitis (AAp) is a very common disease, with a lifetime risk of approximately is 8.6% for males and 6.7% for females.[1] AAp represents the most common abdominal emergency, but its diagnosis can be a challenge even for experienced surgeons, as it is mainly based on anamnesis and proper clinical presentation. However, diagnosis based only on clinical presentation has a low sensitivity and specificity.[2] The gold standard treatment option for AAp is appendectomy which is generally considered a routine and safe procedure. AAp may cause a variety of symptoms and patients may seek medical attention at different time intervals after the onset of the symptoms.[3] Kulvatunyou et al.[4] showed that patients

Cite this article as: Akbulut S, Koç C, Şahin TT, Şahin E, Tuncer A, Demyati K, et al. An investigation into the factors predicting acute appendicitis and perforated appendicitis. Ulus Travma Acil Cerrahi Derg 2021;27:434-442.

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Ulus Travma Acil Cerrahi Derg 2021;27(4):434-442 DOI: 10.14744/tjtes.2020.60344 Submitted: 31.05.2020 Accepted: 07.06.2020

older than 50 years, prehospital admission later than 12 hours, fecalith as the etiology of the luminal obstruction and leukocyte count >15.000 cells/mm^3 were considered as risk factors for perforated AAp. However, these are non-specific findings and more specific bedside tests are required to discriminate between non-perforated and perforated AAp to guide the management of patients. Perforated AAp carries significant risks and has consequences that results in increased length of hospitalization, morbidity and mortality even with appropriate treatment.[3] This can be prevented by a simple surgery if timely diagnosis is performed before perforation develops. Management of patients with perforated AAp is very different from patients with non-perforated AAp; thus, distinguishing perforated AAp is important during the preoperative period. Technical improvements in imaging systems, such as ultrasonography (US) and computerized tomography (CT)[5,6] and the developments in clinical scoring systems and algorithms,[6,7] have reduced the incidence of negative appendectomy (normal appendix vermiformis) and perforated AAp. Furthermore, early surgery to manage perforated AAp also reduces morbidity and mortality related to perforation.[8,9] Determining such factors would help achieve a more accurate diagnosis reducing the negative appendectomy rate and its morbidity and predicting the existence of perforation, which influences management and may reduce morbidity and mortality.[10] This study was designed to investigate the factors predicting non-perforated AAp and perforated AAp in patients who underwent surgery with a preliminary diagnosis of AAp.

MATERIALS AND METHODS

Between May 2009 and December 2018, 1504 patients underwent an appendectomy in Department of Surgery, Inonu University Faculty of Medicine. The patients' data were obtained by entering two different ICD codes (610.130 and 610.131) in the electronic patient database system used in our hospital. Demographic, clinical and histopathological data of all patients were obtained from the patient archives and recorded to both excel and SPSS software. Patients younger than 17 years were excluded from this study. Patients who underwent laparotomy for any reason other than a preliminary diagnosis of AAp were excluded from this study. Therefore, patients who underwent incidental/prophylactic appendectomy for various indications were excluded from this study. Briefly, 72 patients who underwent incidental appendectomy during living donor hepatectomy, which is one of the most commonly performed surgical procedures in our transplant institute, and 32 patients who underwent incidental appendectomy during or after liver transplantation were also excluded from this study. Although the colonic specimens including appendix vermiformis, the patients who underwent right hemicolectomy for malignancy were also excluded from this study. Patients who underwent incidental appendectomy during gynecological surgery were also excluded from the study. In conclusion, 1316 patients who underwent appendectomy with the preliminary diagnosis of AAp were found to eligible for inclusion criteria in this study. The inclusion and exclusion criteria are summarized in the flowchart in Figure 1.

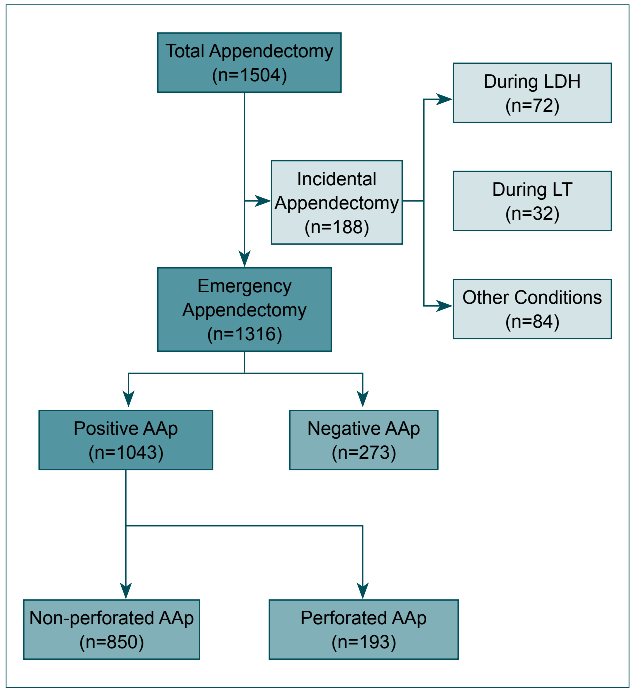

Figure 1. Demonstration of inclusion and exclusion criteria with flowchart scheme (AAp: Acute appendicitis; LDH: Living donor hepatectomy, LT: Liver transplantation).

Study Parameters

The following demographic and clinical parameters were used for the design of this study: age (years), gender (male, female), white blood cell (WBC), neutrophil, lymphocyte, platelets, red blood cell distribution width (RDW), platelet distribution width (PDW), mean corpuscular hemoglobin (MCH), mean platelet volume (MPV), mean corpuscular volume (MCV), total bilirubin (TBil), c-reactive protein (CRP), white cell neutrophil ratio (WNR), white cell lymphocyte ratio (WLR), neutrophil to lymphocyte ratio (NLR), platelets lymphocyte ratio (PLR), platelets neutrophil ratio (PLR), surgical choice (open, laparoscopic), ultrasonographic findings (positive, negative), length of the appendix (mm), width of the appendix (mm) and histopathological findings (non-perforated AAp, perforated AAp, normal appendix vermiformis).

Diagnostic Approaches

The diagnosis of AAp was made after evaluating the patient's history, physical examination, abdominal x-ray graphy, which is routinely performed on any patient who admits with acute abdominal pain, complete blood count parameters, CRP (most patients) and urine analysis together. Patients with the suspected diagnoses were followed up in the emergency department for repeated physical examinations and routine blood tests. A gynecologist was routinely consulted to exclude tub ovarian diseases in female patients of reproductive age who were not diagnosed with AAp by clinical and radiological instruments. To summarize, patients with an Alvarado score between 1 to 4 points were discharged with recommendations as the risk of AAp was very low. In patients with Alvarado score between 5 to 6 points, a detailed examination was performed with the US and abdominal CT when necessary. Patients with an Alvarado score of 7–10 points were considered to have AAp, and patients in the last group were operated on directly for appendectomy. In recent years, all patients with AAp who present to our emergency department are routinely evaluated by the abdominal US regardless of the Alvarado score. Almost none of the patients with obvious signs of AAp in our clinic were followed up with medical treatment, which is known as the non-operative treatment of AAp.

Objectives and Study Design

The first aim of this study was to compare the patients who had histopathological proven AAp with the patients who had histopathological proven normal appendix vermiformis concerning demographic and clinical features. For this purpose, patients were divided into two groups as AAp group (n=1043) and non-AAp group (n=273). The second aim of this study was to compare the patients who had histopathological proven non-perforated AAp with the patients who had histopathological proven perforated AAp in terms of demographic and clinical features. For this purpose, patients were divided into two groups as non-perforated AAp (n=850) and perforated AAp (n=193). We divided entire cohort into two groups based on their age (≥50 vs <50 years) and compared these groups in terms of demographic and clinical characteristics. This retrospective study was approved by the Inonu University Institutional Review Board for Non-interventional Studies (Approval No: 2019/10-22).

Statistical Analysis

The statistical analyses were performed using IBM SPSS Statistics v25.0 (Statistical Package for the Social Sciences, Inc, Chicago, IL, USA). The quantitative variables were expressed as Median and interquartile range (IQR). The qualitative variables were reported as number and percent (%). Kolmogorov–Smirnov was used to assess the normality of quantitative variables' distribution. Nonparametric Mann-Whitney U test was used to compare quantitative variables. Pearson's chi-square test was used to compare qualitative variables. Receiver operating characteristics (ROC) analysis was used to identify the optimum cut-off value of quantitative variables. The cut-off value for these variables was determined to obtain an ideal sensitivity and specificity. Variables with a significance of p≤0.20 in the univariate analyses were then taken into a multivariate analysis via Backward Stepwise logistic regression model to investigate whether an independent risk factor for AAp or perforated AAp. Hosmer–Lemeshow test was used for the goodness of fit of logistic regression models. P≤0.05 was considered a statistically significant value.

RESULTS

Overall Assessment

In this study, 1316 patients whose median age was 33 years (IQR=24) and underwent appendectomy with a presumed diagnosis of AAp were included. Of the patients, 711 (54%) were male (median 33 years; IQR=23) and 450 (46%) were female (median: 33 years; IQR=25.5) patients. Histopathologically, 1043 (79.3%) of the patients had inflammatory changes in appendectomy specimen, which was defined as AAp group, and 273 (20.7%) of the patients had no inflammation in appendectomy specimen, which was defined as non-AAp group (negative appendectomy). Appendiceal perforation was also detected in 193 (18.5%) of 1043 patients who were clinical and histopathologically proven to have AAp. Of the 1316 patients included in this study, 1188 were evaluated using the US and 774 (65.2%) of these patients had changes that might be compatible with AAp. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy value of the US to detect AAp were 70.0 %, 54.7 %, 86.3 %, 30.9 % and 67.0 %, respectively. Median WBC, Neutrophil, CRP, NLR, PNR, WLR, WNR and TBil values were 13.1 (IQR=6.4), 10.5 (IQR=6.7), 2.92 (IQR=9.0), 5.93 (IQR=7.0), 22.8 (IQR=15.6), 7.36 (IQR=7.5), 1.27 (IQR=0.25) and 0.7 (IQR=0.61), respectively. One thousand eighty-one (82.1%) patients underwent an open appendectomy and the remaining 235 (17.9%) patients underwent laparoscopic appendectomy. The median length of appendectomy specimens was 60 mm (IQR=30), and the median width was 10 mm (IQR=7).

Comparison of Patients with and without AAp

Patients were divided into two groups according to histopathological features: AAp (n=1043) and Non-AAp (n=273). Optimal cut-off points were calculated using ROC analysis to show whether demographic and clinical parameters predict AAp and after then, optimal cut-off points obtained for each parameter are shown in first column of Table 1. Univariate analysis revealed that there were statistically significant differences between the both groups concerning gender (p<0.001; OR=1.7), WBC (p<0.001; OR=2.9), neutrophil (p<0.001; OR=3.1), lymphocyte (p=0.001; OR=1.6), TBil (p<0.001; OR=1.9), CRP (p<0.001; OR=1.6), NLR (p<0.001; OR=2.7), PNR (p<0.001; OR=3.3), WLR (p<0.001; OR=2.5), WNR (p<0.001; OR=2.5), appendix length (p<0.001), appendix width (p<0.001) and ultrasonographic findings (p<0.001; OR=2.8). Detailed results of univariate analysis used to compare both groups are summarized in Table 1.

All parameters with a p≤0.20 were included in the logistic regression model to determine whether an independent factor for AAp. Multivariate analysis showed that gender (male; p=0.034; OR=1.4), WBC (≥10.900; p=0.022; OR=1.5), MPV (≥29.1; p=0.006; OR=1.6), TBil (≥0.61; p=0.034; OR=1.4), CRP (≥0.725; p=0.002; OR=1.7), NLR (≥5.13; p=0.034; OR=1.5), PNR (<24.04; p=0.001; OR=1.9), and the US

(App+; p<0.001; OR=2.9) were independent factors for predicting AAp. Detailed information about multivariate analysis is summarized in Table 2.

Comparison of AAp Patients with and without Perforation

Patients who had histopathologically proven AAp were divided into two groups considering appendiceal perforation status: non-perforated AAp (n=850) and perforated AAp (n=193). Optimal cut-off points were calculated using ROC analysis to show whether parameters predict perforated AAp and after then, optimal cut-off points obtained for each parameter are shown in first column of Table 3. Univariate analysis revealed that there were statistically significant differences between the both groups concerning age (p<0.001; OR=2.8), WBC (p=0.032; OR=1.4), neutrophil (p=0.014;

Table 1. Comparison of patients with and without AAp

Patients' characteristics	AAp (n=1043)	Non-AAp (n=273)	OR (95% CI)	p
Age (years) (≥28.5)	643 (61.6)	163 (59.7)	NS	0.558
Gender (male)	593 (56.9)	118 (43.2)	1.7 (1.3–2.3)	<0.001
White blood cell (≥10.900)	758 (72.7)	130 (47.6)	2.9 (2.2–3.8)	<0.001
Neutrophil (≥7.950)	771 (73.9)	130 (47.6)	3.1 (2.4–4.1)	<0.001
Lymphocyte (<1.655)	544 (52.2)	112 (41.0)	1.6 (1.2–2.1)	0.001
Platelets (≥234.000)	542 (52.0)	157 (57.5)	NS	0.102
Red blood cell distribution width (≥13.2)	631 (60.5)	176 (64.5)	NS	0.230
Platelet distribution width (≥16.05)	612 (58.7)	176 (64.5)	NS	0.082
Mean corpuscular hemoglobin (≥29.1)	555 (53.2)	144 (52.7)	NS	0.891
Mean platelet volume (≥8.35)	644 (61.7)	152 (55.7)	NS	0.068
Mean corpuscular volume (≥84.9)	633 (60.7)	170 (62.3)	NS	0.634
Total bilirubin (≥0.61)	692 (66.3)	139 (50.9)	1.9 (1.5–2.5)	<0.001
C-reactive protein (≥0.725)	796 (76.3)	180 (65.9)	1.6 (1.2–2.2)	<0.001
Neutrophil lymphocyte ratio (≥5.13)	659 (63.2)	106 (38.8)	2.7 (2.1–3.5)	<0.001
Platelets lymphocyte ratio (≥126.5)	644 (61.7)	152 (55.7)	NS	0.068
Platelets neutrophil ratio (<24.04)	601 (57.6)	78 (28.6)	3.3 (2.5–4.5)	<0.001
White cell lymphocyte ratio (≥5.77)	739 (70.9)	133 (48.7)	2.5 (1.9–3.4)	<0.001
White cell neutrophil ratio (<1.29)	606 (58.1)	98 (35.9)	2.4 (1.9–3.3)	<0.001
Ultrasonography findings (AAp+)	668 (70.0)	106 (45.3)	2.8(2.1–3.8)	<0.001

AAp: Acute appendicitis; OR: Odds ratio; CI: Confidence interval.

Table 2. Determination of factors predicting AAp using Backward stepwise logistic regression model

Variables	B	SE	Wald	Sig.	Exp(B)	95% CI for EXP(B)	
						Lower	Upper
Gender (male)	0.348	0.164	4.515	0.034	1.4	1.0	2.0
White blood cell (≥10.900)	0.419	0.183	5.223	0.022	1.5	1.1	2.0
Mean platelet volume (≥29.1)	0.450	0.164	7.506	0.006	1.6	1.1	2.0
Total bilirubin (≥0.61)	0.349	0.165	4.476	0.034	1.4	1.0	2.0
C-reactive protein (≥0.725)	0.535	0.172	9.651	0.002	1.7	1.2	2.4
Neutrophil lymphocyte ratio (≥5.13)	0.397	0.187	4.500	0.034	1.5	1.0	2.2
Platelets neutrophil ratio (≥24.04)	-0.643	0.201	10.268	0.001	1.9	1.3	2.9
Ultrasonography (App+)	1.056	0.158	44.606	0.000	2.9	2.1	3.9
Constant	1.145	0.092	155.012	0.000	3.1		

Hosmer and Lemeshow test sig. 0.250, Omnibus tests for model coefficients X^2: 150.14. sig: <0.001.

OR=1.5), lymphocyte (p<0.001; OR=1.9), TBil (p<0.001; OR=1.9), CRP (p<0.001; OR=3.9), NLR (p<0.001; OR=2.6), PLR (p<0.001; OR=2.4), PNR (p=0.034; OR=1.4), WLR (p<0.001; OR=2.5), WNR (p<0.001; OR=1.9), and appendix width (p<0.001). Detailed results of univariate analysis used to compare both groups are summarized in Table 3.

All parameters with a p≤0.20 were included in the logistic regression model to investigate whether an independent factor for perforated AAp. Multivariate analysis also showed that age (≥32 years; p<0.001; OR=2.5), TBil (≥0.67; p=0.046; OR=1.5), CRP (≥3.75; p<0.001; OR=3), and NLR (≥5.69; p=0.006; OR=1.8) were independent factors for predicting perforated AAp. Detailed information about multivariate analysis is summarized in Table 4.

Evaluation of Patients according to Age (<50 years versus ≥50 years)

Three hundred and six of the patients who underwent appendectomy were ≥50 years old, which consisted of 23.2 % of all patients. Eighty-three patients (43%) of the 193 patients with perforated AAp were ≥50 years and were considered to be a high-risk group in accordance with age. Furthermore, 34% of the patients (n=83) older than 50 years had perforated AAp. To sum up, low WBC (p=0.007) and lymphocyte (p<0.001)

Table 3. Comparison of AAp patients with and without appendiceal perforation

Patients' characteristics	Perforated App (n=193)	Non-perforated AAp (n=850)	OR (95% CI)	p
Age (years) (≥32)	136 (70.5)	392 (46.1)	2.8 (2.0–3.9)	<0.001
Gender (Male)	112 (56.9)	481 (56.6)	NS	0.715
White blood cel (≥13.550)	111 (57.5)	416 (48.9)	1.4 (1.1–1.9)	0.032
Neutrophil (≥10.850)	114 (59.1)	419 (49.3)	1.5 (1.1–2.0)	0.014
Lymphocyte (<1.475)	106 (54.9)	329 (38.7)	1.9 (1.4–2.6)	<0.001
Platelets (≥222)	119 (61.7)	505 (59.4)	NS	0.566
Red blood cell distribution width (≥13.2)	118 (61.1)	458 (53.9)	NS	0.067
Platelet distribution width (≥16.0)	107 (55.4)	505 (59.4)	NS	0.312
Mean corpuscular hemoglobin (≥28.9)	109 (56.5)	473 (55.6)	NS	0.834
Mean platelet volume (≥8.65)	102 (52.8)	458 (53.9)	NS	0.795
Mean corpuscular volume (≥85.4)	116 (60.1)	467 (54.9)	NS	0.192
Total bilirubin (≥0.67)	141 (73.1)	497 (58.5)	1.9 (1.4–2.7)	<0.001
C-reactive protein (≥3.75)	150 (77.7)	403 (47.4)	3.9 (2.7–5.6)	<0.001
Neutrophil lymphocyte ratio (≥5.69)	145 (75.1)	455 (53.5)	2.6 (1.8–3.7)	<0.001
Platelets lymphocyte ratio (≥134.5)	141 (73.1)	451 (53.1)	2.4 (1.7–3.4)	<0.001
Platelets neutrophil ratio (<19.9)	93 (48.2)	339 (39.9)	1.4 (1.1–1.9)	0.034
White cell lymphocyte ratio (≥7.30)	141 (73.1)	446 (52.5)	2.4 (1.7–3.5)	<0.001
White cell neutrophil ratio (<1.22)	107 (55.4)	343 (40.4)	1.8 (1.3–2.5)	<0.001
Ultrasonography findings (AAp+)	123 (69.9)	545 (70.1)	NS	0.966

AAp: Acute appendicitis; OR: Odds ratio; CI: Confidence interval.

Table 4. Determination of factors predicting perforated AAp using Backward stepwise logistic regression model

Variables	B	SE	Wald	Sig.	Exp(B)	95% CI for EXP(B)	
						Lower	Upper
Age (≥32)	0.930	0.179	26.893	0.000	2.5	1.8	3.6
Total bilirubin (≥0.67)	0.377	0.189	3.996	0.046	1.5	1.0	2.1
C-reactive protein (≥3.75)	1.096	0.193	32.313	0.000	3.0	2.1	4.4
Neutrophil lymphocyte ratio (≥5.69)	0.612	0.223	7.567	0.006	1.8	1.2	2.9
Constant	-1.914	0.111	300.070	0.000	0.2		

Hosmer and Lemeshow test sig. 0.179, Omnibus tests for model coefficients X^2: 119.93. sig: <0.001.

Table 5. Comparison of patients according to cut-off value age of 50 (<50 yr versus ≥50 yr)

Patients' characteristics	≥50 years (n=306)	<50 years (n=1010)	OR (95% CI)	p
Gender (male)	161 (52.6)	550 (54.4)	NS	0.571
White blood cell (<10.900)	119 (38.9)	309 (30.6)	1.4 (1.1–1.9)	0.007
Neutrophil (≥7.950)	196 (64.1)	705 (69.8)	NS	0.058
Lymphocyte (<1655)	181 (59.2)	475 (47.0)	1.6 (1.2–2.1)	<0.001
Platelets (≥234.000)	151 (49.3)	548 (54.3)	NS	0.132
Red blood cell distribution width (≥13.2)	238 (77.8)	509 (56.3)	3.0 (2.3–4.1)	<0.001
Platelet distribution width (≥16.05)	189 (61.8)	599 (59.3)	NS	0.442
Mean corpuscular hemoglobin (≥29.1)	158 (51.6)	541 (53.6)	NS	0.553
Mean platelet volume (≥8.35)	182 (59.5)	614 (60.8)	NS	0.680
Mean corpuscular volume (≥84.9)	203 (66.3)	600 (59.4)	1.3 (1.1–1.8)	0.029
Total bilirubin (≥0.61)	235 (76.8)	596 (59.0)	2.3 (1.7–3.1)	<0.001
C-reactive protein (≥0.725)	268 (87.6)	708 (70.1)	3.0 (2.1–4.3)	<0.001
Neutrophil lymphocyte ratio (≥5.13)	203 (66.3)	562 (55.6)	1.6 (1.2–2.1)	0.001
Platelets lymphocyte ratio (≥126.5)	208 (68.0)	588 (58.2)	1.5 (1.2–2.0)	0.002
Platelets neutrophil ratio (<24.04)	152 (49.7)	527 (52.2)	NS	0.442
White cell lymphocyte ratio (≥5.77)	224 (73.2)	648 (64.2)	1.5 (1.1–2.0)	0.003
White cell neutrophil ratio (<1.29)	183 (59.8)	541 (51.6)	1.3 (1.1–1.7)	0.012
Histopathology (AAp+)	243 (79.4)	800 (79.2)	NS	0.939
AAp status (perforated)	83 (34.2)	110 (13.7)	3.2 (2.3–4.5)	<0.001
Ultrasonography findings (AAp+)	169 (62.8)	605 (65.8)	NS	0.363

AAp: Acute appendicitis; OR: Odds ratio; CI: Confidence interval.

counts were significantly higher in patients ≥50 years. However, RDW (p<0.001), MCV (p=0.029), TBil (p<0.001), CRP (p<0.001), NLR (p=0.001), PLR (p=0.002), WLR (p=0.003), WNR (p=0.012) and presence of AAp (p<0.001) were significantly higher in patients ≥50 years. All demographic, clinical and biochemical data are summarized in Table 5.

DISCUSSION

AAp is one of the most common acute surgical emergencies, with incidence of approximately 100 per 100,000 people.[1,11] Its incidence changes according to age, geographic location and diet.[1,12,13] The pathogenesis of AAp is believed to reflect an initial insult to the mucosa resulting from luminal obstruction by a fecalith, a fragment of undigested food, or lymphoid hyperplasia, followed by bacterial infection that progressively spreads from the mucosa into the wall. Inflammation of the appendiceal wall leads to ischemia, necrosis and eventually perforation, which may result in a localized abscess, plastron formation or generalized peritonitis.[14]

Despite its high incidence, diagnosis is challenging due to non-specific symptoms and atypical presentations. Accurate diagnosis is challenging as there is no single symptom or sign that accurately predicts perforated AAp. The diagnosis is usually based on patient history and physical examination. Physical examination and history are supported by imaging and laboratory markers, such as WBC and CRP.[10] We found that determining appendix in the ultrasound was an independent risk factor for the diagnosis of AAp and perforated AAp as well. In patients ≥50 years, rate determination of perforated AAp was significantly higher. Thus, the routine use of imaging, including the US and CT, as an adjunct to the clinical diagnosis of AAp can provide valuable information regarding the complications and should be employed in the evaluation of obscure and high-risk cases.[5]

Many authors stated that negative appendectomy rates ranged from 15% to 50% and it was reported that appendectomy carried similar morbidity regardless of whether the appendix was inflamed.[10,15,16] With laparoscopy and the availability of radiological instruments, such as CT and US, some units have seen a decrease in their acceptable negative appendectomy rate to less than 10%.[17] However, the wide availability of laparoscopy has lowered the threshold of surgeons to perform a diagnostic procedure and increase the rate of incidental and negative appendectomies.[15] In the present study, the negative appendectomy rate was calculated as 20.7%, in which rate is lower than in many studies. In either case, in our institution, we are not against negative appendectomies and we perform appendectomy if the exploration of the abdomen does not yield any other cause or macroscopic examination of the appendix is suspicious concerning inflammation. Some researchers suggest that all appendices, even when grossly normal, should be removed during surgery for suspected AAp. Appendectomy should be carried out even if the gross appearance is normal because the microscopic evaluation may show a subtle acute inflammatory process.[11,18]

Various scoring systems that incorporate symptoms and various laboratory markers, such as leukocytes and c-reactive protein, have been developed to help aid the diagnosis of AAp. One of the most widely used is the Alvarado score described in 1986.[7] However, none of the scoring systems are actually related to the severity of the disease and appendiceal perforation to improve the diagnostic accuracy of AAp.[6,7,19–22] We also favor the Alvarado scoring system for the evaluation of our patients. Unfortunately, the data regarding this scoring system are missing due to the retrospective nature of this study which is one of the limitations of the present study.

The present study aims to report the diagnosis of AAp, staging the severity and predicting perforation, which is a very important point. Many studies reported that perforated AAp rates ranged from 16% to 46%.[4] In our opinion, this variation is the result of a lack of accurate diagnostic tests to predict the severity of AAp that will guide the physicians to take the necessary precautions. Diagnosis of perforated AAp in patients with signs and symptoms of acute abdomen and peritoneal irritation is straightforward. The main problem is the (early) diagnosis of high-risk groups and predicting the perforation in these group of patients where the mortality and morbidity are high.[8,23] In the present study, 193 patients had perforated AAp which made up 18.5% of the patients with AAp. Eighty-three patients (43%) of the 193 patients with perforated AAp were ≥50 years old and were considered to be high-risk group in accordance with age. Furthermore, 34% of the patients ≥50 years old perforated AAp.

Ramasamy Ramu and colleagues[24] showed that the frequency distribution of age groups in AAp peaked at the second followed by the third decade, whereas perforation peaked in the third decade followed by the second decade. In the same study, men dominated women in sex distribution. Multivariate analysis of the present study showed that while male sex was a risk factor for AAp, gender was not significantly associated with perforation. However, the present study also showed that male sex in addition to patients ≥50 years old was at a significantly increased risk of developing perforated AAp.[25]

Certain variables, such as WBC, NLR and CRP, are correlated to the inflammatory process and have been associated with the diagnosis of AAp. The markers that have been reported to be correlated with AAp include high WBC counts, high NLR, elevated neutrophil counts, elevated CRP, and elevated platelet counts and the diameter and wall thickness of appendix vermiformis on conventional imaging studies, such as the US or CT.[26–31] Furthermore, severe infections and sepsis itself lead to hyperbilirubinemia by bacteremia and endotoxemia, causing imparted bile excretion from the canaliculi.[4,21,32–34] Our results are in accordance with the previous studies, and we found that WBC (≥10.900), MPV (≥29.1), TBil (≥0.61), CRP (≥0.725), NLR (≥5.13) and PNR (≥24.04) were independent risk factors determining AAp. Furthermore, TBil (≥0.67), CRP (≥3.75) and NLR (≥5.69) were independent risk factors predicting perforated AAp. Therefore, these readily available routine tests can be used to diagnose AAp and perforated it whenever the clinical characteristics of the patient are obscure. The WBC, platelet, and selective lymphocyte counts were significantly lower with patients ≥50 years. However, inflammatory markers, such as RDW, MCV, TBil, CRP, NLR, PLR, WLR and WNR, were significantly higher in patients ≥50 years old when compared to younger patients. This makes these markers useful tools for the diagnosis of acute in a high-risk vulnerable group.

While this study has identified several factors that correlated significantly with the presence of AAp and perforated AAP, several limitations are present. The main limitation of this study is that it is a retrospective study, with the data being secondary. Data were often incomplete, and some of the required information was poorly recorded or missing. As a retrospective study, there were some other expected disadvantages. Some data were missing and some of the medical records could not be traced to assess the clinical parameters. Patient delay time and system delay time could not be assessed as well. Furthermore, we performed open surgery more often because the facilities and trained personnel related to laparoscopy are not readily available during an emergency operation performed in non-working hours. This may be the reason for the high open appendectomy rate in the present study.

In addition to clinical assessment, laboratory tests, imaging studies and diagnostic scores increase the accuracy of diagnosis of AAp with some parameters found to predict the diagnosis of AAp in patients that were evaluated. Other parameters were significantly associated with perforated AAp. The use of these results will provide surgeons with valuable data for decision-making, reducing the rate of negative appendicectomies and avoiding delays in diagnosis and treatment of perforated cases and also for evaluation of high-risk cases with vague signs and symptoms.

Ethics Committee Approval: This study was reviewed and approved by the Inonu University institutional review board for non-interventional studies (Approval No: 2019/10-22).

Peer-review: Internally peer-reviewed.

Authorship Contributions: Concept: S.A., C.K., T.T.S.; Design: S.A., C.K.; Supervision: S.A., S.Y.; Resource: S.A., T.T.S., C.K.; Materials: C.K., E.Ş., A.T., E.Ş.,K.D.; Data: C.K.,

S.A., E.S., A.T.; Analysis: S.A., T.T.S., C.Ç; Literature search: S.A., K.D., A.T.; Writing: S.A., K.D.; Critical revision: S.A., T.T.S., E.Ş., S.Y.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study has received no financial support.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Akut apandisit ve perfore apandisiti öngören faktörlerin belirlenmesi

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AMAÇ: Akut apandisit (AAp) ön tanısıyla ameliyata alınan hastalarda AAp ve perfore AAp'yi öngören faktörlerin belirlenmesidir.
GEREÇ VE YÖNTEM: Mayıs 2009 ile Aralık 2018 arasında 1316 hastaya AAp ön tanısıyla apandektomi yapıldı. AAp'yi öngören faktörlerin belirlenmesi için apendiks'teki enflamatuvar değişikliklerin varlığı gözönünde bulundurularak hastalar iki gruba ayrıldı: AAp (AAp grubu; n=1043) ve normal appendiks (Non-AAp; n=273). Ayrıca apendiks perforasyonunu öngören faktörlerin belirlenmesi için AAp tespit edilen hastalar perforasyon varlığı gözönünde bulundurularak iki gruba ayrıldı: AAp (AAp grubu; n=850) ve perfore AAp grubu (perfore AAp grubu; n=193). Kantitatif değişkenler için optimal kesim noktalarının belirlenmesi için ROC eğri analizi kullanıldı. Gruplar univariate analiz yöntemelri ile karşılaştırıldı ve p≤0.20 değeri alan değişkenler multivariate alojistik regresyon modeline (backward stepwise) alındı.
BULGULAR: AAp'yi öngören faktörlerin belirlenmesi için yapılan multivariate analiz cinsiyet (erkek; p=0.034; OR: 1.42), WBC (≥10.900; p=0.022; OR: 1.52), MPV (≥29.1; p=0.006; OR: 1.57), TBil (≥0.61; p=0.034; OR: 1.42), CRP (≥0.725; p=0.002; OR: 1.71), NLR (≥5.13; p=0.034; OR: 1.50), PNR (≥24.04; p=0.001; OR: 0.53) ve US bulgularının (AAp+; p<0.001; OR: 2.88) AAp'yi öngörmede bağımsız birer faktör olduğunu göstermiştir. Apendiks perforasyonunu öngören faktörlerin belirlenmesi için yapılan multivariate analiz yaş (≥32 yıl; p<0.001; OR: 2.54), TBil (≥0.67; p=0.046; OR: 1.46), CRP (≥3.75; p<0.001; OR: 2.99) ve NLR (≥5.69; p=0.006; OR: 1.84) perforasyonu öngörmede bağımsız birer faktör olduğunu göstermiştir.
TARTIŞMA: Hem AAp hem de perforasyonun öngörülmesinin, acil servise AAp ön tanısıyla başvuran hastaların değerlendirmesinde klinisyene yardımcı olacağına inanıyoruz. Bu yaklaşım aynı zamanda negatif apendektomi ve perforasyon oranlarının azaltılmasına katkıda bulunacaktır.

Anahtar sözcükler: Akut apandisit; apendiks vermiformis; negatif apendektomi; öngören faktörler; perfore akut apandisit.

Ulus Travma Acil Cerrahi Derg 2021;27(4):434-442 doi: 10.14744/tjtes.2020.60344