

CLINICAL STUDY

Laboratory in complicated appendicitis prediction and predictive value of monitoring

Aydin OU¹, Soylu L¹, Dandin O², Uysal Aydin E³, Karademir S¹Güven Hospital, Department of Surgery, Ankara, Turkey. oguzguraydin71@gmail.com**ABSTRACT**

OBJECTIVES: The purpose of the study was that monitoring, which is used in diagnosis of acute appendicitis, and laboratory values, were evaluated for verifying diagnosis of complicated appendicitis and these parameters revealed cut-off values in complicated acute/non-complicated appendicitis.

METHODS: 195 patients, who had had an operation for acute appendicitis between January 2012 and March 2015 and who were proved to have acute complicated/non-complicated appendicitis from the results of histopathology consideration, were included in this study. Patients' age, preoperative serum, WBC, CRP, NLR and BT with USG results were evaluated.

RESULTS: Among the groups, there were no meaningful differences in the sense of age. Meaningful difference was obtained in between ($p > 0.05$), WBC, NLR, CRP and appendix diameter values.

Serum in WBC > 13800 (AUC = 0.614, $p = 0.006$, %95 GA: 0.541–0.682), in NLR > 4.87 (AUC = 0.641, $p = 0.001$, %95 GA: 0.569–0.708), in CRP > 5.98 (AUC = 0.651, $p < 0.000$, %95 GA: 0.580–0.718), in the measurement > 11 mm (AUC = 0.630, $p = 0.002$, %95 GA: 0.558–0.698) values were obtained. The values that were obtained, were confirmed to be descriptive in analysis of complicated appendicitis and non-complicated appendicitis.

According to the obtained cut-off values, serum WBC, diameter of appendicitis, NLR and CRP values', (OR) ratios were calculated for complicated appendicitis by being classified (odds ratio respectively; 3.103 (1.713–5.621), 2.765 (1.496–5.109), 3.025 (1.665–5.494), 2.313 (1.295–4.130)).

CONCLUSION: It is important that treatment options are evaluated to be able to discriminate complicated appendicitis fast and with a high accuracy. In the case that serum WBC is higher than 13800. CRP is higher than 5.98, NLR is higher than 4.87 and appendicitis diameter is longer than 11mm, inflammation of appendicitis is complex with gangrene, perforation and abscess and it emphasizes the suggestion of surgical treatment option to patients (Tab. 4, Fig. 1, Ref. 28). Text in PDF www.elis.sk.

KEY WORDS: appendicitis, leucocyte count, diameter, complicated.

Introduction

Complicated acute appendicitis; perforation namely, intraabdominal abscess, plastron and gangrenous can be seen between 20 % and 30 % of all appendicitis. Diagnosis of acute non-complicated appendicitis is performed with a high accuracy by using monitoring methods (USG/BT) in a widespread manner. Especially, the usage of BT in diagnosis reduces negative appendectomy below 2 % (1). Unfortunately, early diagnosis of complicated appendicitis cannot succeed in the same way. Therefore, early diagnosis of complicated appendicitis is effective at reducing risks, which are related to these complications. Also, papers revealed recently activity of non-complicated appendicitis conservative treatment (2, 3). Thus, a safe guess, which is done in preoperative way, ranges from a possible surgery to morbidity and mortality which are re-

levant to surgery. Different inflammatory indicators (White blood cell (WBC), C-reactive protein (CRP) (4), D-lactate level (5), level of calprotectin (6), level of procalcitonin (7), many interleukins (8) and usage of monitoring methods in diagnosis of appendicitis are available in many studies related to discrimination of complicated/non complicated. Neutrophil and lymphocyte ratio (NLR) starts to find place for itself recently between these indicators (9).

The purpose of this study was to research the effectiveness of histopathology diagnosed patients with acute appendicitis laboratory parameters CRP, WBC, NLR studied in the preoperative period along with evaluation of the effectiveness of USG and BT's discrimination of complicated/non-complicated, which are monitoring examinations.

Materials and methods

195 patients, who had had appendectomy between January 2012 and May 2016 in our Hospital's general surgery clinic, were included for consideration. The patients, who were confirmed to have acute appendicitis from examination results were included in the study. Demographic data that belonged to patients, laboratory parameters and monitoring examination with histopathology

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Tab. 1. Comparison of two groups [Median (Min–Max)].

	Group I* (n=103)	Group II** (n=92)	p***
Age	35 (17–90)	36 (17–80)	0.442
WBC	12.300 (1.400–23.700)	14.250 (5.740–30.900)	0.006
NLR	4.3 (0.06–32.09)	5.98 (1.65–28.65)	0.001
CRP	4.7 (0.46–215.55)	13.6 (0.45–300.35)	0.000
Diameter	10 (6–26)	11 (7–88.4)	0.002

* N

Tab. 2. Comparison of the groups).

		Group I* n (%)	Group II** n (%)	p***
Sex	Female	49 (47.6)	36 (39.1)	0.235
	Male	54 (52.4)	56 (60.9)	
USG	No	75 (90.4)	57 (86.4)	0.615
	Yes	8 (9.6)	9 (13.6)	
CT	No	20 (95.2)	25 (96.2)	1.000
	Yes	1 (4.8)	1 (3.8)	
Complicated	No	103 (100.0)	–	
	Yes	–	92 (100.0)	
	Phlegmon		77 (83.7)	
	Abscess		2 (2.2)	
	Perforation		13 (14.1)	

* Non-Complicated Appendicitis, ** Complicated Appendicitis, *** Ki-Kare

analysing results were evaluated. Analysing, the patients, who were determined to have an acute focal/supportive appendicitis were evaluated as the non-complicated (Group 1) and the patients who were determined to have phlegmonous and perforation appendicitis with periappendiceal abscess were evaluated as the complicated (Group 2). Blood samples were taken before the usage of antibiotic. Patients were firstly evaluated by USG, which is one of the examinations of monitoring. BT was taken with oral contrast app by the patients whose appendicitis could not be monitored. Upper limit of normal appendicitis diameter in USG and BT was specified as 7 mm, which is accepted as normal in our hospital. Patients with normal abdominal examinations, under 16 years old, pregnant, using steroid and antibiotic were excluded from the study.

In physical examination, in case when tenderness, defence and rebound were observed in the right lower quadrant of abdominal, rising at least one of the laboratory parameters WBC, CRP, NLR and along with appendicitis diameter that was above the normal range in BT or USG, section decision was settled for these patients.

Consideration of data

Analysis of data were done by using IBM SPSS 23.0 and MedClac 15.8 statistical programs. While considering the study

data, illustrative statistical methods (frequency, percentage, median, min–max) were used as well as Ki-Square (χ^2) test was used for comparing qualitative data. Suitability of the data to normal distribution were evaluated with Kolmogorov–Smirnow and Shapiro–Wilk tests and they did not indicate normal distribution. In the research, Mann–Whitney test was used, while comparing groups. Roc curve (Receiver Operating Characteristic) method was used to obtain distinctiveness of variables. Relative odds ratios were calculated. Values that have $p < 0.05$ were accepted as meaningful.

Power analysis

Power analysis was done using the G*Power 3.1.9.2 statistical packet program and power obtained was $(1-\beta)=0.92$ with respect to $n_1 = 103$, $n_2 = 92$, $\alpha = 0.05$, effect size $d = 0.5$.

Results

Meaningful difference between groups could not be obtained in terms of age, gender, USG and CT values ($p > 0.05$). Serum WBC, NLR, CRP and results of appendicitis diameter measurements were found high in the complicated group (Group II) with respect to the non-complicated group (Group I) ($p < 0.05$) (Tabs 1 and 2).

Cut-off values were obtained for WBC > 13800 (AUC = 0.614, $p = 0.006$, %95 GA: 0.541–0.682), for NLR > 4.87 (AUC = 0.641, $p = 0.001$, %95 GA: 0.569–0.708), for CRP > 5.98 (AUC = 0.651, $p < 0.000$, %95 GA: 0.580–0.718), for appendicitis diameter > 11 mm (AUC = 0.630, $p = 0.002$, %95 GA: 0.558–0.698) (Tab. 3 and Fig. 1). Serum WBC value, NLR, CRP and appendicitis diameter measurement obtained were distinguishing parameters in discrimination of acute appendicitis to become complicated or not.

According to the cut-off values, when variables (WBC, NLR, CRP and Diameter) that are classified as normal-pathological are compared among complicated and non-complicated appendicitis groups, it was found out that there were statistically meaningful differences and pathology ratios were higher in the complicated groups (Group II) than the non-complicated groups (Group I) ($p < 0.05$). These variables' relative odds ratio was calculated later. If Serum WBC value was over 13.800, complicated appendicitis developed 3.1 times according to the ones that were below this value, if NLR values were over 4.87, complicated appendicitis developed 3 times according to the ones that were below this value, if CRP value was over 5.98, complicated appendicitis developed 2.3 times according to the ones that were below this value and if appendix diameter was over 11 mm, complicated appendicitis developed 2.8 times according to the ones that were below this value (Tab. 4).

Tab. 3. Cut-off values for prediction complicated appendicitis.

	AUC	Cut Off	Sensitivity	Specificity	+LR	–LR	%95 CI	p*
WBC	0.614	>13.800	53.3	67.0	1.61	0.70	0.541–0.682	0.006
NLR	0.641	>4.87	70.7	56.3	1.62	0.52	0.569–0.708	0.001
CRP	0.651	>5.98	71.7	54.4	1.57	0.52	0.580–0.718	0.000
DIAMETER	0.630	>11	45.7	76.7	1.96	0.71	0.558–0.698	0.002

* ROC Curve

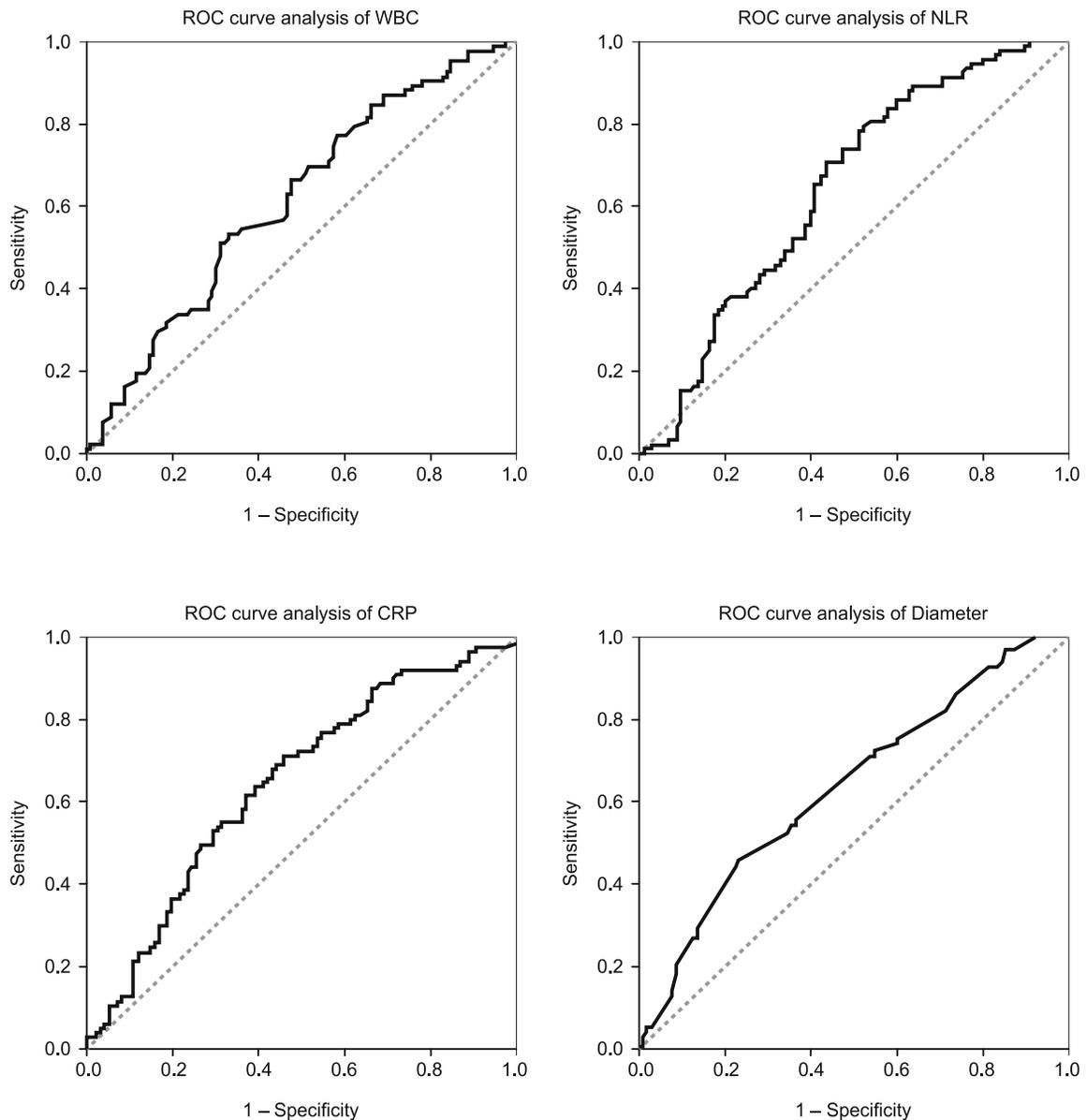


Fig. 1. ROC curves.

Discussion

Acute appendicitis is seen in about 7% of the population. The reasons (fecalith, lymph node, parasite and tumor) that causes obstruction of appendix lumen are blamed in aetiopathogenesis. However, spontaneous resolution that is coming into existence in some cases and healing with antibiotic treatment support the obstruction theory. Thus, it is not wrong to think that complicated and non-complicated appendicitis are different illnesses that develop due to different aetiology. Thought of non-operative treatment that saves patients from risks of surgery in acute non-complicated appendicitis has increased the importance of doing discrimination of complicated/non-complicated appendicitis with a high accuracy.

There are studies, which state that antibiotic treatment is as safe as surgery in acute non-complicated appendicitis (10–13).

Complicated appendicitis is related to perforation, necrosis and formation of intraabdominal abscess and appendix perforation is the basic pathology that reveals a complicated situation. To separate complicated appendicitis, studies that used laboratory parameters (13) or monitoring methods (14, 15) are available. In this study, cut-off ratios were investigated to reach out discrimination of complicated and non-complicated appendicitis by evaluating laboratory and monitoring parameters together.

Counting leucocytes are laboratory values, which are used most frequently. It is the early indication of inflammation in organ. Specificity and sensitivity in many studies are distributed in a wide

Tab. 4. Estimated relative risk ratio (Odds Ratio) for the parameters.

		Group I*	Group II**	p***	Odds Ratio (OR)	95 CI
CRP	Normal	69 (67.0)	43 (46.7)	0.004	2.313	1.295–4.130
	Pathologic	34 (33.0)	49 (53.3)			
WBC	Normal	58 (56.3)	27 (29.3)	0.000	3.103	1.713–5.621
	Pathologic	45 (43.7)	65 (70.7)			
NLR	Normal	56 (54.4)	26 (28.3)	0.000	3.025	1.665–5.494
	Pathologic	47 (45.6)	66 (71.7)			
Diameter	Normal	79 (76.7)	50 (54.3)	0.001	2.765	1.496–5.109
	Pathologic	24 (23.3)	42 (45.7)			

* Non-complicated appendicitis, ** Complicated Appendicitis, *** Chi-Square

	Sensitivity	Specificity	Odds Ratio (OR)	%95 CI
CRP	53.3	67.0	2.313	1.295–4.130
WBC	70.7	56.3	3.103	1.713–5.621
NLR	71.7	54.4	3.025	1.665–5.494
CAP	45.7	76.7	2.765	1.496–5.109

interval (16). Also, our study results of counting WBC sensitivity and specificity are compatible with literature (respectively, 70.7 % and 56.3 %). There are studies indicating that counting WBC is significantly higher as well as there are also studies indicating that seriousness of appendix inflammation cannot be obtained because of low specificity and sensitivity (17). Atema and his friends stated that WBC values that were over 13.000/mm³ are meaningful for distinguishing complicated/non-complicated appendicitis in their study (18) so as 13.800/mm³, which is close to 13.000/mm³, which was obtained in our study.

CRP is an indicator, which is rising in acute phase with progressing inflammation in many illnesses. Specificity and sensitivity of CRP's diagnostic accuracy in meta-analysis, which was done recently, had been designated in a wide range (7). In our study, identification sensitivity of CRP's complicated appendicitis was 53.3 % and sensitivity was 67.0 % and they were compatible with literature. Moon and his friends had showed that risen CRP level was related to complicated appendicitis (19). Also, when CRP values that were over 5 mg/dL were compared with leucocytosis, there were studies indicating that the only meaningful factor was the discrimination of complicated and non-complicated appendicitis (20). CRP values that were over 5.98 mg/dL had been obtained as meaningful for complicated appendicitis.

Neutrophile/lymphocyte ratio is an indicator of systematic or local inflammation. Many inflammatory diseases, sepsis and neoplastic diseases are indicators of morbidity and mortality (21, 22). Also, there exist studies, which are related to diagnostic value in acute complicated/non-complicated appendicitis (23, 24). Although, it is lower in comparison with the results in literature, NLR value had been found significantly high in complicated appendicitis group in proportion to non-complicated group in our study.

While early diagnosis ratio is increasing by using monitoring methods in diagnosis of acute appendicitis, morbidity ratios, which are connected to complicated appendicitis had decreased. Specificity and sensitivity of BT is high in diagnosis of acute appendicitis (25). Appendix diameter, which is over 7 mm in BT images, supports the diagnosis of acute appendicitis (26, 27). In the case that appendix was over 10 mm, there were studies showing

that appendicitis is complicated. In the study, which was done by Salminen and his friends, conservative treatment was applied in non-complicated acute appendicitis, which was detected by BT and most of the patients did not need surgery. Postoperative complication had been seen significantly low as meaningful for the patients, who needed surgery (28). In our study, it was determined that the patient with over 11 mm appendix diameter is related to complicated appendicitis. Abdominal ultrasonography, which is the preferred one monitoring method, is a diagnostic tool that is fast, easy to use, low cost and readily available. Sensitivity is at a level of 85–99 % and specificity is at a level of 90–99 %. However, appendix cannot be monitored in some patients. In this study, it was found out that sensitivity for distinguishing complicated appendicitis of appendix diameter was 45.7 % and specificity was 76.7 % and when appendix diameter, which is monitored with USG or BT in complicated group was compared to non-complicated group, it has been found out that it was higher as meaningful.

When all these symptoms are evaluated, making diagnosis of acute appendicitis is important for both forecasting whether complicated appendicitis is developed or not and designating strategy of surgeon, who operates and for applying medical treatment in appendicitis that are not considered as complicated. In many studies, it has been indicated that there are no basic and only laboratory or monitoring method that designates complicated appendicitis. When high serum leucocyte level (> 13800/mm³), CRP values that are over 5.98, NLR that is over 4.87 and wide appendix diameter (in USG/BT > 11 mm) are evaluated together, we are of the opinion that inflammation period is complicated with gangrene, perforation and abscess. Our study is retrospective and did not include young age group where atypical symptoms and appendicitis are in common and did not include the group to whom conservative treatment was applied and these are the limiting properties of our study.

Finally, we think that measurement of appendicitis diameter and counting serum leucocyte in acute period are sufficient in complicated appendicitis for quick diagnosis and discrimination of measurement of NLR and CRP.

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