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Effectiveness of D-dimer, CRP, procalcitonin and white blood cell count in non-traumatic acute abdomen

Non-Traumatic Acute Abdomen Syndrome and Laboratory Parameters

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Abstract
Aim: This prospective study investigates the effects of changes in leukocyte, CRP, D-dimer and procalcitonin levels during the treatment process of patients admitted to hospital with pre-diagnosis of non-traumatic acute abdominal pain on the decision about the treatment method.
Material and Methods: Patients included in the study were divided into 3 groups: those who underwent surgical treatment within the first 24 hours (Group-1), those who underwent surgical treatment within 24-48 hours (Group-2), and those who were discharged without surgical treatment after at least 48 hours of follow-up (Group-3). At the end of the treatment process, the change in the levels of leukocytes, CRP, D-Dimer and PCT values were examined in each group.
Results: A total of 141 patients (Group-1: 41 patients, Group - 2: 33 patients and Group - 3: 67 patients) were included in the study. The level of WBC tended to decrease in Group - 3 patients (p=0.001). The level of CRP tended to increase in Group - 2 patients (p=0.001) and decrease in Group - 3 patients (p=0.067) compared to the levels at the time of admission. The level of PCT was lower in Group-3 patients from the time of admission (p=0.005). D-dimer level in Group-3 patients tended to decrease compared to the level at the time of admission (p=0.096).
Discussion: Changes in these laboratory values add valuable information for clinicians and may prevent unnecessary surgical intervention in some patients.

Keywords
Abdominal Pain, Acute Abdomen, Emergency Surgery

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Introduction

All pathologies resulting from non-traumatic causes with a sudden onset and that last less than a week, and progress with abdominal findings, are examined under "acute abdomen (AA)" [1,2]. In this syndrome, which is widely encountered in emergency services and constitutes an important part of emergency surgeries, reaching the right diagnosis as soon as possible is significant because the pathological condition can progress rapidly and reach life-threatening levels [1]. The most important step in diagnosis is to decide whether the etiological cause requires surgical treatment or medical treatment.

Early determination of the etiologic factor in non-traumatic acute abdominal pain and rapid intervention in a patient with surgical pathology are among the most important factors in decreasing mortality and morbidity rates [1]. When abdominal pain is evaluated in all patients admitted to emergency departments, etiological factors were non-specific in 75-80% of the patients, and these patients could be treated without requiring hospitalization, and the remaining 20-25% of patients required hospitalization for further examinations [3]. Despite all the examinations carried out at the time of admission to the hospital, a clear decision could not be made about whether surgical intervention is necessary for 40-45% of this hospitalized patient group, and medical treatment decision was made according to the results of clinical follow-up [4].

In the diagnosis of non-traumatic AA, the laboratory parameters that were evaluated when making surgical decisions were blood leukocyte levels and C-Reactive Protein (CRP) level [5]. In recent years, clinical studies have shown that D-dimer and procalcitonin (PCT) levels are valuable in making a decision about surgery for patients in need of emergency surgery [6]. However, studies in the literature were conducted using the values of these laboratory parameters, measured only at the time of admission to the hospital, that is, based on the results of a single evaluation of these parameters [7,8].

In this study, it was investigated whether changes in WBC, CRP, D-dimer and PCT levels in patients admitted to the hospital with AA pre-diagnosis could be effective in determining the treatment method.

Material and Methods

The study was carried out in Sakarya University Faculty of Medicine Hospital between August 2013 and January 2015. For this prospective study, approval was obtained from Sakarya University Faculty of Medicine Clinical Research Ethics Committee (Ethics committee no: 16214662.050.01.04/24). The study was recorded in Clinical Trials with the reference number 2013-08-06-002. Informed consent was obtained from the patients.

This study was carried out with the patients, aged 18-65 years, who were admitted to the General Surgery Clinic with a prediagnosis of non-traumatic acute abdominal pain and were volunteer to participate in the study. Patients who were <18 years of age, >65 years of age, those with a history of external trauma (blunt or penetrating) in the last 6 months, pregnant women, those who gave birth in the last 6 months, or in lactation at the time of admission, and those with a history of abdominal or extra-abdominal major surgery in the last 1 year were excluded from the study.

Design of study groups: Patients were grouped as follows: patients whose surgery decision was made on the day of admission to the hospital (within the first 24 hours) (Group - 1), and patients whose surgery decision was made within 24-48 hours after the first 24 hours of medical follow-up (Group - 2), and patients who were discharged after at least 48 hours of medical follow-up without making surgery decision (Group - 3).

Collecting blood samples: D-dimer and PCT values were studied in addition to the routine Hemogram and CRP tests carried out in the groups once a day, for the periods specified. According to this protocol, the above-mentioned laboratory tests were performed one time before surgery in Group - 1; two times in Group - 2, on Day 0 and Day 1; and three times in Group - 3, on Day 0, Day 1 and Day 2.

Statistical Analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) software was used for statistical analysis. When evaluating the study data, along with descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum), the Kruskal-Wallis test was used to compare three or more groups that did not show a normal distribution in quantitative data and Mann-Whitney U test was used to determine the group that caused the difference. The Friedman test and Wilcoxon Signed Ranks test were used for intra-group comparisons of non-normally distributed variables and evaluation of binary comparisons, respectively. Diagnostic and screening tests (sensitivity, specificity, PKD, NKD) and ROC Curve analysis were used for cut-off parameters. The level of significance was $p<0.01$ and $p<0.05$.

Results

The study was performed with the total of 141 patients, including 41 patients (29.1%) whose surgery decision was made on Day zero, 33 patients (23.4%) who were operated on Day 1, and 67 patients (47.5%) who were followed up without surgery. Sixty (42.5%) of the patients were female and 81 (57.5%) were male, and the mean age was 44 (18-65) years.

Group - 1 included 13 female (31.7%) and 28 (68.3%) male patients, 41 patients in total. The mean age of the patients was 35 (25-52) years. The final diagnosis of patients was as follows: acute appendicitis in 24 patients (58.6%), intestinal obstruction in six patients (14.6%), intestinal phytobezoar in four patients and colorectal malignancy in two patients, incarcerated

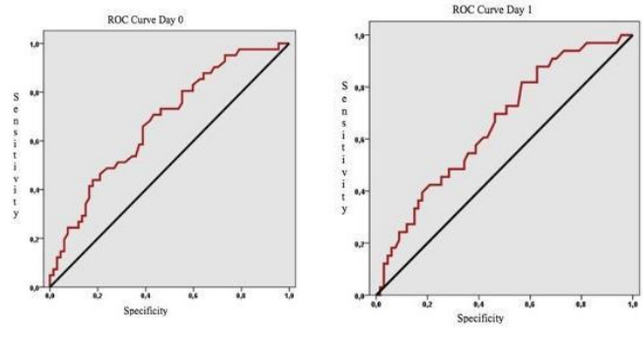

Figure 1. ROC Curve Graph for WBC Based on the Decision of the Day 0 and Day 1 of the Surgery

inguinal hernia in four patients (9.8%), acute cholecystitis in two patients (4.9%), necrosis of the appendix epiploica in two patients (4.9%), intestinal perforation due to colon malignancy in one patient (2.4%) and mesenteric ischemia in one patient (2.4%), negative laparotomy (with the preliminary diagnosis of mesenteric ischemia) in one patient (2.4%). The average length of hospitalization was three (2-5) days. Two patients (4.9%) developed a superficial surgical site infection without mortality. Group - 2 consisted of 33 patients, 14 (42.4%) were females and 19 (57.6%) were males. The mean age of the patients was 35 (26-40) years. Final diagnoses of patients were as follows: Acute appendicitis in 25 patients (75.7%), acute cholecystitis in three patients (9.1%), intestinal obstruction in two patients (6.1%), segmental intestinal ischemia in one patient (3%), peptic ulcer perforation in one patient (3%) and incarcerated inguinal hernia in one patient (3%) (clinical follow-up due to spontaneous reduction one day ago). The average length of hospitalization was three (3-5) days. Three patients (9.7%) developed a superficial surgical site infection with no mortality. Group - 3 involved 67 patients, 33 (49.3%) were females and 34 (50.7%) were males. The mean age of the patients was 54 (41-62) years. Final diagnoses of patients were as follows: Cholecystitis in 25 patients (37.3%), ileus in 18 patients (26.9%), non-specific abdominal pain in 17 patients (25.4%), reduced inguinal hernia in two patients (3%), colon diverticulitis in two patients (3%), acute pancreatitis in two patients (3%), and ureteral stone one patient (1.5%) The average length of hospitalization was 4.3 (4-5) days. There was no morbidity or mortality. The diagnosis of diverticulitis and pancreatitis patients was known at the first admission and they were followed up to see if surgery would be needed. The patient with a diagnosis of ureteral stone could not be diagnosed at the first admission and was followed up with a diagnosis of abdominal pain. Ureteral stone was detected in the urinary system ultrasonography, performed 48 hours later.

Table 1, Table 2 and Table 3 showed WBC, CRP, D-Dimer and PCT results of the groups.

According to the groups, there was a statistically significant difference between the patients' WBC measurements at day 0 ($p=0.002$; $p<0.01$). According to the results of the Mann-Whitney U test, the WBC value of the patients who were followed without surgery was significantly lower on Day 0 and Day 1, compared to the patients who were operated ($p=0.002$; $p=0.011$; $p<0.05$). No statistically significant difference existed among the CRP measurements of the patients on day 0, according to the groups ($p>0.05$). There was no statistically significant difference among the D-dimer measurements of the patients on day 0, according to the groups ($p>0.05$). No statistically significant difference was found among the procalcitonin measurements of the patients on day 0, according to the groups ($p>0.05$).

The mean decrease of 254.55±2548.79 in the WBC measurement on the 1st day was not statistically significant compared to day 0 ($p> 0.05$). The mean decrease of 20.61±61.25 in the CRP measurement on the 1st day was statistically significant compared to day 0 ($p=0.003$; $p<0.01$).

The mean decrease of 150.55±459.97 in the D-Dimer measurement on the 1st day was statistically significant compared to day 0 ($p=0.027$; $p<0.05$). The mean decrease of 0.48±1.39 in the procalcitonin measurement on the 1st day was statistically significant compared to day 0 ($p=0.001$; $p<0.01$).

There was a statistically significant difference among the WBC measurements of the patients on days 0, 1 and 2 ($p=0.001$; $p<0.01$). According to the results of the Wilcoxon Signed Ranks test, conducted to determine the difference, the mean 1370.15±1980.51 decrease in WBC measurement on day 1 was statistically significant compared to day 0 ($p=0.001$; $p<0.01$). The mean 2076.12±2772.76 decrease in WBC measurement on day 2 was statistically significant compared to day 0 ($p=0.001$; $p<0.01$). The mean 705.97±1801.67 decrease in WBC measurement on day 2 was statistically significant compared to day 1 ($p=0.002$; $p<0.01$). WBC values of the patients who were followed up without surgery were significantly lower

Table 1. Evaluation of WBC, CRP, D-Dimer and Procalcitonin Measurements on Day 0 by Groups

		Group 1 (n = 41)	Group 2 (n = 33)	Group 3 (n = 67)	ap
WBC on 0 Day	Min-Max (Median)	4.600-3.7200 (12,300)	4.900-22.700 (11,700)	3.900-23.600 (10.000)	0.002**
CRP on Day	Min-Max (Median)	3.45-267 (27)	3.45-311 (23)	3.45-313 (23)	0.936
D-dimer on Day	Min-Max (Median)	27.88-12.737 (245)	5-2.122 (216)	16-3.947 (258)	0.526
Procalcitonin on Day	Min-Max (Median)	0.05-1.55 (0.05)	0.05-14.9 (0.06)	0.05-21.79 (0.05)	0.259

a Kruskal-Wallis Test **p<0.01

Table 2. Evaluation of WBC, CRP, D-Dimer and Procalcitonin Measurements on Day 0 by Groups 1 and 2

		Group 1 (n = 41)	Group 2 (n = 33)	Difference	bp
WBC	Min-Max (Median)	4.900-22.700 (11.700)	5.600-0.900 (11.800)	-254.55±2548.79	0.978
CRP	Min-Max (Median)	3.45-311 (23)	3.45-430 (30)	20.61±61.25	0.003**
D-dimer	Min-Max (Median)	5-2.122 (216)	4.74-3.252 (346)	150.55±459.97	0.027*
Procalcitonin	Min-Max (Median)	0.05-14.9 (0.06)	0.05-16.43 (0.1)	0.48±1.39	0.001**

b Wilcoxon Signed Ranks Test *p<0.05, **p<0.01

Table 3. Evaluation of WBC, CRP, D-Dimer and Procalcitonin Measurements on Day 0, Day 1 and Day 2 (patients followed without surgery)

		Day 0	Day 1	Day 2	cp	0-1. Day bp	0-2. Day bp	1-2 Day
WBC	Min-Max (Median)	3900-23600 (10000)	3600-21800 (8000)	3600-18200 (7900)	0.001**	0.001**	0.001**	0.002**
CRP	Min-Max (Median)	3.45-313 (23)	3.2-386 (19)	3.2-330 (19)	0.001**	0.308	0.067	0.009**
D-Dimer	Min-Max (Median)	16-3947 (258)	19-8128 (199)	13-2187 (236)	0.001**	0.104	0.096	0.020*
Procalcitonin	Min-Max (Median)	0.05-21.79 (0.05)	0.05-13.75 (0.05)	0.05-6.8 (0.05)	0.005**	0.328	0.086	0.043*

b Wilcoxon Signed Ranks Test, c Friedman Test *p<0.05, **p<0.01

than in those who were operated on day 0 (p=0.002; p <0.01). According to ROC analysis, a WBC cut-off value ≥108 predicted the diagnosis with a sensitivity of 70.73%, specificity of 56.72%, a positive predictive value of 50.0% and a negative predictive value of 76.0% (Figure 1).

There was a statistically significant difference among the CRP measurements of the patients on days 0, 1 and 2 (p=0.001; p<0.01). According to the results of the Wilcoxon Signed Ranks test, conducted to determine the difference. The mean 3.06 ± 26,02 decrease in CRP measurement on day 2 was statistically significant compared to day 1 (p=0.009; p<0.01).

There was a statistically significant difference among the D-Dimer measurements of the patients on days 0, 1 and 2 (p=0.001; p<0.01). According to the results of the Wilcoxon Signed Ranks test conducted to determine the difference. The mean 118.16±966.23 decrease in D-Dimer measurement on day 2 was statistically significant compared to day 1 (p=0.020; p<0.01).

There was a statistically significant difference among the Procalcitonin measurements of the patients on days 0, 1 and 2 (p=0.005; p<0.01). According to the results of the Wilcoxon Signed Ranks test conducted to determine the difference. The mean 0.18±2.31 decrease in Procalcitonin measurement on day 2 was not statistically significant compared to day 0 (p=0.086; p<0.01). The mean 0.15±1.50 decrease in Procalcitonin measurement on day 2 was statistically significant compared to day 1 (p=0.043; p<0.01).

Discussion

In patients in whom it was impossible to decide whether treatment should be surgical or medical for patients who were admitted to the hospital due to non-traumatic AA at the time of admission, the parameters indicated in the literature as a guideline can be listed as PCT [9], D-Dimer [10], Interleukin-1, Interleukin-1 receptor, Interleukin-1 receptor antagonist [11], Interleukin-6 [12], Plasma lactate concentration [13] and Neopterin [14] in addition to leukocyte and CRP [5]. In our study, the values of 4 parameters, which were used more frequently within the above-mentioned parameters, were examined not only at the time of admission to hospital but also during treatment process.

In our study, the leukocyte level was higher in the groups with surgical treatment than in the group treated without surgery, and this was an expected result, consistent with the literature. However, using leukocyte level alone could be misleading among laboratory parameters because some patients with normal leukocyte levels (Group - 1: 4.600/mm3, Group - 2: 4.900/mm3) underwent surgical treatment and also there were patients with a significantly higher leukocyte level (23.600/mm3) at the time of admission to the hospital in the group that did not undergo surgical treatment.

Considering the facts that there was no statistically significant difference among the CRP measurements in all groups in day 0 in our study and there was a decrease in CRP levels in follow-up in Group - 2, whereas there was a decrease in the follow-up in Group - 3, we believe that the value of CRP at the time of patient's admission alone should not be effective in determining the treatment method, and that the change in CRP in the treatment process is more valuable. On the other hand, the fact that CRP levels were higher in the group who underwent surgery than in the group without surgery supports the idea that CRP may be a useful parameter in deciding about surgery; however, we think that only evaluating the CRP level at the time of admission may be misleading.

Considering the facts that no statistically significant difference was found between D-Dimer measurements at the time of admission of the patients according to the groups in our study, and the D-dimer level, which was high in all groups at the time of admission, continued to increase in the group who underwent surgery during follow-up, but decreased in the medical treatment group, it is thought that the change in D-Dimer level, rather than the value at the time of admission of the patient, may be more valuable in determining the treatment modality. In addition, we think that the statistically significant decrease in D-dimer levels on the 2nd day of measurements in Group - 3 patients, who showed no statistically significant increase on Day 1, according to the value of day 0, and the increase in the D-dimer value in the early period will not support the right decision for surgery, on the contrary, a decrease in D-dimer value in the following days is more valuable in supporting the decision to move away from the surgery decision.

In our study, we attribute a normal PCT level to the fact that pathological event has just started in patients (Group -1) with the decision to undergo surgery and the result of the PCT reflecting the time of admission to the hospital. A statistically significant increase in PCT measurement on day 1 compared to day 0 in patients operated on day 1 (Group -2) and an increase in the level of PCT during the follow-up period can be interpreted as helpful in deciding on surgery. Furthermore, the fact that the PCT values in patients in Group - 3 were low from the day of the admission and continued to decrease in the follow-up period supports this interpretation. Dias et al. analyzed a total of 58 patients who presented with acute abdomen [15]. Plasma PCT (value >5 ng/mL) could be used to predict the requirement for surgery in patients presenting with acute abdomen. In our study, the PCT value was not found to be statistically significant.

Conclusion

In conclusion, in patients with non-traumatic acute abdominal pain, changes in CRP, D-Dimer and PCT values are more valuable in the clinical process than their level at the referral stage in determining the main treatment methodology (surgical treatment or medical treatment), and that the evaluation in the clinical process may prevent unnecessary surgical interventions.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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