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Klinik Çalışma

The value of D-dimer test in the diagnosis of patients with nontraumatic acute abdomen

Travma dışı akut karınlı hastaların tanısında D-dimer testinin değeri

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BACKGROUND

A patient with acute abdominal pain requires rapid evaluation. In these patients, it is very important to distinguish between surgical and nonsurgical pathology. Our aim was to compare the accuracy of the leukocyte count and D-dimer test in the diagnosis of acute abdomen.

METHODS

In this prospective study, 225 patients admitted to the emergency unit due to nontraumatic acute abdomen between June 2006 and November 2007 were evaluated. The patients were divided into two groups: Group 1 patients who needed immediate laparotomy and Group 2 patients who did not. Age, gender, leukocyte count, D-dimer level, causes of acute abdominal pain, and operative findings were investigated. P values of <0.05 were considered statistically significant.

RESULTS

There was a positive correlation between the plasma D-dimer level and leukocyte count. D-dimer acted similarly to the leukocyte count in emergency abdominal conditions. The area under the receiver operating characteristic curve was statistically higher with the D-dimer test ($p<0.0001$). Additionally, in patients needing immediate laparotomy, the sensitivity of the D-dimer test was 95.7% versus 74.8% for leukocyte counts.

CONCLUSION

In a patient with acute abdomen, D-dimer test may be a strong alternative or an adjuvant to the leukocyte count.

Key Words: Acute abdomen; D-dimer; leukocyte.

AMAÇ

Akut karınlı bir hasta hızlıca değerlendirilmeyi gerektirir. Bu hastalarda karın ağrısının cerrahi bir nedenden mi yoksa cerrahi olmayan bir nedenden mi olduğunu anlamak çok önemlidir. Bu çalışmada, akut karın tanısında lökosit sayısının ve D-dimer testinin doğruluğu karşılaştırıldı.

GEREÇ VE YÖNTEM

Bu prospektif çalışmada, Haziran 2006 ile Kasım 2007 tarihleri arasında travmaya bağlı olmayan akut karın nedeniyle acil servise başvuran 225 hasta değerlendirildi. Hastalar iki gruba ayrıldı: grup 1 acil cerrahi girişim gerektirenler ve grup 2 gerektirmeyenler. Yaş, cinsiyet, lökosit sayısı, D-dimer seviyesi, akut karın ağrısının nedeni ve ameliyat bulguları araştırıldı. P değerlerinden 0,05'den küçük olanlar istatistiki olarak anlamlı kabul edildi.

BULGULAR

D-dimer seviyesi ve lökosit sayısı arasında pozitif bir korelasyon bulundu. Acil karın içi durumlarda D-dimer ve lökosit sayısı benzer şekilde davrandı. ROC eğrisi altında kalan alan ise D-dimer testinde anlamlı olarak daha yüksekti ($p<0,0001$). Ek olarak, acil laparotomi gereken hastalarda bu testin duyarlığı %95,7 iken lökosit sayısınınki ise %74,8 olarak saptandı.

SONUÇ

Akut karınlı bir hastada D-dimer testi lökosit sayısına güçlü bir alternatif veya yardımcı olabilir.

Anahtar Sözcükler: Akut karın; D-dimer; lökosit.

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Acute onset of intense abdominal pain necessitates rapid evaluation. The physician must take into account many entities. The most important step is the decision of whether the pain is from a surgical or nonsurgical pathology. A delay in diagnosis will increase morbidity and mortality. Thus, the differential diagnosis is essential and sometimes life-saving.

A brief history and complete physical examination are obligatory for proper immediate therapy. Prompt radiographs and laboratory tests are usually helpful in the differential diagnosis. Chest X-rays, a plain abdominal X-ray, abdominal ultrasonography, and leukocyte counts are used most often. Today, modern computed tomography is more widely available, less invasive, can be performed quickly, and can provide further information. Nevertheless, there are many conditions that restrict its use, such as technical problems, renal insufficiency and severe allergic reaction. These cases, who generally have more than one comorbidity, are common in the surgical departments of many hospitals in large cities.

Fibrin degradation fragment, also known as D-dimer, is a fibrinolytic marker that is used to diagnose venous thromboembolism, pulmonary embolism, disseminated intravascular coagulopathy, and intraabdominal pathologies. A positive D-dimer test indicates an abnormally high level of fibrin degradation products of a blood clot caused by venous or arterial thromboembolism.[1-7]

In this prospective clinical study, our aim was to evaluate the accuracy and usefulness of D-dimer testing in the differential diagnosis of patients with acute abdomen by comparing its sensitivity and specificity to those of leukocyte count.

MATERIALS AND METHODS

The study was approved by the research ethics committee of Erciyes University Medical Faculty and was undertaken at the general surgery department of that facility. Between June 2006 and November 2007, the patients who admitted to the department of surgery due to abdominal pain were enrolled. All traumatic patients, patients who used warfarin or heparin, patients with vascular occlusion or with a suspicion of vascular occlusion except for the mesentery vascular system (deep vein thrombosis, pulmonary emboli, acute or chronic ischemic events, acute or chronic ischemia of the extremities, etc.), pregnant patients, and patients with recent surgical procedures (less than 6 months) were excluded from the study.

The remaining 225 patients were evaluated prospectively. Blood samples were taken on admission for analysis of the fibrinolytic marker D-dimer, white blood cells, and arterial blood. D-dimer concentration was determined with a quantitative immunofiltration assay method (MDA® D-dimer, bioMérieux, Durham, North Carolina, USA; normal value >0.6 µg fibrinogen equivalent units (FEU)/ml). A leukocyte level higher than 12,000 was considered as leukocytosis.

Age, gender, causes of acute abdominal pain, and operative findings were investigated. Following a brief history, physical examination, prompt diagnostic modalities, and laboratory tests, the patients were divided into two groups as: Group 1, patients who needed immediate laparotomy and Group 2, patients without need for immediate laparotomy. Patients who had been operated after initial conservative treatments were included in Group 1 according to their postoperative pathologies or continued to be a subgroup of Group 2 if the laparotomy was negative.

Statistical Analysis

Data from the study were evaluated with the statistical SPSS package version 13.0 (Chicago, IL). Data were expressed as mean ± standard deviation (SD) or median (range). Differences between categorical variables were compared with chi-square test; Mann-Whitney U tests were used to evaluate the statistical values of leukocyte counts, D-dimer levels and age. Spearman correlation coefficient was calculated to determine the significance level of the relationship between leukocyte counts, D-dimer levels and age. The cutoff values, area under curves (AUC), sensitivity, and specificity were calculated by the receiver operating characteristic (ROC) curve technique for leukocyte counts and D-dimer levels. Agreement between the leukocyte counts and D-dimer level was analyzed using Bland-Altman plots. P values of <0.05 were considered statistically significant.

RESULTS

Two hundred twenty-five patients (female: 105, male: 120) with a mean age of 56.67±14.17 years were evaluated. Group 1 consisted of 110 patients and Group 2 of 115 patients. Etiologic distributions of groups are described in Table 1. One hundred fifty-eight patients were operated. Sixty-seven patients were treated conservatively or were operated later under elective conditions. There was no significant difference between groups with regard to patients' demographics. In patients requiring immediate laparotomy (Group 1), the

Table 1. Etiological distribution of groups

Group 1	n	Group 2	n
Patients	110	Cholecystitis	33
Intestinal necrosis	56	Late stage cancer	24
Ulcer perforation	29	Acute appendicitis	23
Gallbladder necrosis	14	Acute pancreatitis	20
Perforated appendicitis	11	Negative laparotomy	15

Table 2. Sensitivity and specificity values of the leukocyte counts and D-dimer levels

	Cut-off value	Sensitivity	Specificity	AUC-ROC (95%CI)
Leukocyte	> 14200	70	58	0.62 (0.54-0.67)**
D-dimer	> 1.6	64	86	0.82 (0.76-0.86)***

AUC: Area under ROC curve; ROC: Receiver operating characteristics; CI: Confidence interval.
Statistically significant (p=0.004)**; (p<0.0001)***.

means of the D-dimer levels and leukocyte counts were 4.49±3.00 µg FEU/ml and 15211±7100/mm^3, respectively. In Group 2, these values were 1.87±1.43 µg FEU/ml and 13071±5092/mm^3, respectively.

D-dimer levels and leukocyte counts showed a weak positive correlation in all patients (Spearman rho = 0.16, p=0.014). The sensitivity and specificity values and cutoff values of the leukocyte counts and D-dimer levels are shown in Table 2. The sensitivity and specificity curves of these parameters are shown in Fig. 1. Leukocyte counts higher than 14200/mm^3 (p<0.004) and D-dimer levels higher than 1.6 µg FEU/ml were more sensitive (p<0.0001). At the mean value of D-dimer level of patients needing immediate laparotomy, D-dimer test sensitivity increased to 95.7%. The AUC of the D-dimer test was significantly larger than the AUC of the leukocyte count (82 versus 62; Table 2, Fig. 1). In addition to correlation analysis, the compliance between the leukocyte counts and D-dimer levels in both groups was evaluated with Bland-Altman plots (Fig. 2). We observed a moderate correlation and demonstrated the agreement of the similar fields of the two parameters. D-dimer levels acted similarly to the leukocyte counts in emergency abdominal conditions.

With regard to D-dimer levels, there were no significant differences between subgroups of Group 1, and all of the 110 patients had a D-dimer level above the normal value. In this group, there were only 12 patients with D-dimer levels below the cutoff value (1.6 µg FEU/ml) and interestingly, the majority of these patients (9 patients) were in the mesentery vascular occlusion subgroup. Two of the remaining patients were in the perforated appendicitis subgroup and one was in the gallbladder necrosis subgroup.

Comorbidities were present in 52 patients in Group 1 (98 comorbidities) and in 49 patients in Group 2 (70 comorbidities). Approximately half of these patients had more than one comorbidity (51 patients, 50.5%). The comorbidity rates were similar between groups except for the high rate of atrial fibrillation seen in the subgroup of Group 1 patients with mesentery vascular occlusion (Table 3).

DISCUSSION

D-dimer is an indirect measure of thrombin generation and subsequent clot formation. A positive D-dimer test indicates an abnormally high level of fibrin degradation products. An elevated D-dimer level may be seen in many conditions such as venous thromboembolism, acute ischemic stroke, sudden arterial occlusion of lower extremities, pulmonary embolism, acute aortic dissection, symptomatic abdominal aortic aneu-

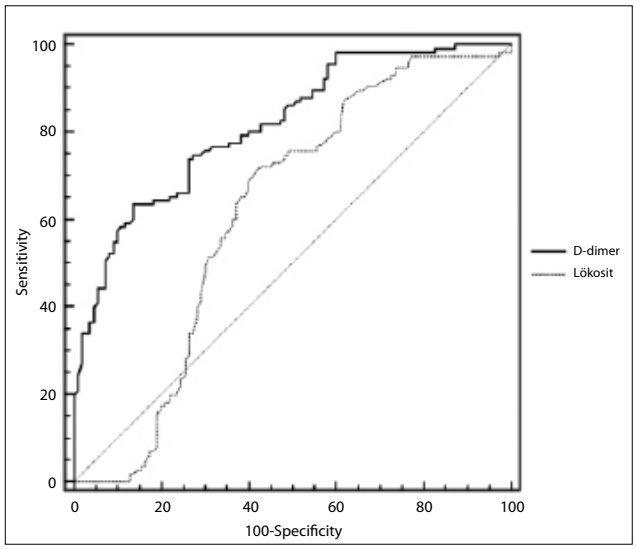

Fig. 1. Sensitivity and specificity curves for D-dimer and leukocyte count. Pairwise comparison of ROC curves (p<0.0001).

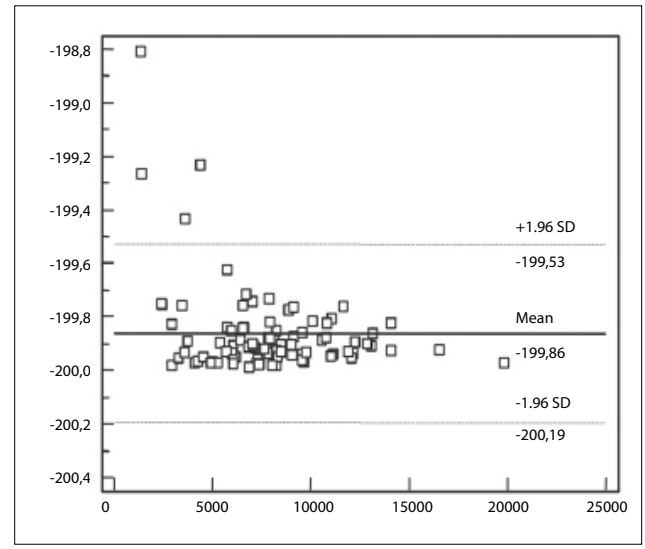

Fig. 2. Bland-Altman plots for leukocyte counts and D-dimer levels in the two groups. The dotted lines mark the upper and lower limits of the 95% confidence interval (mean ± 2 SD) and the dashed lines indicate the bias.

Table 3. Comorbidities in Groups 1 and 2

	Group 1 52 patients	Group 2 49 patients
HT	29	30
AF	40	4
CHF	12	15
COLD	9	12
DM	8	9

HT: Hypertension; AF: Atrial fibrillation; CHF: Congestive heart failure; COLD: Chronic obstructive lung disease; DM: Diabetes mellitus.

rysm, severe trauma, liver disease, pregnancy, eclampsia, cancer, and recent surgery.[8-12] D-dimer is a stable molecule with 4-8 hour *in vivo* half-life and attains higher plasma levels when fibrin begins to degrade. Therefore, it is very useful in acute conditions.[13]

D-dimer levels in intraabdominal pathologies are a relatively new area of investigation. In patients with acute thromboembolic occlusion of the superior mesenteric artery, with strangulated intestinal hernia or with unclear nontraumatic acute abdomen, D-dimer levels were reported to be significantly higher.[4-6] Although these reports and high sensitivities were harmonious with our results, in this study, the sensitivity of D-dimer test at the cutoff point was lower. This difference was probably due to the high selection criteria and the very limited number of patients in the other studies.

As described in the Bland-Altman plots, the agreement of the similar fields of the two parameters (plasma D-dimer level and leukocyte count) demonstrated the accuracy of plasma D-dimer level for evaluating patients with acute abdomen as an alternative or as an adjuvant to the leukocyte count. At cutoff levels, although the sensitivity of the D-dimer test was lower than that of the leukocyte count, its area under the ROC curves, which is much more important, was significantly larger ($p<0.0001$). This difference in areas revealed that the D-dimer test was more accurate and useful for more patients than the leukocyte count. Another superiority of the D-dimer test over the leukocyte count in distinguishing surgical from nonsurgical pathology was the p values of the cutoff levels ($p<0.0001$ versus $p<0.004$). Additionally, the mean value of D-dimer levels in patients needing immediate laparotomy (4.49±3.00 µg FEU/ml) had a sensitivity of 95.7%, whilst the mean value of leukocyte counts ($15211 \pm 7100/mm^3$) for the same patients had a sensitivity of 74.8%.

There is no generally accepted explanation of why D-dimer levels rise in acute abdominal conditions. The increase in D-dimer levels in these patients may be explained by the following mechanism: a generalized inflammatory process in every patient who needed emergency laparotomy may cause at least impaired local circulation; coagulation parameters like D-dimer show significant changes corresponding to changes found in the intestinal circulation, and respectively, local intestinal changes in coagulation and fibrinolysis mimic the systemic response in a generalized inflammatory state.[5,14,15]

Laparotomy or laparoscopy in patients with multiple comorbidities carries a high risk of morbidity and mortality. Therefore, with these kinds of patients, the surgeon needs to be sure of a surgical pathology. Additionally, in case of emergency, in patients with acute abdomen who require intensive care because of comorbidities such as basal pneumonia, diabetes mellitus, vascular pathology, renal diseases, and cardiac pathology, the decision is much more difficult. There are no precise predictors of which patients have surgical pathology and to what degree they have it. These cases are common in the surgical departments of many universities. Despite the advances in radiology in terms of speedy high resolution images, this technology is not helpful in all cases for many reasons as mentioned before, such as renal failure and contrast hypersensitivity, etc.

This prospective study including 225 patients demonstrated that in patients with acute abdomen, D-dimer test may be used as an important adjuvant to other diagnostic modalities, and it even performed better than leukocyte count. Further clinical and experimental studies are warranted in order to evaluate the precise value and place of D-dimer level in acute and chronic abdominal conditions and to better understand its relationship with the inflammatory process and acute phase reactants.

In conclusion, in a patient with acute abdomen, if the D-dimer level is higher than 1.6 µg FEU/ml (3 times normal value), the physician can predict a surgical pathology with 64% sensitivity and 86% specificity. The sensitivity becomes higher with the increase in D-dimer levels, and in patients requiring immediate laparotomy (mean D-dimer value for these patients was 4.49±3.00 µg FEU/ml), the sensitivity of the D-dimer test was 95.7% versus 74.8% for leukocyte count.

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