ORIGINAL ARTICLE

The efficacy of hemogram parameters in the differential diagnosis of renal colic and acute appendicitis in the emergency department

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ABSTRACT

BACKGROUND: To investigate the efficacy of WBC, PLR and NLR for use in the differential diagnosis of acute appendicitis and renal colic in the emergency department.

METHODS: This study was conducted after consent was received from the Cukurova University Medicine Faculty Noninvasive Clinical Research Ethics Committee. In this study, 440 patients for whom file data could be accessed in the hospital automation and archive system who were admitted to the hospital with abdominal pain were included.

RESULTS: Of the 440 patients included in this study, 59.5% were male and 40.5% were female. The average age of the patients was 37.74±13.39 years. According to the pathological diagnosis, 207 patients were diagnosed with acute appendicitis. When the efficacy of differential diagnosis using hematological parameters was examined with ROC analysis, the neutrophil/lymphocyte ratio (NLR) value had the strongest predictive ability (AUC, 0.716, SS=0.024, 95% GA 0.668–0.764). After NLR, the platelet/lymphocyte ratio (PLR) value was the second-best concerning predictive ability for differential diagnosis (AUC, 0.608 SS=0.027, 95%, GA 0.555–0.661).

CONCLUSION: Patients with acute appendicitis and renal colic often present to the emergency department with abdominal pain. While patients with acute appendicitis are usually treated with surgical methods, medical treatment is used for renal colic in the acute period. The differential diagnosis of these two patient groups is important. We believe that the PLR and NLR values can be used when an exact differential diagnosis cannot be made.

Keywords: Acute appendicitis; neutrophil/lymphocyte ratio; platelet/lymphocyte ratio; renal colic.

INTRODUCTION

Abdominal pain causes 10% of all admissions to the emergency department. Demographic findings (age, gender, ethnicity, family history, cultural practices, and geographical location) affect the clinical features and incidence of abdominal pain. Medical history, vital signs and physical examination findings may not lead to a specific diagnosis, and sometimes laboratory findings are not useful. Although there is often no definite cause underlying a patient's pain, the examination should be conducted to exclude life-threatening conditions, and the differential diagnosis should be narrowed for further investigation.

Acute appendicitis is one of the most common causes of hospitalization for patients admitted to the emergency department due to abdominal pain. In addition, appendectomy is one of the most common emergent surgical procedures.[1]

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Renal colic is a condition that can be diagnosed rapidly among patients admitted to emergency departments with a complaint of acute pain. Abdominal pain lasting less than 12 hours, low back pain or costovertebral angle sensitivity and hematuria (>10 erythrocytes/microscope field) are among the most important findings of acute renal colic. Patients with urinary stones generally describe acute onset pain that begins in the lumbar region and spreads towards the groin that causes much suffering and is intermittent.

In addition to using the available laboratory tests and imaging methods, some investigators have conducted studies in which several hemogram parameters, such as the white blood cell (WBC) count, neutrophil-lymphocyte ratio (NLR), platelet neutrophil ratio (PNR), platelet count (PLT), mean platelet volume (MPV) and red cell distribution width (RDW), have been frequently used to increase the validity of the diagnosis of acute appendicitis and renal colic, and these tests are available in almost all clinics.[2]

The present study aimed to investigate the efficacy of the use of WBC, PLR and NLR values for the differential diagnosis of acute appendicitis and renal colic in the emergency department.

MATERIALS AND METHODS

Patient Selection

This study was conducted after the decision by the Cukurova University Medical Faculty Non-Interventional Clinical Research Ethics Committee dated 7 July 2017 (meeting number: 66 and decision number: 42). In this study, 440 patients whose information was stored in the archives of the automation system and who were admitted to the emergency department of our hospital between January 01, 2016 and December 31, 2017 with a complaint of abdominal pian and diagnosed with acute appendicitis and renal colic were included. The age, sex, abdominal ultrasonography reports, computed abdominal tomography (CAT) reports, pathology reports, emergency department outcomes and the hospitalization period of the patients were recorded. Patients for whom some information was missing in the file data or who were under 18 years of age, were referred to another center, who refused treatment, whose final diagnosis was not acute appendicitis and/or renal colic or who had additional diseases (coronary artery disease, hypertension, diabetes mellitus, chronic liver disease, chronic renal disease, asthma, or chronic obstructive pulmonary disease) were excluded from this study. In this study, 207 patients who were confirmed to have been diagnosed with acute appendicitis were defined as Group 1 and 233 patients who were confirmed to have been diagnosed with renal colic were defined as Group 2.

Laboratory Analysis

The hemogram and biochemical parameters of the patients included in this study were measured using venous blood samples taken from the antecubital region upon admission to the emergency department. The WBC, hemoglobin, hematocrit, RDW, MPV, PLR and NLR values were determined and recorded. The glucose, urea, creatinine, aspartate aminotransferase (ALT), alanine aminotransferase (AST), sodium and potassium levels, which are biochemical parameters, were determined and recorded. Whole blood count measurements were performed using a Sysmex XN 10 automated measuring device (Automated Hematology Analyzer XN series, Sysmex Corporation, 1-5-1 Wakinnohama-Kaigandori Chuo-ku, Kobe 651-0073, Japan). Biochemical parameters were measured using a Beckam Coulter AU5800 automated measuring device (Beckman Coulter GmbH Europark Fichtenhain B 13 47807, Krefeld, Germany).

Statistical Analysis

For the statistical analysis, the 'SPSS for Windows Version 21' program was used. While analyzing the data, descriptive statistical methods (mean, standard deviation) were used, and Student's t-test was used to analyze the distribution of the quantitative data. The Mann-Whitney U test was used for the analysis of data that did not show a normal distribution. The chi-square test was used for qualitative evaluation. Statistical values below $p<0.01$ were considered significant. Using the hematological parameters and the analysis of the receiver operating characteristics (ROC) curve of the cardiac markers and area under the curve calculations (AUC), the efficacy of the values in predicting the differential diagnosis were calculated. The cut-off values of the strongly predictive parameters with the highest specificity and sensitivity ratios were determined and recorded.

RESULTS

Of the patients included in this study, 59.5% were male (n=262), and 40.5% (n=202) were female. The mean age of the patients was 37.74±13.39 years.

The data regarding the hematological and biochemical parameters of the patients are given in Table 1.

Abdominal ultrasonography (USG) was not performed on 305 (69.3%) patients, while it was performed on the remaining 135 (30.7%) patients. Of the patients for whom USG was performed, 59 (13.4%) were reported to be normal, while 36 (8.2%) patients had acute appendicitis (Group 1), and 40 (9.1%) patients were reported to have urinary stones (Group 2).

The findings showed that computed abdominal tomography (CAT) was not performed for 59 (13.4%) patients, but it was performed for the remaining 381 patients (86.6%). While 58 (13.2%) of the patients for whom CAT was performed were reported to be normal, 131 (29.8%) patients were reported to have acute appendicitis (Group 1), and 192 (43.6%) patients were reported to have urinary stones (Group 2).

Table 1. Evaluations hematological and biochemical parameters of patients

	n	Minimum	Maximum	Average±Standard deviation
White blood cell (10^3/μl)	440	4.00	32.40	11.88±4.16
Hemoglobin (g/dL)	440	7.84	19.10	13.69±1.85
Hematocrit (%)	440	26.40	58.20	41.03±5.21
Platelet (10^3/μl)	440	97.00	600.00	262.05±72.25
Mean platelet volume (fL)	440	4.49	98.00	9.09±4.47
Red cell distribution width (%)	440	11.00	21.70	13.87±1.49
Platelet/lymphocyte ratio	440	29.88	880.00	146.39±93.75
Neutrophil/lymphocyte ratio	440	0.65	47.25	5.48±5.43
Glucose (mg/dL)	440	63.00	569.00	114.44±44.35
Urea (mg/dL)	440	8.00	43.00	27.30±7.38
Creatinine (mg/dL)	440	0.27	1.40	0.82±0.22
Alanine aminotransferase (U/L)	440	5.00	44.00	20.30±9.20
Aspartat aminotransferase (U/L)	440	3.40	44.00	23.19±8.15
Sodium (mmol/L)	440	135.00	145.00	139.13±2.22
Potassium (mmol/L)	440	3.50	5.50	4.23±0.39

When the patients were examined for surgical suitability, 207 (47%) patients diagnosed with acute appendicitis underwent surgery, and their pathology reports were consistent with acute appendicitis. The remaining 233 patients were diagnosed with renal colic and did not undergo surgery. Of the patients who underwent surgery, 207 (47%) patients were admitted to the general surgery clinic, 28 (6.4%) of 233 patients diagnosed with renal colic were admitted to the urology clinic, and 205 (46.6%) patients were discharged after treatment in the emergency department was completed.

An evaluation was performed regarding the practical efficacy of the use of biochemical and hematological parameters for differential diagnosis. Acute appendicitis patients comprising Group 1 and renal colic patients comprising Group 2 were compared. As a result, no statistically significant difference was found between the hemoglobin, hematocrit, platelet count, MPV, RDW, glucose, ALT, AST, sodium and potassium values (p-values for each parameter were p=0.596, p=0.075, p=0.193, p=0.328, p=0.608, p=0.245, p=0.711, p=0.633, p=0.038 and p=0.561, respectively). When the groups were compared

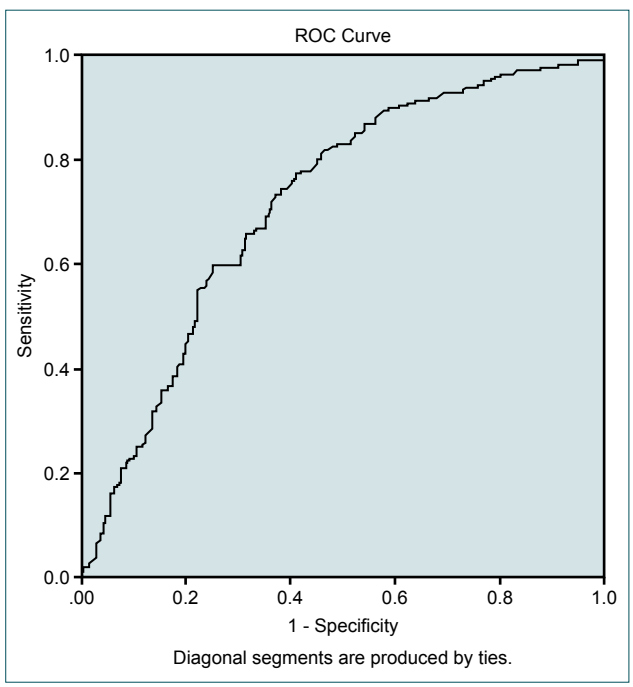

Figure 1. ROC analysis of neutrophile-lymphocyte ratio.

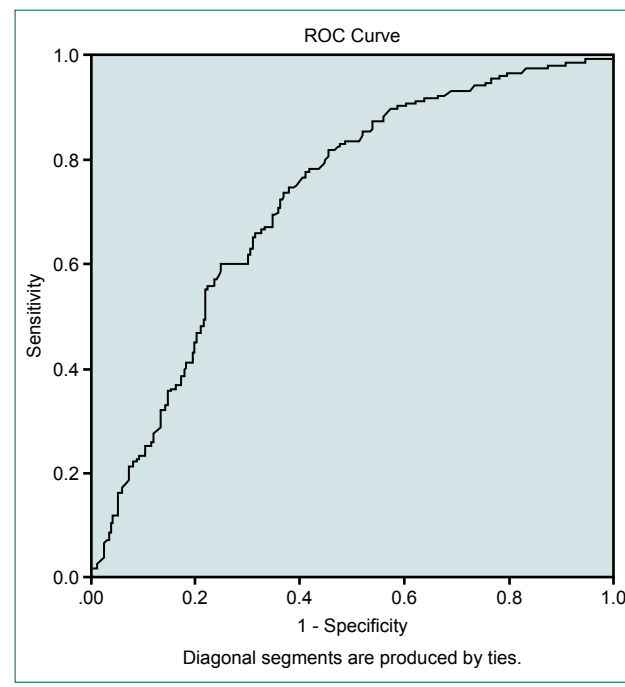

Figure 2. ROC analysis of platelet- lymphocyte ratio.

Table 2. Comparison of hematological and biochemical parameters in the differential diagnosis of groups

Parameter	Groups	N	Average±Standard deviation	p-value
White blood cell	Group 1	207	13.59±3.97	<0.001
	Group 2	233	10.36±3.72	
Hemoglobin	Group 1	207	13.64±1.91	0.596
	Group 2	233	13.73±1.80	
Hematocrit	Group 1	207	41.50±5.29	0.075
	Group 2	233	40.61±5.11	
Platelet	Group 1	207	266.81±66.62	0.193
	Group 2	233	257.82±76.81	
Mean platelet volume	Group 1	207	9.31±6.35	0.328
	Group 1	233	8.89±1.24	
Red cell distribution width	Group 1	207	13.91±1.59	0.608
	Group 2	233	13.84±1.40	
Platelet/lymphocyte ratio	Group 1	207	158.84±100.16	0.009
	Group 2	233	135.36±86.38	
Neutrophil/lymphocyte ratio	Group 1	207	6.86±6.02	<0.001
	Group 2	233	4.26±4.50	
Glucose	Group 1	207	111.83±42.91	0.245
	Group 2	233	116.76±45.56	
Urea	Group 1	207	24.96±7.13	<0.001
	Group 2	233	29.38±6.98	
Creatinine	Group 1	207	0.74±0.18	<0.001
	Group 2	233	0.89±0.23	
Alanine aminotransferase	Group 1	207	20.47±9.76	0.711
	Group 2	233	20.15±8.68	
Aspartat aminotransferase	Group 1	207	22.99±8.32	0.633
	Group 2	233	23.36±8.01	
Sodium	Group 1	207	138.90±2.13	0.038
	Group 2	233	139.34±2.29	
Potassium	Group 1	207	4.25±0.38	0.561
	Group 2	233	4.22±0.40	

concerning the WBC, PLR, NLR, urea and creatinine values, the difference between the groups was statistically significant (p-values for each parameter were p<0.001, p=0.009, p<0.001, p<0.001, and p<0.001, respectively) (Table 2).

Table 3. Area under the curve for PLR and NLR

	Area	SD	p-value	95% CI	
				Lower Bound	Upper Boundr
PLR	0.608	0.027	<0.000	0.555	0.661
NLR	0.716	0.024	<0.000	0.668	0.764

PLR: Platelet/lymphocyte Ratio; NLR: Neutrophil/lymphocyte ratio; CI: Confidence interval.

When the practical efficacy of the use of hematologic parameters for differential diagnosis was examined using ROC analysis, the NLR value had the strongest predictive capability (AUC, 0.716, SD=0.024, 95% CI 0.668–0.764). When the cut-off value of NLR was set to 3.67, it was found that it had 72.0% sensitivity and 63.5% specificity (Fig. 1, Table 3). Following NLR, PLR was the second strongest predictor of the differential diagnosis (AUC, 0.608, SD=0.027, 95% CI 0.555 0.50.661). When the cut-off value of the PLR was set to 124 at the end of the analysis, it was found to have a sensitivity of 60.4% and a specificity of 56.2% (Fig. 2, Table 3).

DISCUSSION

This study demonstrates that the WBC, PLR, and NLR values can be used to differentiate among patients with acute

appendicitis and renal colic who have been treated in the emergency department due to acute abdominal pain. It has also been shown that the PLR and NLR cut-off values can be considered when making this distinction.

Acute appendicitis is the most common cause of surgery in patients who have been admitted to the emergency department with the complaint of acute abdominal pain. The incidence of appendicitis throughout the life span of a human being has been reported to be 6–7%.[3,4] It is more common in males than in females, and the ratio of males to females is 1.3/1.[5,6] The incidence of appendicitus usually reaches a peak in the 2nd and 3rd decades of life.[3,7] Renal colic is the most common reason for patients to be admitted to the emergency department due to side pain, but the complaint may also be acute abdominal pain. Renal colic is a disease for which diagnosis and treatment are performed in the emergency department, and it usually does not require emergent surgery. Renal colic is 2-fold more common in men than in women, and attacks usually occur in the 3rd and 5th decades of life.[8,9] The data we obtained are consistent with the data in the literature.

Acute appendicitis and renal colic are the most common causes of abdominal pain. Renal colic can be confused with acute appendicitis, which occurs with a frequency of 4%. Therefore, additional laboratory tests and imaging procedures are needed.[10] Physicians working in emergency departments encounter this condition many times every day and attempt to perform the differential diagnosis of these two diseases. Tan et al.[11] emphasized the importance of computed abdominal tomography (CAT) in the differential diagnosis of suspected patients. In their study, the rate of negative appendectomy was 5.7% in patients for whom a CT evaluation was performed; however, this rate increased to 17.9% in those without a CT evaluation. Emergency physicians have difficulties in diagnosing these diseases, especially in emergency departments where advanced diagnostic tools, such as ultrasonography (USG) and CT, are not available.[12] In particular, right ureteral stones can be confused with acute appendicitis when radiological imaging is not available. Physicians cannot fully protect themselves against medical and legal consequences if they have to rely only on physical examination.[13] Because of this, objective data should be used to differentiate between these two groups of patients with abdominal pain complaints. When the data of the patients included in our study were examined, we found that CAT was performed on 381 patients, 131 (29.8%) of whom were diagnosed with acute appendicitis. When abdominal USG, which is one of the diagnostic methods, was used as the basis diagnosis, we found that only 8.2% of the patients were diagnosed with acute appendicitis. However, we observed that 207 (47%) of 235 hospitalized patients had acute appendicitis pathology. Despite the advanced radiological diagnostic methods in our third-level hospital, the diagnosis of acute appendicitis could not be made using CT in 17.3% (n=76) of patients and using USG in 38.9% (n=171) of patients. The usefulness of USG is dependent on the patient; the patient may be obese, for example. The optimal conditions often cannot be achieved because elective preparations, such as fasting and bowel cleansing for USG in emergent conditions, cannot be performed, which may be factors that prevent diagnosis.[14] Additional indicators that will assist those working in emergency departments where such advanced diagnostic tools are not available are needed, and these will be useful in cases when there are disadvantages related to the use of advanced methods.

The WBC, MPV, RDW, NLR and PLR are known to reflect inflammatory processes. There have been some studies showing that these inflammatory markers are valuable.[15,16] Acute appendicitis is caused by inflammation of the appendix vermiformis through direct inflammatory processes. Therefore, some inflammatory markers are still under investigation. As reported in many studies, these inflammatory markers have led many inexperienced physicians and surgeons to choose surgery.[17] In a study conducted by Tanrikulu et al.,[18] patients diagnosed with acute appendicitis were compared with a control group. As a result, the findings showed that the MPV, RDW and WBC were significantly higher in the group of patients with acute appendicitis. In a meta-analysis in which 3382 patients and 14 studies were analyzed, the sensitivity and specificity of leukocytosis (leukocyte count >10000) in the diagnosis of acute appendicitis were reported to be 83% and 67%, respectively. During the acute phase of renal colic, increased intraluminal pressure causes pain. While inflammation is not yet seen in the acute phase, inflammatory processes develop through mediators, such as prostoglandins and nitric oxide.[19] A high WBC value is not a specific marker because it is increased by many inflammatory processes.[20] In this study, in which we investigated the efficacy of the use of the WBC in the differential diagnosis of renal colic and acute appendicitis, we found that the WBC was significantly higher in patients with acute appendicitis than in those with renal colic. Since acute appendicitis starts with an inflammatory process, but renal colic is not associated with inflammation but with increased luminal pressure, we are of the opinion that the WBC may be a useful marker for the differential diagnosis in emergency departments in the early disease period.

Another inflammatory marker is the NLR. In a study conducted by Kahramanca et al. in 1062 patients, a point that they particularly emphasized was the determination of the cut-off value for the NLR. The researchers pointed out that when the NLR cut-off value was 4.68, it was a marker of acute appendicitis; when it was 5.74, it was an important marker of complicated perforated appendicitis.[19] The importance of the NLR in the differential diagnosis of renal colic and acute appendicitis was highlighted in a study conducted by Acar et al.,[13] which indicated that the NLR could be used in differential diagnosis. However, when we examined the data in the literature, we did not find any data indicating the use of the NLR cut-off value for the differential diagnosis of acute appendicitis and renal colic. When the NLR cut-off

value obtained in our study was set to 3.67, we found that it had a sensitivity value of 72% and a specificity value of 63.5%. We are of the opinion that a value above this cut-off value can be used as an indicator of acute appendicitis, whereas a value below this may indicate renal colic. The data from our study differ from that of the literature in this case.

PLR is an indicator of severe inflammation. It has been used to assess the inflammatory process leading to the release of proinflammatory cytokines and the proliferation of megakaryocytes.[21] The activation of platelets is a marker that could also be used to assess the course of cancer since this leads to angiogenesis, degradation of the extracellular matrix, and the release of adhesion molecules and growth factors.[22,23] Lee et al.[24] emphasized that the PLR may be used as an independent predictor of the prognosis of gastric cancers. There have also been studies showing that this value can be used to determine the prognosis of colorectal cancers.[25,26] Yıldırım et al.[21] investigated the importance of the PLR value in the diagnosis of patients with complicated acute appendicitis and emphasized that it is an important marker. In a study conducted by Acar et al.,[13] the importance of the PLR value in the differential diagnosis of renal colic and acute appendicitis was emphasized, and the researchers stated that it could be used in differential diagnosis. Nevertheless, a cut-off value for PLR was not determined in these studies, and no data on the usability of the cut-off value for the distinction of acute appendicitis from renal colic were given. When the PLR cut-off value obtained in our study was 124, we found that it had a sensitivity value of 60.4% and a specificity value of 56.2%. We think that values above this cut-off value can be used as an indicator of acute appendicitis, whereas values below the cut-off may indicate renal colic. The data from our study differ from that of the literature in this case.

The platelet count is performed as part of the complete blood count. It plays an important role in inflammation, as well as in stopping bleeding and maintaining hemostasis. Inflammation can be defined as the efforts of living tissues to combat pathological factors to remove a pathogen and initiate the healing process.[27] The MPV acts as an acute phase reactant and is a biological marker of platelet activation that is associated with the morphology of platelets.[28] The RDW is a measure of the variability in the sizes of red cells. Inflammation and oxidative stress possibly cause an RDW increase by altering erythrocyte hemostasis.[29,30] Among studies on the MPV and RDW conducted in different patient groups, some studies have found meaningful results for both high and low levels of these indicators. In studies concerning patients with ischemic stroke, there have been cases in which high levels were meaningful.[31–34] However, another study concerning ischemic stroke subtypes did not reveal a significant relationship. Sevinç et al.[35] conducted a study on 3329 patients and found that a low MPV value was significant in patients with acute appendicitis, whereas Acar et al.[13] found that high MPV and RDW values were significant in patients with renal colic. MPV and RDW values are known to be associated with inflammatory processes. However, although there is a slight association between acute appendicitis and inflammation, the acute phase of renal colic is unrelated to inflammation; increases during this phase cannot be explained through already known physiopathological processes. In light of the data obtained in our study, we found that the MPV and RDW values had no efficacy in the differential diagnosis.

It is recommended that the serum urea and creatinine levels in patients with urinary system stones who are admitted to the emergency department be evaluated.[30] In a study of 342 patients by was evaluated, the majority of patients (80%) had normal blood urea nitrogen (BUN) and creatinine values at admission.[36] In our study, although the urea and creatinine values were in normal ranges, we found significantly higher values in patients with renal colic than in patients with acute appendicitis. We believe that urea creatinine values may be higher in patients with renal colic than in patients with acute appendicitis, even if they are within normal ranges, as a result of deterioration in renal tissue caused by luminal pressure due to the presence of stones.

Conclusion

Patients with acute appendicitis and renal colic are frequently admitted to the emergency department with acute abdominal pain. Patients with acute appendicitis are treated using surgical methods, while patients with renal colic receive medical treatment in the acute phase. It is important that the differential diagnosis of these two patient groups be made clearly. The use of laboratory parameters, as well as advanced radiological imaging tools, such as CT and USG to aid in the diagnostic process, will further facilitate accurate differential diagnosis. The data of our study show that the PLR, NLR, and WBC values can be used in cases where a differential diagnosis cannot clearly be made.

Ethics Committee Approval: This study was approved by Ethics Committee of Non-Interventional Clinical Researches of Cukurova University (meeting number: 66, decision number: 42-2017).

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Authorship Contributions: Concept: A.A., S.A., A.K.; Design: A.A., S.A.; Supervision: A.A., S.S.; Resource: M.G., A.S.; Materials: M.G., A.S.; Data: G.S., B.Ş.A.; Analysis: A.A., S.A.; Literature search: B.Ş.A.; G.S.; Writing: A.A., S.A.; Critical revision: A.A., S.A., A.K.

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ORİJİNAL ÇALIŞMA - *ÖZET*

Acil serviste akut apandisit ile renal kolik ayırıcı tanısında hemogram parametrelerinin etkinliği

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AMAÇ: Acil serviste akut apandisit ile renal kolik'in ayırıcı tanısında WBC, PLR ve NLR değerlerinin etkinliğini araştırmaktır.
GEREÇ VE YÖNTEM: Çalışmaya Çukurova Üniversitesi Tıp Fakültesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu'nun onayı alındıktan sonra başlandı. Hastane otomasyon ve arşiv sisteminde dosya verilerine tam olarak ulaşılan toplam 440 hasta çalışmaya dahil edildi.
BULGULAR: Çalışmaya alınan 440 hastanın %59.5'i erkek (n=262), %40.5'i (n=202) ise kadındı. Hastaların yaş ortalaması 37.74±13.39/yıl idi. Hastaların patolojik tanısına göre, 207 hastanın akut apandisitle uyumlu olduğu tespit edildi. Hematolojik parametrelerin ayırıcı tanıda kullanım etkinliği ROC analizi ile incelendiğinde en güçlü tahmin etme özelliğine nötrofil/lenfosit oranının (NLR) sahip olduğu saptandı (AUC, 0.716, SS=0.024, %95 GA 0.668–0.764). NLR'den sonra ikinci sırada platelet/lenfosit oranının (PLR) ayırıcı tanıda güçlü tahmin edici olduğu saptandı (AUC, 0.608, SS=0.027, %95 GA 0.555–0.661).
TARTIŞMA: Akut apandisit ve renal kolik akut abdominal ağrı ile acil servise sıklıkla başvurmaktadır. Akut apandisitli hastalar cerrahi yöntemler ile tedavi edilirken, renal kolikli hastalarda akut dönemde tıbbi tedavi uygulanmaktadır. Bu iki hasta grubunun ayırıcı tanısının net olarak yapılması önem arz etmektedir. PLR ve NLR değerlerinin ayırıcı tanının net olarak yapılamadığı durumlarda kullanılabileceğini düşünmekteyiz.
Anahtar sözcükler: Akut apandisit; NLR; PLR; renal kolik.

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