Clinical Value of the Platelet-to-Lymphocyte Ratio for Diagnosing Complicated Acute Appendicitis

Platelet-Lenfosit Oranının Komplike Apandisit Tanısı Koymada Klinik Etkinliği

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ABSTRACT

Aim: Acute appendicitis (AA) is the most common acute surgical disease worldwide. Despite the use of preoperative advanced radiological instruments, preoperative determination of complicated cases is still difficult and remains an important concern. The aim of this study is to evaluate the predictive value of the platelet-to-lymphocyte ratio and of the presence of elevated white blood cells to discriminate between complicated and uncomplicated AA.

Method: All patients who were admitted to the emergency care unit and underwent urgent laparotomy for AA were analyzed retrospectively. The platelet-to-lymphocyte ratio and white blood cell count were measured. Patients were divided into two groups: uncomplicated cases (group 1) and complicated cases (group 2). White blood cell count and platelet-to-lymphocyte ratio were compared between the two groups.

Results: There were 196 patients in group 1 and 43 patients in group 2. The gender distribution between groups was homogeneous (p=0.020); the mean age of group 2 was higher than group 1 (p<0.001). The platelet-to-lymphocyte ratio was significantly higher in group 2; there was also a significant difference in the white blood cell count (p<0.001 and p=0.029 respectively). The platelet-to-lymphocyte ratio was significantly higher in group 2, and was predictive of complications independently of age and gender (p<0.001). The cutoff value of the platelet-to-lymphocyte ratio was 169.7, giving a sensitivity of 74.4% and specificity of 73.5%.

Conclusion: The platelet-to-lymphocyte ratio could predict complicated cases with a higher sensitivity and specifity than white blood cell count.

Keywords: Acute appendicitis, perforated appendicitis, platelets, lymphocytes, white blood cells

ÖZ

Amaç: Akut apandisit (AA) dünyada en yaygın gözüken acil cerrahi hastalıktır. Preoperatif olarak bakılan ileri radyolojik görüntüleme yöntemlerine rağmen, komplike olguların değerlendirilmesi hala önemli bir sorun teşkil etmektedir. Bu çalışmada, platelet-lenfosit oranının ve beyaz küre değerinin komplike ve komplike olmayan apandisit olgularının ayrımında klinik etkinliğini ortaya koymaya amaçladık.

Yöntem: Acil servise akut karın bulgularıyla başvurup AA ön tanısıyla acil laparotomi yapılan hastalar çalışmaya dahil edildi. Platelet-lenfosit oranı ve beyaz küre değerleri ölçüldü. Hastalar komplike olmayan olgular grup 1, komplike olgular ise grup 2 olarak karşılaştırıldı. Her iki grup arasında beyaz küre ve platelet-lenfosit oranları istatistiksel olarak karşılaştırıldı.

Bulgular: Yüz doksan altı hasta grup 1, 43 hasta grup 2'de idi. Cinsiyet dağılımı gruplar arasında homojendi (p=0,020); grup 2 ortalama yaşı grup 1'e göre daha yüksekti (p<0,001). Platelet-lenfosit oranı grup 2'de anlamlı ölçüde yüksekti. Beyaz küre sayımı da grup 2'de anlamlı oranda yüksekti (sırasıyla p<0,001 ve p=0,029). Platelet-lenfosit oranı aynı zamanda yaş ve cinsiyetten bağımsız olarak komplike olguları öngörebilmekteydi (p<0,001). Platelet-lenfosit oranının cut-off değeri 169,7 iken, %74,4 sensitivitesi ve %73,5 spesifitesi mevcuttu.

Sonuç: Platelet-lenfosit oranı komplike apandisit olgularını beyaz küre sayımına oranla daha yüksek bir sensitivite ve spesifite ile öngörebilmektedir.

Anahtar Kelimeler: Akut apandisit, perfore apandisit, platelet, lenfosit, beyaz küre

Introduction

Acute appendicitis (AA) is one of the most common surgical emergency in modern surgical era.[1] Its incidence rate is 100 per 100.000 inhabitants and lifetime risk for appendicitis is 8.6% for males and 6.7% females.[2] Natural history of disease remains unclear, it means progression to perforation is not predictable and spontaneous resolution is common,[3] so noncomplicated and complicated appendicitis may be discussed as different diseases.[4] Traditionally, management of the patient is based on several steps like medical history, physical findings, laboratory tests and imaging studies; negative appendectomy only within reasonable limits is acceptable for fear of morbidity and mortality due to perforation. Therefore many scoring systems and serum biomarkers were investigated in order to diagnose the disease properly to avoid negative laparotomies.[5,6,7]

In literature, many of the studies focused on diagnosis of AA. Although the increased use of computerized tomography (CT) lowered the rate of negative appendectomies,[8] the rate of misdiagnosed cases are still an important problem (15%).[9,10]

But major mortality of appendicitis is arising from complicated cases which fewer diagnostic biomarkers were investigated and stated in literature. Following uncomplicated appendectomy complication rates are lower than complicated cases.[11]

Studies have shown inconsistent information regarding the use of white blood cells (WBC) count. Most studies show an association between elevated WBCs count in diagnostic process, however its significance varies greatly. Several reports suggest an elevated leukocyte count is usually the earliest serum biomarker to show appendiceal inflammation.[12]

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are associated with worse outcome in various diseases stated in literature. Also, NLR is a new biomarker.[13,14] Nevertheless we did not find any other study investigating PLR in case of discrimination of complicated cases of AA.

In this study, we aimed to investigate the predictive value of PLR on discrimination of complicated and noncomplicated AA.

Materials and Methods

A retrospective analysis of collected data was carried out on all patients admitted to emergency care unit with abdominal pain and underwent urgent laparotomy who prediagnosed as acute appendicits over a 2 year period (from January 2012-December 2014). AA was diagnosed preoperatively by clinical history, laboratory tests and in some patients by imaging studies like ultrasonography (USG) or CT. Laboratory tests were performed on blood samples. PLR which obtained from complete blood count sample and WBCs count were measured. According to intraoperative surgical findings and pathology reports, patients were divided into two groups. Group 1 was noncomplicated appendicitis group and group 2 was complicated appendicitis groups (cases with perforation, plastrone appendicitis, periappendicular abscess). WBC and PLR results were compared between two groups.

Immunocompromised patients, patients who had transfused blood within seven days, patients with coronary artery disease, cerebrovascular event, malignity, hematologic disorders and patients with negative appendectomies were excluded from this study. The leukocyte count and platelet count percentages were measured by an automated hematology analyzer (Coulter Counter Model S-Plus Jr, Coulter Electronics, Hialeah, FL). The reference interval of WBC was 4500-10.300/mm^3.

Statistical Analysis

The data was analyzed by using the Statistical Package for the Social Sciences for Windows, version 17.0 (SPSS Inc, Chicago, IL, USA). Shapiro-Wilk test was showed whether the distributions of continuous variables were normal or not. Data were shown as mean ± standard deviation or median (minimum-maximum), where applicable. Student's t or Mann-Whitney U test were used to compare the differences between groups, where appropriate. Categorical data were analyzed by Pearson's chi-square test, where appropriate. Receiver operating characteristic (ROC) analysis was used to determine discriminative results by cutoff values of parameters between groups. At each value, the sensitivity and specificity for each outcome under study were plotted, thus generating an ROC curve. A p value less than 0.05 was considered statistically significant.

Results

Median value for 239 patients age who were included to the study was 28 (12-85) and male/female ratio was 1.37. There were 196 patients in group 1 and 43 patients in group 2.

When gender disribution between groups was analyzed there was male dominancy in group 1 and female dominancy in group 2 (p=0.020), furthermore mean age of group 2 was higher than group 1 (p<0.001). Demographic characteristics were shown at Table 1.

When groups were compared considering PLR and WBC values, PLR and WBC values are significantly higher in group 2 (p<0.001 and p=0.029 respectively). Distribution of PLR and WBC values between groups is given in Figure 1 and Figure 2. Multivariate Cox regression analysis showed

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that PLR could predict complications independently of age and gender (p<0.001) (Table 2).

Cutoff value of PLR which was assessed by Roc curve analysis was 169.7, giving a sensitivity of 74.4% and specificity of 73.5% (Roc curve analysis is given in Figure 3).

However cutoff value of WBC which was assessed by Roc curve analysis was 13.45, giving a sensitivity of 55.8% and specifity 55.6.

Discussion

Diagnostic process of AA is not always easy. Preventing complications by means of observing the patient until the

Table 1. Patients demographic specialities

Specialities	Group 1	Group 2	Total	p
Age (year)	27 (15-85)	36 (12-74)	28 (12-85)	<0.001
Gender (F/M)	76/120	25/18	101/138	0.020
Patients	196	43	239	

Group 1: Non-complicated appendicitis; Group 2: complicated appendicitis
F: Female, M: male

Table 2. Multivariate Cox regression analyse (age, gender and platelet-to-lymphocyte ratio)

Independent factors	p
Age	0.150
Gender	0.254
PLR	<0.001

PLR: Platelet-to- lymphocyte ratio

diagnosis becomes obvious or operating early seems to be a serious dilemma for surgeons. Rapid intervention may result in the removal of uncomplicated appendicitis with a small risk of morbidity.[15] Delay in the diagnosis may lead to appendix rupture and secondary complications.[16] Considering surgeons who work in rural areas, they may not have radiological imaging facilities. Furthermore, USG or CT imaging may not always help to achieve an accurate diagnosis.[15] Increased use of CT lowered the rate of negative

Figure 2. Distribution of white blood cell inter groups
White blood cell group 1: 12.9 (4.4-28.0)
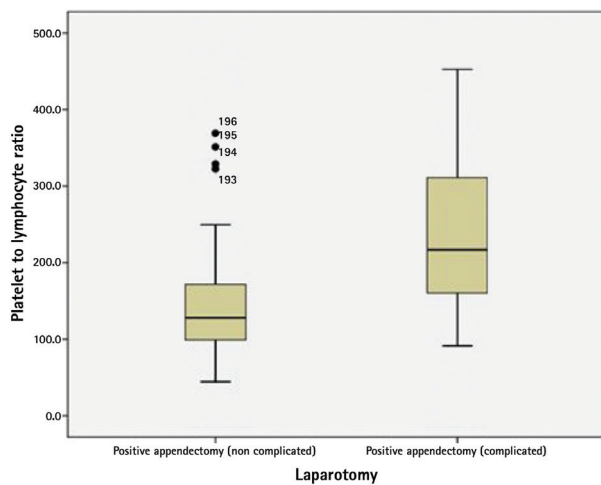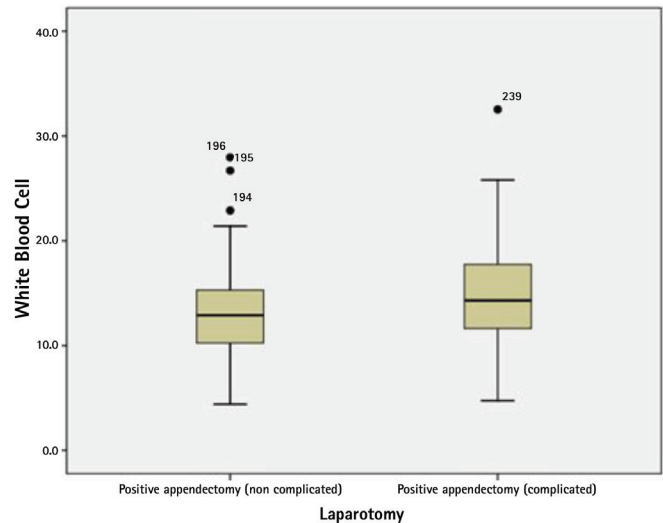*White blood cell group 2: 14.3 (4.8-32.5)*
p=0.029

Figure 1. Distribution of platelet-to-lymphocyte ratio inter groups
Platelet-to-lymphocyte ratio group 1: 127.95 (44.60-369.10)
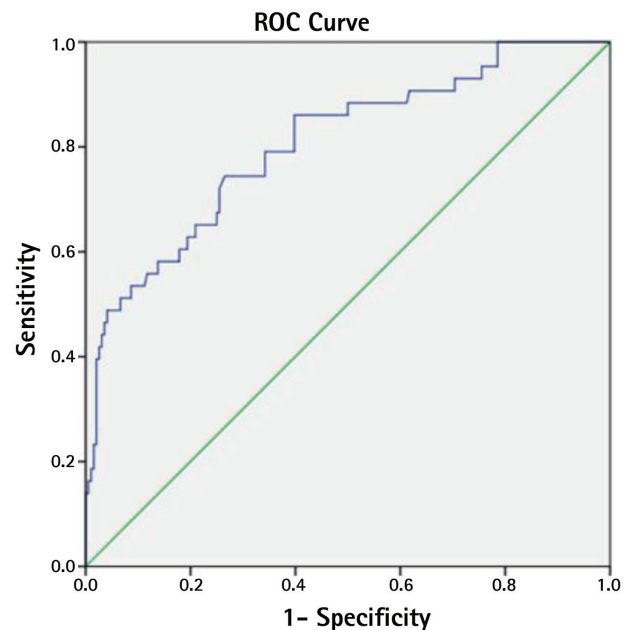*Platelet-to-lymphocyte ratio group 2: 216.84 (91.30-452.40)*
p<0.001

Figure 3. Receiver operating characteristic curve analysis of groups in terms of platelet-to-lymphocyte ratio results
ROC: Receiver operating characteristic

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appendectomies[8] however the rate of misdiagnosed cases are still an important problem (15%).[9,10] There is also an increasing concern over radiation exposure and long-term cancer risk related with CT.[17] Consequently surgeons are still seeking of an consistent and easy laboratory test to diagnose appendicitis appropriately.

Our results revealed that PLR with a cutoff value off 169.7, giving a sensitivity of 74.4% and specificity of 73.5%. These results showed that PLR could be an important marker to predict complicated cases.

Our study has some limitations like the retrospective nature of the study. Only a two year of period for collected data and 239 patients may not show the real potential of WBCs count and PLR in discrimination of noncomplicated and complicated appendicitis.

The degree of WBC elevation in appendicitis has been analyzed widely in many studies. It is usually elevated in patients who had AA. Nevertheless it is not an accepted specific marker and is usually raised higher laboratory degrees in patients with other inflammatory conditions.[17] In our study when groups were compared considering WBC values, there was significant difference in terms of WBC values.

Although Sack et al.[18] showed that WBCs count was elevated in children with complicated appendicitis, Mughal and Soomro[19] found leucocytes elevated in all their patients. Also, Yokoyama et al.[20] reported that WBCs count are not a useful for surgical indication.

PLR is a marker of serious inflammation and it was used in various clinical conditions to determine the degree of inflammatory process which leads to the release of proinflammatory cytokines and it promotes megakaryocytes' proliferation. The activation of platelets is a hallmark in the course of cancer, by promoting neoangiogenesis, degradation of extracellular matrix, release of adhesion molecules, and growth factors.[21,22] Lee et al.[23] demonstrated that PLR was an independent prognostic factor for overall survival with advanced gastric cancer. Another studies showed that PLR may be a valuable marker for determination of prognosis in colorectal cancer.[24,25] There are also some studies about the role of PLR in terms of prognosis of the patients with breast and gynaecological malignancies.[26,27] However we did not find any study about PLR and AA in literature. There are also few data about serum biomarkers for discrimination of complicated and non-complicated AA.

In our study PLR value was significantly higher in complicated appendicitis group and, PLR could predict complicated cases indepently of age and gender. Moon et al.[28] reported that complicated appendicitis was significantly high in patients who were older than 40 years. Our study showed similar result that mean age of group 2 was higher than group 1 which was significant statistically.

In our study the number of complicated cases in group 2 may be also a limitation. It seems surgeons participated in this study did not wait until cases were complicated and difference in number between groups may lead this result. However, Drake el al.[29] showed that perforation was not associated with elapsed time from hospital presentation to operating room start among adult patients. This result is compatible with the view that disease progression in appendicitis has a more complex pathophysiology and complicated appendicitis may be a separate biological or host-response entity.[29]

Laboratory markers may contribute to the diagnostic process of AA however they can not to change the diagnosis of suspected cases on their own. When they used in a combination with physical examination, medical history and radiological findings they show greater promise.[17]

In conclusion, our results showed that PLR could predict complicated cases more accurately with a high sensitivity and specifity than WBCs count.

Ethics

Ethics Committee Approval: The study was approved by the Kafkas University Local Ethics Committee (Approval no: 80576354-050-99/76), Informed Consent: Due to its retrospective nature of study informed consent was not needed however preoperative detailed surgical informed consent was filled out by all patients.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ali Cihat Yıldırım, Turgut Anuk, Burak İrem, Concept: Ali Cihat Yıldırım, Design: Ali Cihat Yıldırım, Data Collection or Processing: Ali Cihat Yıldırım, Turgut Anuk, Elnare Günal, Analysis or Interpretation: Ali Cihat Yıldırım, Saygı Gülkan, Literature Search: Ali Cihat Yıldırım, Elnare Günal, Saygı Gülkan, Writing: Ali Cihat Yıldırım, Turgut Anuk.

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References

1. Williams RG. Presidential Address: a history of appendicitis. With anecdotes illustrating its importance. Ann Surg 1983;197:495-506.

2. Addiss DG, Shaffer N, Fowler BS, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol 1990;132:910-925.

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3. Andersson RE. The natural history and traditional management of appendicitis revisited: spontaneous resolution and predominance of prehospital perforations imply that a correct diagnosis is more important than an early diagnosis. World J Surg 2007;31:86-92.

4. Livingston EH, Woodward WA, Sarosi GA, Haley RW. Disconnect between incidence of nonperforated and perforated appendicitis: implications for pathophysiology and management. Ann Surg 2007;245:886-892.

5. Alvarado A. A practical score for the early diagnosis of acute appendicitis. Ann Emerg Med 1986;15:557-564.

6. Lintula H, Kokki H, Pulkkinen J, Kettunen R, Gröhn O, Eskelinen M. Diagnostic score in acute appendicitis. Validation of a diagnostic score (Lintula score) for adults with suspected appendicitis. Langenbecks Arch Surg 2010;395:495-500.

7. Eskelinen M, Ikonen J, Lipponen P. Sex-specific diagnostic scores for acute appendicitis. Scand J Gastroenterol 1994;29:59-66.

8. Weyant MJ, Eachempati SR, Maluccio MA, Rivadeneira DE, Grobmyer SR, Hydo LJ, Barie PS. Interpretation of computed tomography does not correlate with laboratory or pathologic findings in surgically confirmed acute appendicitis. Surgery 2000;128:145-153.

9. Flum DR, Morris A, Koepsell T, Dellinger EP. Has misdiagnosis of appendicitis decreased over time? A population-based analysis. JAMA 2001;286:1748-1753.

10. Flum DR, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: nationwide analysis. Arch Surg 2002;137:799-804.

11. Masoomi H, Nguyen NT, Stamos MJ, Smith BR. Overview of outcomes of laparoscopic and open Roux-en-Y gastric bypass in the United States. Surg Technol Int 2012;22:72-77.

12. Al-Gaithy ZK. Clinical value of total white blood cells and neutrophil counts in patients with suspected appendicitis: Retrospective study. World J Emerg Surg 2012;7:32.

13. Markar SR, Karthikesalingman A, Falzon A, Kan Y. The diagnostic value of neutrophil: lymphocyte ratio in adults with suspected acute appendicitis. Acta Chir Belg 2010;110:543-547.

14. Yazici M, Ozkisacik S, Oztan OM, Gursoy H. Neutrophil/lymphocyte ratio in the diagnosis of childhood appendicitis. Turk J Pediatr 2010;52:400-403.

15. Kahramanca S, Ozgehan G, Seker D, Gökce EI, Seker G, Tunç G, Küçükpınar T, Kargıcı H. Neutrophil-to-lymphocyte ratio as a predictor of acute appendicitis. Ulus Travma Acil Cerrahi Derg 2014;20:19-22.

16. Al-Abed YA, Alobaid N, Myint F. Diagnostic markers in acute appendicitis. Am J Surg 2015;209:1043-1047.

17. Shogilev DJ, Duus N, Odom SR, Shapiro NI. Diagnosing Appendicitis: Evidence-Based Review of the Diagnostic Approach in 2014. West J Emerg Med 2014;15:859-871.

18. Sack U, Biereder B, Elouahidi T, Bauer K, Keller T, Tröbs RB. Diagnostic value of blood inflammatory markers for detection of acute appendicitis in children. BMC Surg 2006;6:15.

19. Mughal SA, Soomro S: Acute appendicitis in children. J Surg Pakistan 2007;12:123-125.

20. Yokoyama S, Takifuji K, Hotta T, Matsuda K, Nasu T, Nakamori M, Hirabayashi N, Kinoshita H, Yamaue H. C-Reactive protein is an independent surgical indication marker for appendicitis: a retrospective study. World J Emerg Surg 2009;4:36.

21. Raungkaewmanee S, Tangjitgamol S, Manusirivithaya S, Srijaipracharoen S, Thavaramara T. Platelet to lymphocyte ratio as a prognostic factor for epithelial ovarian cancer. J Gynecol Oncol 2012;23:265-273.

22. Seretis C, Seretis F, Lagoudianakis E, Politou M, Gemenetzis G, Salemis NS. Enhancing the accuracy of platelet to lymphocyte ratio after adjustment for large platelet count: a pilot study in breast cancer patients. Int J Surg Oncol 2012;2012:653608.

23. Lee S, Oh SY, Kim SH, Lee JH, Kim MC, Kim KH, Kim HJ. Prognostic significance of neutrophil lymphocyte ratio and platelet lymphocyte ratio in advanced gastric cancer patients treated with FOLFOX chemotherapy. BMC Cancer 2013;13:350.

24. Kwon HC, Kim SH, Oh SY, Lee S, Lee JH, Choi HJ, Park KJ, Roh MS, Kim SG, Kim HJ, Lee JH. Clinical significance of preoperative neutrophil-lympocyte versus platelet-lymphocyte ratio in patients with operable colorectal cancer. Biomarkers 2012;17:216-222.

25. Liu H1, DU X, Sun P, Xiao C, Xu Y, Li R. Preoperative platelet-lymphocyte ratio is an independent prognostic factor for resectable colorectal cancer. J South Med Univ 2013;33:70-73.

26. Azab B, Shah N, Radbel J, Tan P, Bhatt V, Vonfrolio S, Habeshy A, Picon A, Bloom S. Pretreatment neutrophil/lymphocyte ratio is superior to platelet lymphocyte ratio as a predictor of long-term mortality in breast cancer patients. Med Oncol 2013;30:432.

27. Wang D1, Yang JX, Cao DY, Wan XR, Feng FZ, Huang HF, Shen K, Xiang Y. Preoperative neutrophil-lymphocyte and platelet-lymphocyte ratios as independent predictors of cervical stromal involvement in surgically treated endometroid adenocarcinoma. Onco Targets Ther 2013;6:211-216.

28. Moon HM, Park BS, Moon DJ. Diagnostic Value of C-reactive Protein in Complicated Appendicitis. J Korean Soc Coloproctol 2011;27:122-126.

29. Drake FT, Mottey NE, Farrokhi ET, Florence MG, Johnson MG, Mock C, Steele SR, Thirlby RC, Flum DR. Time to appendectomy and risk of perforation in acute appendicitis. JAMA Surg 2014;149:837-844.