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The role of C-reactive protein/albumin ratio and prognostic nutritional index in the diagnosis of complicated acute appendicitis

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ABSTRACT

Objective: C-reactive protein (CRP) levels increase and albumin levels decrease in patients with inflammation. CRP/albumin ratio (CAR) is a new inflammation-associated prognostic indicator. The prognostic nutritional index (PNI) was described as a simple and neutral indicator of adverse outcomes not only in chronic diseases but also in acute conditions. The aim of this study was to investigate the clinical significance of the CAR and PNI value in differentiating complicated acute appendicitis (AA).

Material and Methods: We retrospectively examined the medical records of 187 patients with AA. Patients were divided into two groups according to pathological results [non-complicated (n= 161) and complicated (n= 26)]. Demographic, clinical, laboratory, and pathological data were examined and compared between the groups. Logistic regression analyses were performed to determine the independent predictors for complicated AA.

Results: Median age of the study group was 32 (23-41) years, and most of the patients were males (n= 101, 54%). Patients in the complicated AA group were significantly older compared to the patients in the non-complicated AA group [38 (32-49.5) years vs. 30 (22-41) years, p= 0.002]. The complicated AA group had significantly higher CAR level compared to the non-complicated AA group (p= 0.001). The length of hospital stay was significantly longer in the complicated AA group compared to the non-complicated AA group [2.5 (2-4.25) days vs. 1 (1-2) days, p< 0.001]. Other variables (including PNI) did not significantly differ between the groups. In univariate logistic regression analysis, only age was found to be a significant variable (OR= 1.045, 95% CI= 1.016-10.74, p= 0.002), but in multiple variate logistic regression analysis, no variable was found to be significant in predicting complicated AA.

Conclusion: We concluded that CAR and PNI value are not independent predictors of complicated AA.

Keywords: Appendectomy, nutrition, lymphocyte, CAR, PNI

INTRODUCTION

Acute appendicitis (AA) is one of the most common causes of acute abdomen. The lifetime incidence of AA is about 7%, and the risk of being complicated with perforation is between 17% and 20% (1). It is extremely important to determine both AA and its complications. Delay in diagnosis can lead to negative outcomes and make the surgery more challenging. For patients with delayed diagnosis, readmission rate, postoperative complications, and the length of hospital stay increase (2).

Imaging methods, especially ultrasonography and computed tomography, are used in the diagnosis of AA and its complications. Since these require special equipment and an experienced radiologist, simpler diagnostic methods are needed (3). Preoperative diagnosis of AA can be made effectively and quickly with inexpensive laboratory tests plus clinical findings and physical examination (4).

However, specific biomarkers are needed to differentiate between complicated and non-complicated AA.

Prognostic nutritional index (PNI), is calculated by serum albumin level and peripheral leukocyte count (5). It is an independent adverse prognostic risk factor for critically ill patients, both in the short and long term (6). Also, it has been reported that the C-reactive protein (CRP)/albumin ratio (CAR) is useful in predicting the prognosis and mortality risk of patients with AA (7).

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In this study, we aimed to explore the correlations between complicated AA and CAR and PNI.

MATERIAL and METHODS

The local ethics committee approval was obtained for the study (2021/2097). Two hundred and thirty-two patients had undergone appendectomy in two years (January 2017-January 2019). We determined the inclusion criteria as follows; age> 18 years and primary diagnosis of AA.

Exclusion criteria were defined as elective appendectomy, normal pathological result, mucocele, mesenteric cyst, and appendectomies that were performed for another procedure (e.g. laparoscopic colon resection or gynecological surgery). Finally, one hundred and eighty-seven patients were included in the study. Age, sex, the length of the complaints (hour), laboratory data [white blood cell (WBC) (10^3/uL), mean platelet volume (MPV) (fL), platelet distribution width (PDW) (fL), platelet (Plt) count (10^3/uL), platelet/lymphocyte ratio (PLR), red cell distribution width (RDW) (fL), CAR, PNI, radiological data [appendix diameter (mm)], length of hospital stay (day), and pathological data were analyzed retrospectively.

We divided the study group into two subgroups according to the pathological results; the non-complicated AA group (n= 161) and the complicated AA group (n= 26). While detecting plastron, perforation, or gangrene in the pathology or operation was defined as complicated AA, detecting edema, suppuration, or inflammation was defined as non-complicated AA. Blood samples were obtained within one hour of admission. AA diagnosis was done and the decision to operate was made via patients' clinical condition, physical examination, laboratory tests, and imaging methods. For all patients, ultrasonography was performed while computed tomography was used selectively. PNI was calculated as 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (per mm^3) (5). The appendix diameter was defined as the largest diameter measured on ultrasonography.

Written informed consent was obtained from the patients before surgery. All operations were performed laparoscopically.

Statistical Analysis

We used the IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA) for statistical analyses. The Shapiro-Wilk test was performed to determine the normality of the distribution of numerical variables. Numerical variables were defined as median (interquartile range) and were compared with the Mann-Whitney U test. Categorical variables were defined as frequency (percentage) and were analyzed by using the Chi-square tests. Univariate logistic regression analysis followed by multiple variate logistic regression analysis containing the variables which had a p< 0.1 in the univariate logistic regression analysis was performed to determine the independent predictors of complicated AA. The results were given as odds ratio (OR), 95% confidence interval (CI), and p values. A two-sided p-value of less than 0.05 was considered significant.

RESULTS

Table 1 shows the demographic, clinical, laboratory, and pathological data of the whole study group and subgroups. Median age of the study group was 32 (23-41) years, and most of the patients were males (n= 101, 54%). The patients in the complicated AA group were significantly older compared to the patients in the non- complicated AA group [38 (32-49.5) years vs. 30 (22-41) years, p= 0.002]. There was no significant difference between the groups in terms of sex, the length of symptoms, WBC count, MPV value, PDW value, Plt count, , PLR, RDW value, PNI, and preoperatively measured appendix diameter.

The complicated AA group had significantly higher CAR level compared to the non-complicated AA group (p= 0.001), and also we found prolonged hospital stay in the complicated AA group compared to the non-complicated AA group and this difference was statistically significant [2.5 (2-4.25) days vs. 1 (1-2) days, p< 0.001]. The most common pathology was AA (n= 134, 71.7%) followed by suppurative appendicitis (n= 27, 14.4%) in the whole study group. The most common pathology of complicated AA was perforated appendicitis (n= 23, 88.5%).

In Table 2, the results of univariate and multiple variate logistic regression analyses of predictors for complicated AA were given. In univariate logistic regression analysis only age was found to be a significant variable (OR= 1.045, 95% CI= 1.016-10.74, p= 0.002), but in multiple variate logistic regression analysis, no variable was found to be significant in predicting complicated AA.

DISCUSSION

In this study, although CAR was higher in the complicated AA group, we found that both CAR and PNI were not independent predictors of complicated AA. Besides, the other variables that were examined in the study were not able to predict complicated AA significantly.

Complicated AA accounts for 20-30% of all AA (1). Complicated AA causes an increase in postoperative complications and financial burden, delay in recovery, and longer stay in hospital. It is important to diagnose complicated AA early to prevent these undesirable situations (8).

Although many other diagnostic tools are available, the patient's clinical condition and physical examination are the cornerstones of diagnosing AA. In addition, laboratory tests are guiding in the diagnosis of AA (9). Previously serum bilirubin value, neutrophil-lymphocyte ratio, WBC value, CRP value, MPV value, RDW value, PLR value, and immature granulocytes were examined to predict

Table 1. Demographic. clinical. laboratory. and pathological data of the whole study group and subgroups

	Study Group (n= 187)	Non-complicated Acute Appendicitis Group (n= 161)	Complicated Acute Appendicitis Group (n= 26)	p
Sex (male)	101 (54)	85 (52.8)	16 (61.5)	0.407
Age (year)	32 (23-41)	30 (22-41)	38 (32-49.5)	**0.002**
Length of symptoms (hour)	24 (12-48)	24 (12-48)	24 (17-48)	0.363
WBC (10^3/uL)	12.6 (10.2-16)	12.5 (10.15-16)	12.95 (11.73-16.6)	0.606
MPV (fL)	10.2 (9.5-10.9)	10.2 (9.4-10.9)	10.5 (9.6-11.2)	0.226
PDW (fL)	12.3 (11.1-14.9)	12.3 (10.95-14.95)	12.25 (11.4-14.18)	0.900
Plt (10^3/uL)	241 (204-286)	248 (203-286)	240 (206.75-271.5)	0.711
PLR	122.07 (91.79-179.78)	118.75 (87.14-177.46)	134.16 (107.63-201.9)	0.168
RDW (fL)	12.9 (12.3-13.65)	12.8 (12.4-13.8)	12.95 (12.3-13.53)	0.932
CRP/albumin ratio	0.53 (0.11-1.57)	0.41 (0.09-1.22)	1.62 (0.42-3.54)	**0.001**
PNI	39.02 (37-42.01)	40.01 (37.01-42.01)	39.01 (34.76-40.26)	0.076
Appendix diameter on USG (mm)	9 (8-11)	9 (8-10)	9.5 (7.75-11)	0.805
Length of hospital stay (day)	2 (1-2)	1 (1-2)	2.5 (2-4.25)	**<0.001**
Pathology				**<0.001**
• Acute appendicitis	134 (71.7)	134 (83.2)	-	
• Suppurative appendicitis	27 (14.4)	27 (16.8)	-	
• Plastrone appendicitis	1 (0.5)	-	1 (3.8)	
• Perforated appendicitis	23 (12.3)	-	23 (88.5)	
• Gangrenous appendicitis	2 (1.1)	-	2 (7.7)	

Significant P values are given as bold.
WBC: White blood cell, MPV: Mean platelet volume, PDW: Platelet distribution width, Plt: Platelets, PLR: Platelet/lymphocyte ratio, RDW: Red cell distribution width, CRP: C-reactive protein, PNI: Prognostic nutritional index, USG: Ultrasonography.

complicated AA (1,3,8,10-12). Haghi et al. have reported that MPV and RDW could be used to diagnose perforated AA (11). Liu et al. have concluded in their meta-analysis that PLR could be used to distinguish between perforated and non-perforated AA. In this study, no relationship was found between complicated AA and WBC value, MPV value, RDW value, and PLR value (13).

CRP is an acute-phase protein that increases with the severity of the inflammation (1). CAR is a highly sensitive indicator of the severity of the inflammation and of the progression of diseases (14). A higher CAR indicates a more serious inflammatory condition due to the positive correlation of CRP and negative correlation of albumin with inflammation (15). There are many studies about the relationship between CAR and poor prognosis (16,17). Additionally, İbrahim et al. have stated that the higher preoperative CAR is a significant predictor for prolonged length of hospital stay, longer duration of operation, and cause of postoperative fever (18). In our study, we found significantly higher CAR in the complicated AA group compared to the non-complicated AA group in intergroup comparisons. However, CAR was not found to be an independent predictor of complicated AA in logistic regression analyses. This may be due to the limited number of patients in the study. PNI is calculated by albumin level and lymphocyte count, which are often used in clinical practice. This index provides information about the nutritional and immunological status of patients (19). The clinical findings of AA occur due to visceral and parietal peritoneum sensitivity with increased inflammation. When inflammation increases, negative acute phase indicators, like serum albumin levels, decrease (20). PNI provides a prediction of adverse outcomes in acute diseases as well as chronic diseases (21). In their study about PNI in patients with aortic dissection, Keskin et al. (6) have found that the intensity of the inflammatory reaction was associated with the decrease in albumin level. As a result, they argued that the albumin level would be low in high risk patients. Unlike the results of that study, a relationship was not found between PNI value and complicated AA in our study.

This study has some limitations. The first is its retrospective design. The second is the limited number of included patients and the limited data. Third, no examination of the relationships between CRP value, CAR, and PNI value with prognosis and postoperative complications.

CONCLUSION

CAR and PNI value are not independent predictors of complicated AA.

Table 2. Univariate and multiple variate analyses of the predictors for complicated acute appendicitis

	Univariate Analysis				Multiple Variate Analysis			
		95% CI				95% CI		
	OR	Lower	Upper	p	OR	Lower	Upper	p
Sex (male)	1.431	0.612	3.342	0.408	-	-	-	-
Age (year)	1.045	1.016	1.074	**0.002**	1.028	0.986	1.072	0.192
Length of symptoms (hour)	1.014	0.998	1.029	0.081	1.013	0.997	1.029	0.111
WBC (10^3/uL)	1.031	0.935	1.137	0.537	-	-	-	-
MPV (fL)	1.203	0.857	1.687	0.285	-	-	-	-
PDW (fL)	0.977	0.826	1.155	0.787	-	-	-	-
Plt (10^3/uL)	0.997	0.991	1.003	0.386	-	-	-	-
PLR	1.001	0.998	1.005	0.514	-	-	-	-
RDW (fl)	0.976	0.842	1.132	0.749	-	-	-	-
CRP/albumin ratio	1.005	0.960	1.052	0.821	-	-	-	-
PNI	0.942	0.866	1.024	0.160	-	-	-	-
Appendix diameter on USG (mm)	0.984	0.898	1.077	0.719	-	-	-	-

Significant P values are given as bold.

OR: Odds ratio, CI: Confidence interval, WBC: White blood cell, MPV: Mean platelet volume, PDW: Platelet distribution width, Plt: Platelets, PLR: Platelet/lymphocyte ratio, RDW: Red cell distribution width, CRP: C-reactive protein, PNI: Prognostic nutritional index, USG: Ultrasonography.

Ethics Committee Approval: This study was approved İnönü University Health Sciences Non-invasive Clinical Research Ethics Committee (Decision date: 18.05.2021, No: 2021/2097).

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Conflict of Interest: The authors have no conflicts of interest to declare.

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ORİJİNAL ÇALIŞMA-ÖZET
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Komplike akut apandisit tanısında C-reaktif protein/albümin oranı ve prognostik beslenme endeksinin rolü

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ÖZET

Giriş ve Amaç: Enflamasyonu olan hastalarda C-reaktif protein (CRP) düzeyleri artarken albümin düzeyleri azalır. CRP/albümin oranı (CAR), enflamasyonla ilişkili yeni bir prognostik göstergedir. Prognostik beslenme endeksi (PNI), yalnızca kronik hastalıklarda değil aynı zamanda akut durumlarda da olumsuz sonuçların basit ve nötr bir göstergesi olarak tanımlanmıştır. Bu çalışmanın amacı komplike akut apandisiti ayırt etmede CAR ve PNI değerinin klinik önemini araştırmaktır.

Gereç ve Yöntem: 187 akut apandisit hastasının tıbbi kayıtları retrospektif olarak incelendi. Hastalar patoloji sonuçlarına göre komplike olmayan (n= 161) ve komplike olan (n= 26) olmak üzere iki gruba ayrıldı. Her iki grup arasında demografik ve klinik veriler, laboratuvar bulguları ve patoloji sonuçları karşılaştırıldı. Komplike akut apandisitin bağımsız belirleyicilerini belirlemek için lojistik regresyon analizleri yapıldı.

Bulgular: Çalışma grubunun ortanca yaşı 32 (23-41) yıl olup, hastaların çoğunluğu erkekti (n= 101, %54). Komplike akut apandisit grubundaki hastalar, komplike olmayan akut apandisit grubuna göre anlamlı derecede daha yaşlıydı [38 (32-49,5) yaş ve 30 (22-41) yaş, p= 0,002]. Komplike akut apandisit grubunun CAR düzeyi komplike olmayan akut apandisit grubuna göre anlamlı derecede yüksekti (p= 0,001). Hastanede kalış süresi komplike akut apandisit grubunda komplike olmayan akut apandisit grubuna göre anlamlı olarak daha uzundu [2,5 (2-4,25) güne karşı 1 (1-2) gün, p< 0,001]. Diğer değişkenler (PNI dahil) gruplar arasında anlamlı farklılık göstermedi. Tek değişkenli lojistik regresyon analizinde sadece komplike akut apandisit tanısında yaş anlamlı değişken olarak bulunurken (OR= 1,045, %95 CI= 1,016-10,74, p= 0,002), çok değişkenli lojistik regresyon analizinde ise anlamlı bir değişken bulunamadı.

Sonuç: CAR ve PNI değerinin komplike akut apandisitin bağımsız belirleyicileri olmadığı sonucuna vardık.

Anahtar Kelimeler: Apendektomi, beslenme, lenfosit, CAR, PNI

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