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Predictive Performance of Admission Hematological Parameters for Adverse Clinical Outcomes in Acute Cholangitis

Akut Kolanjit Hastalarında Olumsuz Klinik Sonuçları Öngörmede Başvuru Hematolojik Parametrelerinin Tahmin Gücü

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ABSTRACT

Objectives: This study aimed to evaluate the prognostic performance of hematological parameters, including red cell distribution width (RDW) and neutrophil-to-lymphocyte ratio (NLR), in patients with acute cholangitis (AC).

Materials and Methods: In this prospective study, 202 patients diagnosed with AC between December 2023 and August 2024 were included. The predictive performance of admission hematological parameters for clinical outcomes, including in-hospital mortality, bacteremia, need for inotropic support, prolonged hospital stay, intensive care unit (ICU) admission, and prolonged ICU stay, was assessed and compared.

Results: Among the 202 patients, 16 (7.9%) died during hospitalization. Multivariate regression analysis identified RDW as an independent risk factor for in-hospital mortality (odds ratio [OR]: 2.25, 95% confidence interval [CI]: 1.48–3.42, p<0.001). For the composite outcome, both NLR (OR: 1.04, 95% CI: 1.01–1.07, p=0.009) and RDW (OR: 1.61, 95% CI: 1.26–2.10, p<0.001) were independent risk factors. Receiver operating characteristic (ROC) analysis showed that RDW had the highest predictive accuracy for both in-hospital mortality (AUC [95% CI]: 0.826 [0.711–0.941]) and the composite outcome (AUC [95% CI]: 0.761 [0.681–0.842]) At a cut-off value of 15.6, RDW yielded a sensitivity of 75% and specificity of 88.2% for predicting in-hospital mortality. Patients with RDW >15.6 had a 21.3-fold higher risk of in-hospital mortality compared to those with lower RDW values (OR: 21.3, 95% CI: 6.3-71.5).

Conclusion: RDW demonstrated the strongest prognostic value among hematological parameters and may serve as a practical and reliable marker for early risk stratification in patients with AC.

Keywords: acute cholangitis, hematological parameters, mortality

ÖZET

Amaç: Bu çalışma, akut kolanjit (AC) hastalarında **eritrosit dağılım genişliği (RDW)** ve **nötrofil-lenfosit oranı (NLR)** dahil olmak üzere hematolojik parametrelerin prognostik performansını değerlendirmeyi amaçlamıştır.

Gereç ve Yöntem: Bu prospektif çalışmaya, Aralık 2023 ile Ağustos 2024 tarihleri arasında AC tanısı almış **202 hasta** dâhil edildi. Başvuru anındaki hematolojik parametrelerin, **hastane içi mortalite, bakteriyemi, inotrop ihtiyacı, uzamış hastane yatışı, yoğun bakım (ICU) yatışı ve uzamış ICU yatışı** gibi klinik sonuçları öngörme gücü değerlendirildi ve karşılaştırıldı.

Bulgular: Çalışmaya dâhil edilen **202 hastanın 16'sı (%7.9) hayatını kaybetti**. Çok değişkenli regresyon analizinde **RDW**, hastane içi mortalite için bağımsız bir risk faktörü olarak bulundu (**odds ratio [OR]: 2.25, %95 güven aralığı [GA]: 1.48–3.42, p<0.001**). **Kompozit sonlanım** açısından hem **NLR (OR: 1.04, %95 GA: 1.01–1.07, p=0.009)** hem de **RDW (OR: 1.61, %95 GA: 1.26–2.10, p<0.001)** bağımsız risk faktörleri olarak bulundu. **ROC analizinde**, hematolojik parametreler arasında **hastane içi mortaliteyi ve kompozit sonlanımı en iyi öngören parametrenin RDW olduğu** belirlendi (sırasıyla, **AUC [%95 GA]: 0.826 [0.711–0.941] ve AUC [%95 GA]: 0.761 [0.681–0.842]**). **15.6 kesme değeri** için **RDW'nin mortalite için duyarlılığı %75, özgüllüğü ise %88.2** olarak hesaplandı. **RDW >15.6** olan hastaların, diğer hastalara kıyasla **21.3 kat daha fazla hastane içi mortalite riski taşıdığı** saptandı (**OR: 21.3, %95 GA: 6.3–71.5**).

Sonuç: RDW, hematolojik parametreler arasında en güçlü prognostik değeri göstermiştir ve AC hastalarında erken risk sınıflandırması için pratik ve güvenilir bir belirteç olarak hizmet edebilir.

Anahtar kelimeler: akut kolanjit, hematolojik parametreler, mortalite

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Introduction

Acute cholangitis (AC) is a condition that occurs due to biliary obstruction and subsequent infection of the biliary tree (1). Although there have been advances in the diagnosis and treatment of AC, if appropriate and timely management is not provided, it may lead to severe implications, such as sepsis and multiorgan failure (2). It is very important to recognize patients who are at high risk for poor outcome in order to direct the management and determine the appropriate timing of biliary drainage (3).

Hematological parameters have emerged as easy to use and cost-effective biomarkers for predicting the severity of disease and the outcome in different inflammatory and infectious diseases (4). Parameters such as white blood cell (WBC) count, neutrophil-to-lymphocyte ratio (NLR), platelet count, and red cell distribution width (RDW) have demonstrated prognostic value in conditions ranging from sepsis to acute pancreatitis (5-7). In recent years, several studies have highlighted the prognostic value of hematological indices, particularly RDW and NLR, in infection-related emergencies such as sepsis, community-acquired pneumonia, and biliary tract infections (8-10). These parameters have been associated with mortality, ICU admission, and prolonged hospitalization in various acute care settings. Nevertheless, their prognostic utility in acute cholangitis has not been fully investigated. Incorporating insights from these recent studies may help improve early risk stratification, particularly in emergency department settings.

The Tokyo guidelines, especially the latest version Tokyo 2018 (TG18) offers a guideline for the management and diagnosis of AC (11). However, the present guidelines do not emphasize the prognostic value of hematological parameters despite presenting clinical, laboratory, and imaging criteria for disease severity (11). Assessing the application of these prominent parameters in AC, which have gained significance in many inflammatory diseases today, will be valuable in understanding their role and providing guidance for future guidelines. In this study, we aim to evaluate the prognostic significance of hematological parameters in patients with AC.

Materials And Methods

Study design and clinical outcomes

This prospective study was conducted between December 2023 and August 2024, including 202 patients. Ethical approval was obtained from the Hospital Ethics Committee (Approval number: E2-22-2101), and written informed consent was obtained from all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki. Patients aged 18 years or older who met the diagnostic criteria for AC according to the TG18 were included in the study. Patients diagnosed with AC at their initial presentation to the emergency department were enrolled, while those who developed AC during hospitalization were excluded. Additionally, patients with a suspected but unconfirmed diagnosis of AC and those with malignancy were excluded.

The prognostic role of hematological parameters, including WBC count, hemoglobin, platelet count, NLR, and RDW, at the time of presentation was investigated in patients with AC. The primary outcome was in-hospital mortality. Secondary outcomes included prolonged hospital stay, intensive care unit (ICU) admission, bacteremia, and the development of inotropic support requirements. Furthermore, patients were also evaluated for composite outcomes, including in-hospital mortality, inotropic support requirement, prolonged ICU stay, and bacteremia.

Definitions and data collection

The diagnosis and severity classification of AC were based on TG18 criteria (11). Patients meeting all three of the following criteria were diagnosed with AC: (1) evidence of systemic inflammation, such as body temperature >38°C, WBC count >10 × 10^9/L, or C reactive protein (CRP) >10 mg/L; (2) evidence of cholestasis, such as jaundice (total bilirubin ≥2 mg/dL) or abnormal liver enzymes (more than 1.5 times the upper limit of normal); and (3) imaging evidence of biliary dilatation or underlying etiology (e.g., stricture, stones, or stent). Patients were classified as having severe AC (Grade III) in the presence of at

least one organ/system dysfunction, including cardiovascular, neurological, respiratory, renal, hepatic, or hematological dysfunction. Moderate AC (Grade II) was defined by the presence of two or more of the following criteria: abnormal WBC count (<4 × 10^9/L or >12 × 10^9/L), fever ≥39°C, age ≥75 years, total bilirubin ≥5 mg/dL, and hypoalbuminemia (<70% of the lower normal limit). Mild AC was diagnosed in cases not meeting the criteria for moderate or severe AC.

Data collected included demographic characteristics, vital signs, comorbid conditions, detailed hematological and biochemical parameters at admission, the presence of bacteremia, length of hospital stay, radiological findings, ICU admission status and duration, and inotropic support requirements. Bacteremia was defined as blood culture positivity deemed clinically significant by the infectious diseases team; contaminants and clinically irrelevant findings were excluded. The time from hospital admission to biliary drainage was recorded in hours. Endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC) were performed as biliary drainage methods in the study cohort. Patients with hospital or ICU stays exceeding the 75th percentile of the overall study population were classified as having prolonged hospital or ICU stays.

Statistical analysis

IBM SPSS software version 26.0 for Windows (IBM Corp., Armonk, NY, USA) was used for statistical analyses. The normality of data distribution was checked with the Kolmogorov–Smirnov test. Continuous variables were presented as mean ± standard deviation or median (interquartile range) and compared with Student's *t*-test or Mann–Whitney *U* test, while categorical variables were presented as number (%) and compared with Pearson's Chi-square or Fisher's exact test. Parameters associated with mortality and composite outcome at $P < 0.1$ level were included in the univariate logistic regression analysis. Parameters found to be associated with mortality and composite outcome at $P < 0.1$ level in the univariate analysis were included in the forward stepwise multivariate logistic regression analysis to determine independent risk factors for in-hospital mortality and composite outcome. The area under the curve (AUC) values of the predictors for primary and secondary endpoints were calculated using the receiver operating characteristic (ROC) curve analysis. The appropriate cut-off values of the independent risk factors were determined based on Youden's index using the ROC curve (12). At the appropriate cut-off values of the predictors, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were also calculated. A $P < 0.05$ was considered statistically significant.

Results

Comparison of baseline characteristics according to mortality

In the total population, 16 patients (7.9%) died. The median age of deceased patients was 84 (76-87) years, compared to 69 (55-79) years for survivors (p<0.001). The proportion of females was higher in the deceased group (p=0.034). The deceased group had lower mean arterial pressure and oxygen saturation (p < 0.001), while heart rate and respiratory rate were higher (p = 0.002 and p < 0.001, respectively). Altered mental status at admission was present in 12 (75%) deceased patients (p < 0.001). The Charlson comorbidity index score was significantly higher in the deceased group (p < 0.001). RDW and NLR values were higher in the deceased group, whereas hemoglobin and platelet levels were lower (p<0.001, p=0.004, p=0.022, and p=0.027, respectively). Comparisons of other baseline characteristics and laboratory parameters are shown in Table 1.

Comparison of clinical outcomes according to mortality

In the deceased group, 13 patients (81.3%) had grade 3 AC according to TG18, compared to 30 patients (16.1%) in the survivor group (p < 0.001). Systemic inflammatory response syndrome (SIRS) score was significantly higher in the deceased group (p < 0.001). Length of hospital stay was similar between the deceased and survivor groups (p = 0.412). The duration from admission to biliary drainage was also comparable between the groups (p = 0.968). Of the 28 pa-

Table 1. Comparison of clinical characteristics and laboratory parameters

Parameter	Overall n = 202	Survivors n = 186	Non-survivors n = 16	p
Age, years	69 (56-80)	69 (55-79)	84 (76-87)	<0.001
Female gender	100 (49.5)	88 (47.3)	12 (75)	0.034
Comorbidities				
Cardiovascular disease	45 (22.3)	37 (19.9)	8 (50)	0.010
Hypertension	117 (57.9)	107 (57.5)	10 (62.5)	0.699
Diabetes mellitus	64 (31.7)	57 (30.6)	7 (43.8)	0.280
Main complaint at admission				
Abdominal pain	198 (98)	184 (98.9)	14 (87.5)	0.032
Jaundice	54 (26.7)	49 (26.3)	5 (31.3)	0.769
Fever	35 (17.3)	29 (15.6)	6 (37.5)	0.026
Vital signs				
Mean arterial pressure	90 (83-99)	92 (84-99)	69 (59-79)	<0.001
Heart rate per minute	85 (79-96)	84 (78-95)	99 (91-106)	0.002
Respiratory rate per minute	15 (14-18)	15 (14-17)	20 (18-24)	<0.001
Oxygen saturation, %	95 (92-98)	96 (93-98)	90 (87-92)	<0.001
Altered mental status	20 (9.9)	8 (4.3)	12 (75)	<0.001
Concomitant acute pancreatitis	88 (43.6)	82 (44.1)	6 (37.5)	0.610
Concomitant acute cholecystitis	47 (23.3)	44 (23.7)	3 (18.8)	0.656
History of cholecystectomy	35 (17.3)	34 (18.3)	1 (6.3)	0.316
Charlson comorbidity index	1 (0-2)	1 (0-2)	4 (2-6)	<0.001
Laboratory parameters				
White blood cell count, 10^9/L	10.3 (7.4-13.9)	10.2 (7.4-13.8)	12.4 (8.4-25.3)	0.175
Neutrophil count, 10^9/L	8.3 (5.5-11.8)	8.3 (5.5-11.8)	8.5 (6-22)	0.435
Lymphocyte count, 10^9/L	0.9 (0.6-1.4)	0.9 (0.6-1.4)	0.5 (0.4-1.2)	0.093
Hemoglobin, g/dL	13.5 (12.1-14.7)	13.5 (12.1-14.9)	12.5 (11.2-13.5)	0.022
Platelet count, 10^9/L	225 (176-288)	226 (183-288)	169 (124-268)	0.027
RDW	14.2 (13.5-14.9)	14.1 (13.5-14.8)	16.8 (15.1-18)	<0.001
NLR	8.9 (4.9-18)	8.4 (4.6-16.6)	19.8 (9.2-33.3)	0.004
Total bilirubin, mg/dL	3.1 (1.7-5.1)	3.2 (1.7-5.1)	2.8 (1.3-7.3)	0.925
Creatinine, mg/dL	0.9 (0.7-1.1)	0.9 (0.7-1)	1.3 (1.1-2.5)	<0.001
Albumin, g/dL	4 (3.7-4.3)	4.1 (3.7-4.3)	3.3 (2.6-3.6)	<0.001
C-reactive protein, mg/L	41 (16-125)	37 (15-114)	98 (44-266)	0.009
Procalcitonin, µg/L	0.5 (0.14-4.06)	0.47 (0.13-3.51)	4.29 (0.35-35)	0.006

Categorical variables are presented as n (%), non-normally distributed numerical variables as median (first quartile, third quartile), and normally distributed numerical variables as mean ± standard deviation. Abbreviations: RDW; red cell distribution width, NLR; neutrophil to lymphocyte ratio,

Table 2. Comparison of disease severity and clinical outcomes

Parameter	Overall n = 202	Survivors n = 186	Non-survivors n = 16	p
TG18 severity grading				<0.001
Grade 1 (mild)	110 (54.5)	109 (58.6)	1 (6.3)	
Grade 2 (moderate)	49 (24.3)	47 (25.3)	2 (12.5)	
Grade 3 (severe)	43 (21.3)	30 (16.1)	13 (81.3)	
SIRS score, ≥2	53 (26.2)	40 (21.5)	13 (81.3)	<0.001
Duration from admission to biliary drainage, hours	96 (34-168)	96 (36-168)	76 (28-252)	0.968
Biliary drainage method				0.145
ERCP	127 (62.9)	124 (66.7)	3 (18.8)	
PTC	5 (2.5)	4 (2.2)	1 (6.4)	
Length of hospital stay, day	9 (7-13)	9 (7-13)	6 (3-25)	0.412
Prolonged hospitalization	42 (20.8)	36 (19.4)	6 (37.5)	0.107
ICU admission	51 (25.2)	36 (19.4)	15 (93.8)	<0.001
Length of ICU stay, day	5 (3-14)	6 (3-12)	4 (2-25)	0.640
Prolonged ICU stay	12 (5.9)	7 (3.8)	5 (31.3)	0.287
Inotrope requirement	20 (9.9)	6 (3.2)	14 (87.5)	<0.001
Bacteremia	28 (13.9)	17 (9.1)	11 (68.8)	<0.001
Gram-negative	19 (9.4)	14 (7.5)	5 (31.3)	
Gram-positive	9 (4.5)	3 (1.6)	6 (37.5)	

TG18; Tokyo 2018 guidelines, SIRS; systemic inflammatory response syndrome, ERCP; endoscopic retrograde cholangiopancreatography, PTC; percutaneous transhepatic cholangiography, ICU; intensive care unit

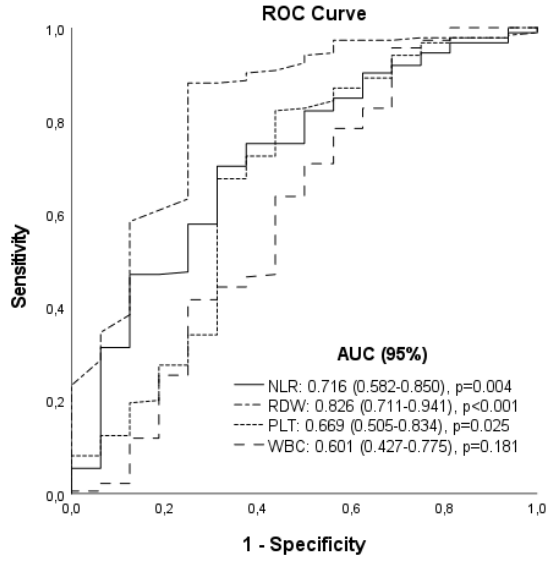

Figure 1. Predictive performance of hematologic parameters for in-hospital mortality.

NLR: Neutrophil-to-Lymphocyte Ratio; PLT: Platelet count; RDW: Red Cell Distribution Width; WBC: White Blood Cell count

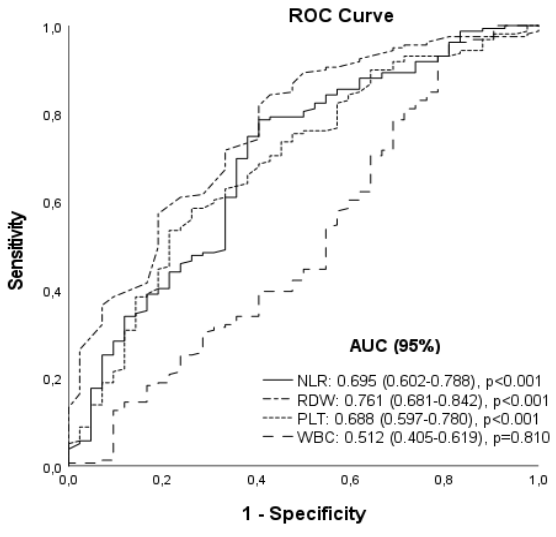

Figure 2. Predictive performance of hematologic parameters for composite outcome.

NLR: Neutrophil-to-Lymphocyte Ratio; PLT: Platelet count; RDW: Red Cell Distribution Width; WBC: White Blood Cell count

Table 3. Univariate and ROC analysis results of hematological parameters for clinical outcomes

		Prolonged hospitalization	ICU admission	In-hospital mortality	Bacteremia
WBC	*AUC*	0.402 (0.300-0.505) p=0.052	0.530 (0.435-0.626) p=0.516	0.601 (0.427-0.775) p=0.181	0.517 (0.385-0.649) p=0.0775
	OR	0.97 (0.92-1.03) p=0.336	1.02 (0.98-1.08) p=0.307	1.09 (1.03-1.16) p=0.006	1.05 (0.99-1.11) p=0.058
NEU	*AUC*	0.401 (0.299-0.504) p=0.050	0.538 (0.443-0.632) p=0.422	0.557 (0.378-0.737) p=0.446	0.532 (0.401-0.663) p=0.586
	OR	0.97 (9.91-1.03) p=0.352	1.03 (0.98-1.09) p=0.252	1.08 (1.01-1.16) p=0.018	1.06 (1.00-1.12) p=0.047
LYM	*AUC*	0.605 (0.514-0.696) p=0.036	0.682 (0.596-0.767) p=<0.001	0.627 (0.463-0.790) p=0.093	0.726 (0.618-0.834) p<0.001
	OR	0.49 (0.25-0.95) p=0.036	0.37 (0.19-0.71) p=0.003	0.79 (0.34-1.87) p=0.602	0.17 (0.06-0.482) p<0.001
HB	*AUC*	0.611 (0.504-0.717) p=0.027	0.639 (0.550-0.728) p=0.003	0.672 (0.551-0.794) p=0.022	0.624 (0.519-0.728) 0.036
	OR	0.79 (0.68-0.95) p=0.012	0.76 (0.64-0.90) p=0.002	0.68 (0.52-0.89) p=0.005	0.75 (0.61-0.93) p=0.008
PLT	*AUC*	0.604 (0.502-0.707) p=0.038	0.686 (0.600-0.773) p<0.001	0.667 (0.503-0.831) p=0.027	0.711 (0.609-0.813) p<0.001
	OR	0.99 (0.99-1.00) p=0.560	0.99 (0.98-0.99) p=0.002	0.99 (0.98-0.99) p=0.027	0.99 (0.98-0.99) p=0.001
RDW	*AUC*	0.642 (0.556-0729) p=0.005	0.697 (0.612-0.781) p<0.001	0.826 (0.711-0.941) p<0.001	0.744 (0.652-0.837) p<0.001
	OR	1.27 (1.05-1.56) p=0.016	1.49 (1.21-1.83) p<0.001	1.90 (1.43-2.51) p<0.001	1.51 (1.20-1.89) P<0.001
NLR	*AUC*	0.538 (0.445-0.631) p=0.538	0.675 (0.586-0.764) p<0.001	0.716 (0.582-0.850) p=0.004	0.708 (0.600-0.816) p<0.001
	OR	0.99 (0.97-1.02) p=0.780	1.04 (1.02-1.06) p<0.001	1.04 (1.01-1.07) p=0.005	1.05 (1.02-1.07) p<0.001

WBC; white blood cells, NEU; neutrophil, LYM; lymphocyte, HB; hemoglobin, PLT; platelet, RDW; red cell distribution width, NLR; neutrophil to lymphocyte ratio, ICU; intensive care unit, ROC; receiver operating characteristic.

tients with bacteremia, the most frequently isolated pathogen was Escherichia coli (n=14), followed by Enterococcus spp. (n=6), Klebsiella spp. (n=3), Pseudomonas spp. (n=2), and Acinetobacter spp. (n=3). Bacteremia was significantly more common in the deceased group (68.8% vs. 9.1%, p < 0.001). Comparative clinical outcomes are summarized in Table 2.

Predictive performance of hematologic parameters

Univariate regression and ROC analyses were conducted to evaluate the predictive performance of WBC, neutrophil (NEU), lymphocyte (LYM), hemoglobin (HB), platelet (PLT), RDW, and NLR for prolonged hospital stay, ICU admission, in-hospital mortality, and bacteremia. RDW demonstrated the highest predictive accuracy for in-hospital mortality, with an AUC (95% CI) of 0.826 (0.711–0.941) (Figure 1). For the composite outcome, which included the need for inotropes, mortality, prolonged ICU stay, and bacteremia, RDW was also the best predictor, with an AUC (95% CI) of 0.761 (0.681–0.842) (Figure 2). The predictive performances of hematologic parameters for

Table 4. Parameters predicting in-hospital mortality and composite outcome

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	**OR (95% CI)**	**p**
In-hospital mortality				
Age	1.12 (1.04-1.17)	0.001		
Mean arterial pressure	0.91 (0.87-0.95)	<0.001		
White blood cell count	1.09 (1.03-1.16)	0.006		
Hemoglobin	0.68 (0.52-0.89)	0.005		
Platelet count	0.99 (0.98-0.99)	0.027		
RDW	1.90 (1.43-2.52)	<0.001	2.27 (1.42-3.62)	**<0.001**
NLR	1.04 (1.01-1.07)	0.005		
Albumin	0.07 (0.03-0.21)	<0.001		
C-reactive protein	1.01 (1.00-1.01)	0.002		
Procalcitonin	1.01 (0.99-1.02)	0.137		
TG18 severity grading	7.83 (2.98-20.6)	<0.001	4.80 (1.41-16.32)	**0.012**
Charlson comorbidity index	1.40 (1.19-1.65)	<0.001		
SIRS score ≥ 2	15.8 (4.3-58.2)	<0.001		
Altered mental status	66.75 (17.56-253.6)	<0.001	42.31 (6.91-259.27)	**<0.001**
Composite outcome				
Age	1.07 (1.04-1.11)	<0.001		
Mean arterial pressure	0.94 (0.92-0.97)	<0.001		
White blood cell count	1.04 (0.99-1.09)	0.087		
Hemoglobin	0.75 (0.63-0.90)	0.002		
Platelet count	0.99 (0.98-0.99)	<0.001		
RDW	1.71 (1.36-2.14)	<0.001	1.61 (1.26-2.1)	**<0.001**
NLR	1.06 (1.03-1.08)	<0.001	1.04 (1.01-1.07)	**0.009**
Albumin	0.16 (0.08-0.33)	<0.001		
C-reactive protein	1.01 (1.00-1.01)	<0.001		
Procalcitonin	1.04 (1.02-1.07)	<0.001		
TG18 severity grading	4.89 (2.96-8.01)	<0.001	3.80 (2.21-6.54)	**<0.001**
Charlson comorbidity index	1.28 (1.12-1.47)	<0.001		
SIRS score ≥ 2	6.93 (3.31-14.51)	<0.001		

Composite outcome includes in-hospital mortality, need for inotropes, prolonged ICU stay, and bacteremia. SIRS; systemic inflammatory response syndrome, RDW; red cell distribution width, NLR; neutrophil to lymphocyte ratio, CRP; C-reactive protein, TG18; Tokyo 2018 guidelines, GCS; Glasgow Coma Scale

prolonged hospital stay, ICU admission, in-hospital mortality, and bacteremia are presented in Table 3.

Predictors of in-hospital mortality

Univariate and multivariate regression analyses were performed to identify predictors of in-hospital mortality and the composite outcome. While many parameters were associated with in-hospital mortality in the univariate analysis, multivariate analysis identified TG18 severity grading ($p = 0.012$), RDW ($p < 0.001$), and altered mental status ($p < 0.001$) as independent predictors of in-hospital mortality. For the composite outcome, multivariate analysis revealed NLR ($p =$

Table 5. Predictive abilities of hematologic parameters for clinical outcomes at different cut-off values

		Cut-off value	Number of patients*	OR (95% CI)	Sens	Spec	PPV	NPV
RDW	Composite outcome	15	46 (22.8%)	6.2 (2.9-13.1)	52.4%	85%	47.8%	87.2%
	In-hospital mortality	15.6	34 (16.8%)	21.3 (6.3-71.5)	75%	88.2%	35.3%	97.6%
NLR	Composite outcome	15.7	59 (29.2%)	5.4 (2.6-11.2)	59.5%	78.8%	42.4%	88.1%
	In-hospital mortality	14.6	66 (32.7%)	5.2 (1.7-15.8)	68.8%	70.4%	16.7%	96.3%
PLT	Composite outcome	150.000	28 (13.9%)	4.3 (1.9-10.1)	52.9%	90.7%	52.9%	80.8%
	In-hospital mortality	150.000	28 (13.9%)	4.5 (1.5-13.5)	31%	90.6%	46.4%	83.3%

*Composite outcome includes in-hospital mortality, need for inotropes, prolonged ICU stay, and bacteremia. PLT; platelet, RDW; red cell distribution width, NLR; neutrophil to lymphocyte ratio, Sens; sensitivity, Spec; specificity, PPV; positive predictive value, NPV; negative predictive value, *Number (%) of patients with values above or below the given cut-off values*

0.009), RDW ($p < 0.001$), and TG18 severity grading ($p < 0.001$) as independent predictors (Table 4).

The optimal cut-off values for independent predictors were determined using ROC analysis with Youden's index. For in-hospital mortality, the optimal RDW cut-off value was 15.6, with a sensitivity of 75% and a specificity of 88.2%. For the composite outcome, the RDW cut-off value was 15, with a sensitivity of 52.4% and a specificity of 85%. Patients with an RDW value > 15.6 had a 21.3-fold increased risk of in-hospital mortality (OR = 21.3, 95% CI: 6.3-71.5) (Table 5).

Discussion

In this prospective study, we evaluated the prognostic significance of routinely available hematological parameters in patients with AC, a condition associated with substantial morbidity and mortality. Our findings revealed that RDW was the most powerful hematological marker for predicting in-hospital mortality. Furthermore, RDW also served as a reliable predictor of adverse composite outcomes, including bacteremia, prolonged ICU stay, in-hospital mortality, need for inotropic support, and prolonged hospital stay.

AC is a critical condition requiring timely intervention, particularly in severe cases, as delays in treatment can lead to poor outcomes such as sepsis and mortality (13, 14). Therefore, the early identification of high-risk patients at presentation is crucial for patient triage and determining the timing of interventional procedures such as ERCP. Currently, the primary guideline for risk stratification and assessing disease severity is the TG18 (11). According to TG18, AC severity is classified into three grades (11, 15). For Grade 3 patients, in addition to appropriate fluid resuscitation and antibiotic therapy, urgent ERCP is recommended, whereas Grade 1 patients are advised to receive more conservative treatment approaches (15). Among hematological parameters, WBC and PLT are the two markers included in the TG18 criteria, classified as Grade 2 and Grade 3 severity markers, respectively (11).

WBC count is widely used as a marker of infection and inflammation in clinical practice due to its rapid and accessible measurement (16). Elevated WBC levels are often indicative of systemic inflammatory responses, such as those observed in sepsis, AC, or other infectious processes (17). In a study by Murayama et al., a WBC count exceeding 20,000 was identified as a poor prognostic factor in AC patients (18). Similar findings have been reported in other studies, where a WBC count above 20,000 was associated with worse outcomes (19, 20). However, the diagnostic specificity of WBC is limited, as elevated levels may also occur in non-infectious inflammatory conditions or due to physiological stress (21, 22). In our study, although WBC was associated with in-hospital mortality in univariate analysis, its prognostic value was lower than other hematological parameters based on ROC analysis.

Another widely used hematological parameter is the PLT count. Beyond its role in hemostasis, PLT count serves as an inflammatory marker in various clinical conditions (23). Thrombocytopenia is frequently associated with severe infections, systemic inflammation, or disseminated intravascular coagulation, reflecting disease severity (24). It is also recognized as a poor prognostic factor in numerous conditions, including AC, where it may indicate advanced disease, systemic involvement, or increased risk of complications (25). In a study by Chen et al., PLT was shown to predict bacteremia, with an AUC of 0.649, a finding consistent with our study (26). TG18 also includes thrombocytopenia (PLT < 100,000/μL) as a marker of poor prognosis (11). Similarly, our findings support the predictive value of PLT for adverse outcomes, in alignment with the TG18 criteria.

In recent years, alongside traditional hematological parameters, novel markers such as the NLR and RDW have been shown to predict poor prognosis, particularly in inflammatory conditions (5, 7, 8). RDW primarily reflects heterogeneity in erythrocyte size and serves as an indicator of the systemic effects of inflammation (27). In states of chronic inflammation and oxidative stress, erythropoiesis is suppressed, iron metabolism is disrupted, and erythrocyte lifespan is shortened (28). These mechanisms lead to increased RDW, which has been associated with the severity of inflammatory diseases and worse clinical outcomes (29). Additionally, elevated RDW may reflect endothelial dysfunction and microvascular injury, further linking it to adverse prognostic outcomes (30).

NLR, on the other hand, is regarded as a marker of the balance between pro-inflammatory and anti-inflammatory responses in the immune system (31). During inflammation, neutrophil mobilization increases, while lymphocyte counts decrease, resulting in an elevated NLR (32). A high NLR indicates an exaggerated immune response, as observed in conditions such as SIRS and sepsis, where immune dysregulation can lead to organ dysfunction or multi-organ failure. NLR is also associated with severe inflammatory responses, such as cytokine storms, and serves as an indirect measure of inflammatory burden (10, 32-34). The distinct mechanisms by which RDW and NLR reflect different aspects of the inflammatory response suggest that these parameters could play complementary roles in assessing disease severity in conditions like AC.

In a study by Yesil et al., NLR was found to predict AC severity (35). Similar findings from other studies have demonstrated NLR as a strong predictor of adverse outcomes in AC (36, 37). In our study, while NLR was a reliable predictor of composite outcomes, its ability to predict in-hospital mortality was lower in multivariate analysis. Moreover, NLR's prognostic value for both in-hospital mortality and composite outcomes was inferior to RDW based on ROC analysis. Our study highlights that RDW outperformed all other hematological parameters in predicting poor prognosis. These findings suggest that incorporating RDW into AC guidelines and severity classifications could enhance patient prognosis and triage decisions. To the best of our knowledge, this is the first prospective study of this scale to demonstrate the superior prognostic value of RDW in AC, emphasizing its potential role in future clinical decision-making.

Our study has some limitations. The primary limitations are the small sample size and the single-center design. However, despite being a single-center study, it is noteworthy that our hospital is one of the largest healthcare institutions in Türkiye, serving a heterogeneous patient population referred from various healthcare facilities. Additionally, our study evaluated hematological parameters obtained at the time of hospital admission. As a result, these values may not fully reflect the initial stages of the disease. Nevertheless, given that studies on AC can only be conducted in advanced tertiary care hospitals, this limitation is inevitable.

In conclusion, our study, which thoroughly investigated the prognostic value of hematological parameters in AC, demonstrated that RDW reflects AC prognosis significantly better than traditionally used parameters such as PLT and WBC. However, for RDW to be incorporated into clinical guidelines and

gain widespread clinical utility in assessing AC severity, future multicenter studies with larger patient cohorts are needed.

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