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Relationships between RDW, NLR, CAR, and APACHE II scores in the context of predicting the prognosis and mortality in ICU patients

M. DENIZ[1], P. OZGUN[2], E. OZDEMIR[1]

[1]Intensive Care Unit, Izzet Baysal State Hospital, Bolu, Turkey
[2]Intensive Care Unit, Sancaktepe Training and Research Hospital, Istanbul, Turkey

Abstract. – OBJECTIVE: Intensive care units (ICU) are tasked with critical care and treatment with a view to improving prognosis. The Acute Physiology and Chronic Health Evaluation II (APACHE II) is one of the most commonly used scoring systems to predict prognosis. In this context, the objective of this study is to evaluate the prognostic value of Red Cell Distribution Width (RDW), Neutrophil-Lymphocyte ratio (NLR), and C-reactive protein to albumin ratio (CAR) in predicting the prognosis and mortality in patients admitted to the ICU.

PATIENTS AND METHODS: The RDW, NLR, and CAR values and APACHE II scores of patients admitted into an ICU, where heterogeneous groups of patients are usually treated, were recorded, categorized based on survival status, and investigated for any correlation between surviving patients' mortality and length of stay (LoS) in ICU and the said parameters.

RESULTS: The ICU mortality among the 2,147 patients included in the study was 43.2%. The most common diagnosis of the patients admitted to the ICU was sepsis. The RDW, NLR, and CAR values and APACHE II scores of the deceased patients were significantly higher than those of the survived patients. There was a significant correlation between LoS in ICU and the said parameters in the positive direction in the survived group only. The APACHE II score had the highest prognostic value in predicting mortality, followed by RDW, CAR, and NLR values in descending order.

CONCLUSIONS: Among the parameters investigated in this study, RDW had the highest prognostic value in predicting the prognosis and mortality. Hence, it may be incorporated into or used alongside the APACHE II scoring system to predict patient outcomes with higher accuracy. However, further randomized controlled studies are needed to determine the cut-off values in predicting the prognosis and mortality.

Key Words:
Intensive care unit, Mortality, Red cell distribution width (RDW), Neutrophil to lymphocyte ratio (NLR), CRP to albumin ratio (CAR), APACHE II.

Introduction

The primary aim of intensive care units (ICUs) is to increase survival by providing care for critically ill patients. Many scoring systems, especially the Acute Physiology and Chronic Health Evaluation II (APACHE II) scoring system, are used to predict mortality at the time of ICU admission. Physiological variables with a high potential to predict prognosis and mortality can be incorporated into the scoring systems to increase their efficacy.

Previous studies have extensively studied complete blood count parameters, including Red Cell Distribution Width (RDW) and Neutrophil to Lymphocyte Ratio (NLR), as well as CRP (C-reactive Protein, a positive acute-phase protein) to albumin (a negative acute-phase protein) ratio (CAR) for predicting mortality and morbidity. The use of these parameters is both more accessible and more affordable compared to APACHE II and other scoring systems.

RDW is a traditionally used parameter for the differential diagnosis of anemias. An increase in RDW reflects impaired erythropoiesis and unregulated erythrocyte homeostasis. Abnormal metabolic conditions such as inflammation, oxidative stress, nutritional disorders, and dyslipidemia have reportedly been associated with RDW values above the upper limit of 14.5%[1]. In cases of infection and other stress-related conditions, neutrophil apoptosis is decreased, subsequently causing a rapid increase in the lev-

Corresponding Author: Mustafa Deniz, MD; e-mail: drmdeniz@gmail.com

el of neutrophils as a result of their mobilization from the bone marrow to the blood. On the other hand, the migration of lymphocytes to inflammatory tissues results in an increase in apoptosis and a decrease in the number of lymphocytes, which eventually increases NLR[2]. High levels of CRP caused by the stimulation of cytokines in inflammatory conditions are associated with poor prognosis and mortality. Low levels of serum albumin are also known to be associated with increased mortality. In parallel, studies focusing on CAR within the context of systemic inflammation have demonstrated this parameter to be a significant predictor of prognosis in cases of infection and malignancy[3].

In view of the foregoing, this study aimed to evaluate the prognostic value of RDW, NLR, and CAR for predicting the prognosis and mortality of ICU patients and the feasibility of using any of these parameters with the APACHE II scoring system or incorporating any of them into the APACHE II scoring system for the aforementioned purpose.

Patients and Methods

The protocol of this retrospective study was approved by the Clinical Research Ethics Committee of Bolu Abant Izzet Baysal University (Decision No.: 2021/139, 25 May 2021). The study population comprised patients admitted to the Intensive Care Department of Bolu Izzet Baysal State Hospital with 4 ICUs and 36 patient beds between January 2018 and December 2020. Patient data, including age and gender, diagnosis at admission, comorbidities, ICU length of stay (LoS), and survival, were obtained from the hospital automation system.

Patients aged < 18 years, patients admitted for active bleeding and COVID-19, and those with liver and kidney transplantation, blood transfusion and albumin replacement in the past two weeks, hematological disorders, liver failure, nephrotic syndrome, and LoS of less than 48 hours were excluded from the study. The study included 2,147 patients. The RDW, NLR, and CAR values and APACHE II scores at ICU admission were recorded. Patients were divided into two groups based on their survival status at the time of discharge: survivors (Group 1) and non-survivors (Group 2). These two groups were comparatively analyzed for factors contributing to differences between the groups, specifically for ICU LoS.

Statistical Analysis

Descriptive statistics were presented as mean ± standard deviation for normally distributed continuous variables, as median, minimum (min), and maximum (max) for non-normally distributed continuous variables, and as numbers and percentages for categorical variables. The Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling tests were used to check whether numerical variables follow a normal distribution.

The Mann-Whitney U test was used to compare two independent groups in the case of non-normally distributed numerical variables. The Pearson's Chi-squared test was used to compare the differences between categorical variables in 2×2 tables.

The receiver operating characteristic (ROC) analysis utilizing the DeLong method with Youden's index was used to determine the cut-off values of RDW, NLR, CAR, and APACHE II scores for predicting mortality. In this respect, the area under the curve (AUC) and the corresponding 95% confidence interval (CI) were calculated. The Kaplan-Meier survival analysis was carried out to determine the temporal correlations between RDW, NLR, CAR, APACHE II scores, and the length of overall survival.

Univariate and multivariate logistic regression analyses were employed to determine the independent risk factors for mortality. Jamovi project (Jamovi, version 2.0.0.0, 2021, retrieved from https://www.jamovi.org), JASP (Jeffreys's Amazing Statistics Program, version 0.15, retrieved from https://jasp-stats.org), and MedCalc (MedCalc statistical software trial version, MedCalc bvba, Ostend, Belgium, 2015, retrieved from http://www.medcalc.org) software packages were used for statistical analyses. A probability p-value ≤ 0.5 was considered statistically significant.

Results

Of the 2,147 patients included in the study, 1,103 (51.4%) were male and 1,044 (48. 6%) were female, with a mean age of 72.1 ± 15.8 years. 928 (43.2%) of the patients died in ICU. The most common diagnosis for ICU admission was sepsis, which was seen in 824 (38.4%) patients, followed by pneumonia and stroke, respectively (Table I). The majority of patients (73.1%) had at least one comorbidity. The distribution of comorbidities is illustrated in Table I.

Table I. Demographic and clinical characteristics of the study groups.

	Overall (n = 2.147)	Group I (survived) (n = 1.219)	Group II (non-survived) (n = 928)	p
Age (year)†,‡	72.1 ± 15.8 76 [17-103]	69.7 ± 17.0 73.0 [17.0-103.0]	75.3 ± 13.4 78.0 [19.0-100.0]	**< 0.001****
Sex¥				
Female	1,044 (48.6)	589 (48.3)	455 (49.0)	**0.777***
Male	1,103 (51.4)	630 (51.7)	473 (51.0)	
Diagnosis¥				
Pneumonia	357 (16.6)	203 (16.7)	154 (16.6)	**< 0.001***
Stroke	293 (13.6)	164 (13.5)	129 (13.9)	
Sepsis	824 (38.4)	377 (30.9)[a]	447 (48.2)[b]	
Acute kidney injury	99 (4.6)	55 (4.5)	44 (4.7)	
Pulmonary thromboembolism	105 (4.9)	69 (5.7)	36 (3.9)	
Trauma	69 (3.2)	64 (5.3)[a]	5 (0.5)[b]	
Intoxications	85 (4)	70 (5.7)[a]	15 (1.6)[b]	
Urinary tract infection	28 (1.3)	12 (1.0)	16 (1.7)	
Others	287 (13.4)	205 (16.8)[a]	82 (8.8)[b]	
Coexisting diseases¥	1,569 (73.1)	818 (67.1)	751 (80.9)	**< 0.001***
Hypertension	537 (25)	254 (20.8)	283 (30.5)	**< 0.001***
Diabetes mellitus	417(19,4)	164 (13.5)	253 (27.3)	**< 0.001***
Chronic obstructive pulmonary disease	393 (18.3)	229 (18.8)	164 (17.7)	0.545*
Coronary artery disease	356 (16.6)	158 (13.0)	198 (21.3)	**< 0.001***
Chronic renal failure	194 (9)	89 (7.3)	105 (11.3)	**0.002***
Cerebrovascular accident	126 (5.9)	51 (4.2)	75 (8.1)	**0.001***
Cancer¥	290 (13.5)	109 (8.9)	181 (19.5)	**< 0.001***

†: Mean ± standard deviation, ‡: Median [min-max], ¥: n (%). *Mann Whitney U test. **Pearson Chi-Square test.

There were 1,219 (56.8%) and 928 (43.2%) patients in Group 1 and Group 2, respectively. There were significant differences between the two groups in terms of age, diagnoses, and comorbidities (Table I). The patients in Group 2 were significantly older than those in Group 1 (75.3 ± 13.4 years *vs.* 69.7 ± 17.0 years, $p<0.001$). The incidence of sepsis was significantly higher in Group 2 than in Group 1 (48.2% *vs.* 30.9%, $p<0.001$). There were more patients with trauma and intoxication in Group 1 than in Group 2 ($p<0.001$). The mortality rates were significantly higher in patients with comorbidities, except for chronic obstructive pulmonary disease (COPD) ($p<0.05$) (Table I). RDW, NLR, CAR, and the APACHE II scores were significantly higher in Group 2 than in Group 1 ($p<0.001$ for all) (Table II). The median ICU LoS was 5 [min: 2.0, max: 98.0] days in Group 1 and 8 [min: 2.0, max: 96.0] days in Group 2. There was a significant difference between the two groups in terms of the median ICU LoS ($p<0.001$, Mann-Whitney U test). The analyses showed significant positive correlations between ICU LoS and the prognostic parameters (RDW, NLR, CAR, and the APACHE II scores) in Group 1 (Table III). The ROC analysis revealed significant differences between the cut-off values of the studied prognostic parameters (Table IV). The APACHE II score had a higher AUC value than the other parameters (Figure 1).

Table II. Comparison of the prognostic parameters between the groups.

	Group I (survived) (n = 1.219)	Group II (non-survived) (n = 928)	p*
RDW (%)‡	15.0 [10.0-30.0]	17.0 [10.0-33.0]	< 0.001
Neutrophil/lymphocyte ratio‡	10.0 [1.0-330.0]	16.0 [1.0-140.0]	< 0.001
CRP/albumin ratio‡	14.0 [0.2-211.0]	40.0 [0.1-160.0]	< 0.001
APACHE score‡	17.0 [2.0-45.0]	29.0 [6.0-54.0]	< 0.001

‡: Median [min-max]. RDW: red cell distribution width, CRP: C-reactive protein, APACHE: The Acute Physiology and Chronic Health Evaluation. *Mann-Whitney U.

Table III. Correlation analysis between the length of the stay in ICU and the prognostic parameters.

		Survived	
		r	*p**
Length of the stay in ICU	- RDW	0.160	< **0.001**
	- Neutrophil/lymphocyte ratio	0.176	< **0.001**
	- CRP/albumin ratio	0.146	< **0.001**
	- APACHE score	0.276	< **0.001**

ICU: intensive care unit, RDW: red cell distribution width, CRP: C-reactive protein, APACHE: The Acute Physiology and Chronic Health Evaluation. Spearman's rho correlation coefficient.

Table IV. ROC analysis of the prognostic parameters in predicting the mortality.

	AUC	Sensitivity	Specificity	Cut-off	95% CI	*p*-value
APACHE score	0.858	75.54	84.17	> 23	0.842-0.872	< **0.001**
RDW	0.730	62.28	73.58	> 16.5	0.711-0.749	< **0.001**
CRP/albumin ratio	0.716	48.49	84.25	> 40	0.696-0.735	< **0.001**
Neutrophil/lymphocyte ratio	0.685	63.54	63.49	> 12	0.665-0.705	< **0.001**

AUC: area under curve, CI: confidence interval, APACHE: The Acute Physiology and Chronic Health Evaluation, RDW: red cell distribution width, CRP: C-reactive protein.

A cut-off value > 23 for the APACHE II score predicted mortality with 75.54% sensitivity and 84.17% specificity (p<0.001). The patients were categorized into higher or lower values of the prognostic parameters based on the cut-off values calculated by ROC analysis (Table V). The number of patients with higher values of any of the prognostic parameters compared to the cut-off values were significantly higher in Group 2 than in Group 1 (p<0.001 for all parameters).

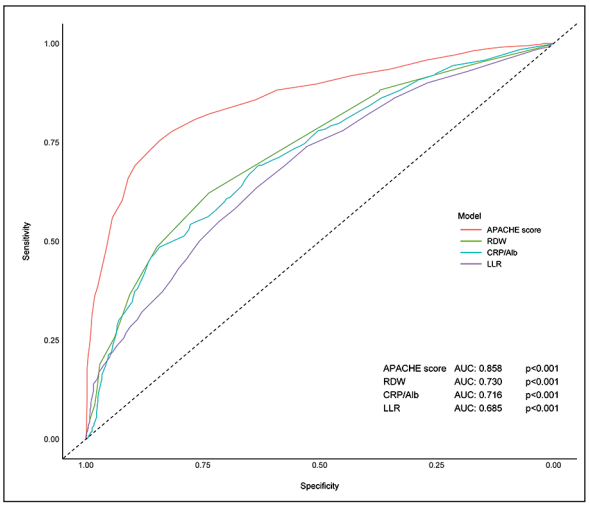

Figure 1. ROC analysis and corresponding AUC values of RDW, NLR, CAR levels, and the APACHE II score.

The results of the Kaplan-Meier log-rank survival analysis are given in Figure 2 (from A to D). Higher RDW, NLR, and CAR values and APACHE II scores compared to the cut-off values were significantly associated with higher mortality rates in the whole study group (p<0.001 for all parameters).

The results of the univariate and multivariate logistic regression analyses for mortality-related risk factors are presented in Table VI. According to the multivariate analysis, the comorbidities of hypertension [Odds Ratio (OR): 1.71, CI 95%: 1.25-2.32, p<0.001], diabetes mellitus (OR: 2.19, CI 95%: 1.58-3.05, p<0.001), coronary artery disease (OR: 1.53, CI 95%: 1.10-2.12, p=0.012), and cerebrovascular accident (OR: 2.65, CI 95%: 1.60-4.41, p<0.001), and a previous history of cancer (OR: 1.94, CI 95%: 1.33-2.84, p<0.001) were independent risk factors for mortality.

Moreover, trauma and chronic renal failure were found to be protective factors for mortality (Table VI).

According to the multivariate logistic regression analysis, higher RDW, NLR, and CAR values and APACHE II scores compared to the cut-off values were significantly associated with higher mortality rates (p<0.001 for all parameters). Furthermore, the multivariate logistic regression analysis showed the highest odds ratio (OR: 10.16,

Table V. Impact of the grouping based on the cut-off values of the prognostic parameters.

	Group I (survived) (n = 1,219)	Group II (non-survived) (n = 928)	p*
RDW			
> 16.5	322 (26.4)	578 (62.3)	**< 0.001**
≤ 16.5	897 (73.6)	350 (37.7)	
Neutrophil/lymphocyte ratio			
> 12	445 (36.5)	589 (63.5)	**< 0.001**
≤ 12	774 (63.5)	339 (36.5)	
CRP/albumin ratio			
> 40	192 (15.8)	450 (48.5)	**< 0.001**
≤ 40	1,027 (84.2)	478 (51.5)	
APACHE score			
> 23	193 (15.8)	701 (75.5)	**< 0.001**
≤ 23	1,026 (84.2)	227 (24.5)	

RDW: red cell distribution width, CRP: C-reactive protein, APACHE: The Acute Physiology and Chronic Health Evaluation. *Pearson Chi-Square test.

CI 95%: 7.99-12.93, $p<0.001$) in patients with high APACHE II scores (>23) compared to those with high values of other three prognostic parameters (Table VI).

Discussion

Most of the relevant studies have demonstrated an association between high levels of RDW,

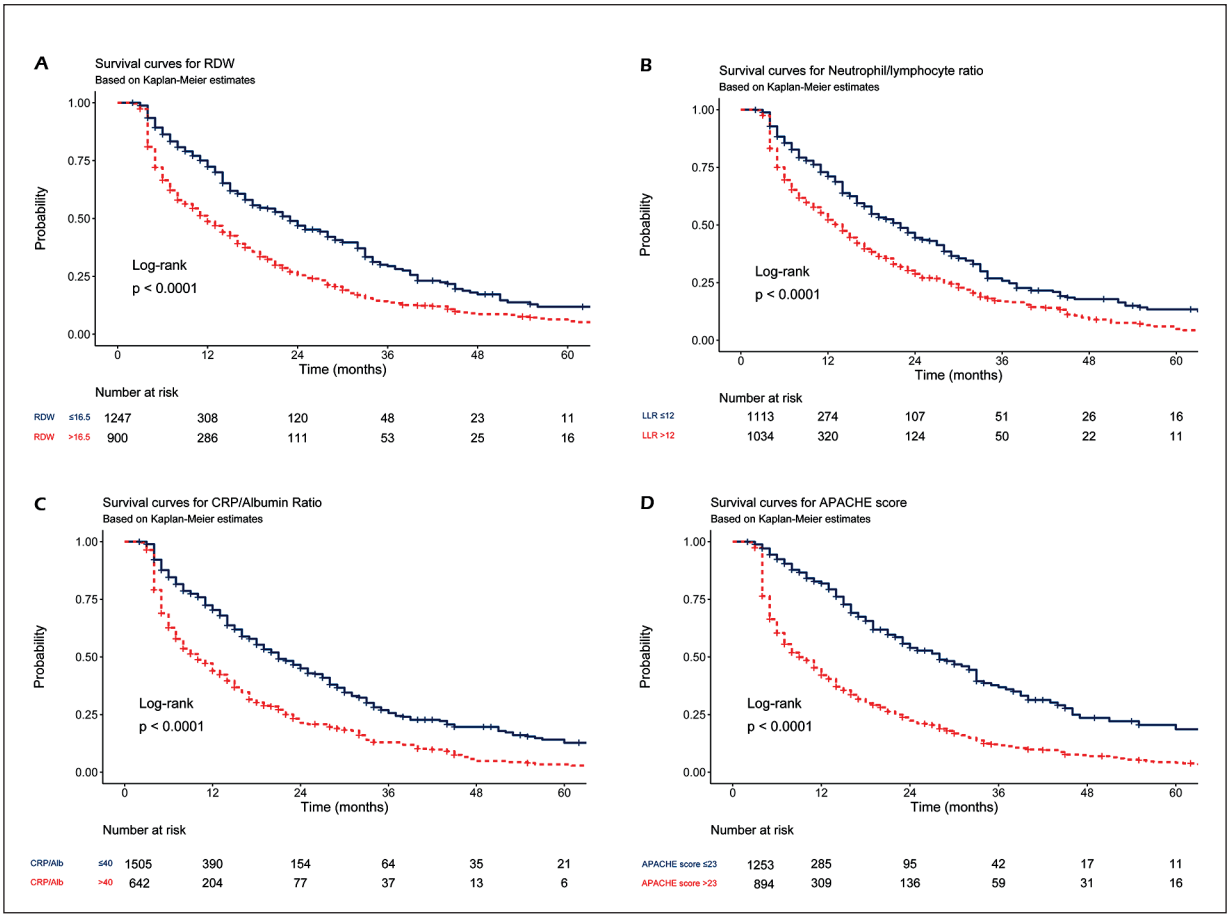

Figure 2. Kaplan-Meier survival curves according to: **A,** RDW; **B,** NLR; **C,** CAR; **D,** the APACHE II score.

Table VI. Univariate and multivariate logistic regression analysis of the variables for the development of mortality.

Variable	Univariate		Multivariate	
	OR [95% CI]	p	OR [95% CI]	p
Diagnosis				
Sepsis	2.08 [1.74-2.48]	**< 0.001**	0.81 [0.63-1.06]	0.122
Trauma	0.10 [0.04-0.24]	**< 0.001**	0.27 [0.09-0.78]	**0.015**
Intoxications	0.27 [0.15-0.47]	**< 0.001**	1.13 [0.51-2.49]	0.766
Presence of any coexisting disease	2.08 [1.70-2.55]	**< 0.001**	0.83 [0.59-1.16]	0.272
Hypertension	1.67 [1.37-2.03]	**< 0.001**	1.71 [1.25-2.32]	**< 0.001**
Diabetes mellitus	2.41 [1.94-3.00]	**< 0.001**	2.19 [1.58-3.05]	**< 0.001**
Coronary artery disease	1.82 [1.45-2.29]	**< 0.001**	1.53 [1.10-2.12]	**0.012**
Chronic renal failure	1.62 [1.20-2.18]	**0.001**	0.48 [0.30-0.76]	**0.002**
Cerebrovascular accident	2.01 [1.40-2.91]	**< 0.001**	2.65 [1.60-4.41]	**< 0.001**
Cancer	2.47 [1.91-3.18]	**< 0.001**	1.94 [1.33-2.84]	**< 0.001**
High RDW	4.60 [3.83-5.53]	**< 0.001**	3.27 [2.58-4.14]	**< 0.001**
High neutrophil/lymphocyte ratio	3.02 [2.53-3.61]	**< 0.001**	1.93 [1.53-2.45]	**< 0.001**
High CRP/albumin ratio	5.04 [4.12-6.16]	**< 0.001**	2.36 [1.81-3.08]	**< 0.001**
High APACHE score	16.42 [13.25-20.35]	**< 0.001**	10.16 [7.99-12.93]	**< 0.001**

OR: Odds ratio, CI: confidence interval, RDW: red cell distribution width, CRP: C-reactive protein, APACHE: The Acute Physiology and Chronic Health Evaluation.

prognosis, and ICU and hospital LoS. One of these studies by Zhang et[4] al with a mixed group of patients followed up in ICU found a significant relationship between the LoS of patients and their RDW levels. Likewise, Fernandez et al[1] reported a significant correlation between ICU and ward LoS, and RDW levels. Moreover, the study of Kim et al[5] on pediatric intensive care patients showed a significant correlation between RDW levels and pediatric ICU LoS. A Turkish study[6] investigating the relationship between RDW levels, prognosis, and mortality reported a significant correlation between RDW levels and ICU LoS. In contrast, a study by Otero et al[7] on critically ill patients followed up in surgical ICU found no significant relationship between high RDW levels and ICU LoS. The results of the present study, on the other hand, revealed a significant correlation between ICU LoS and RDW levels in Group 1, in line with most of the relevant results reported in the literature.

The ICU where this study was conducted is a tertiary ICU serving a mixed group of patients. Separate subgroup analyses were not conducted for each comorbidity and reason for admission since the study sample comprised a mixed group of patients admitted to ICU. Several studies[8-15] have demonstrated an association between high RDW levels and mortality. One of these studies by Özdemir et al[8] demonstrated the association of high RDW levels with mortality in patients admitted to ICU providing care for mixed patients. Another study by Fujita et al[9] found a relationship between high RDW levels and mortality in cardiac patients. Similarly, Safdar et al[10] reported an association between high RDW levels and the 30-day mortality in medical and surgical patients followed-up in ICU. Measuring the RDW levels of patients admitted to ICU, Ochoa et al[11] showed the correlation of high RDW levels with mortality. A study by Rayes et al[12] investigating the relationship between mortality and complete blood count parameters of patients followed up in ICU with cardiac diseases reported a significant correlation between high RDW levels and mortality. A meta-analysis by Zhang et al[13] showed an association between RDW levels, prognosis, and mortality in sepsis patients. Another study by Aydemir and Hoşgün[14] on patients followed up with pulmonary thromboembolism (PTE), community-acquired pneumonia, and COPD attacks found a significant relationship between RDW levels and mortality in respect of all the above-stated three diseases. Wang et al[15] also found a significant association between RDW levels and mortality in patients followed up with acute apoplexy. In line with the relevant studies in the literature, the results of the present study demonstrated a significant relationship between RDW levels and ICU mortality. Moreover, there was also a significant relationship between RDW values

above the cut-off value of 16.5 and mortality. RDW values predicted mortality with 62.25% sensitivity and 73.58% specificity.

Similar to high RDW levels, most of the relevant studies[16-18] have shown an association between high NLR levels and ICU and hospital LoS. One of these studies by Zhao et al[16] on patients followed up with acute apoplexy found NLR levels to be significantly associated with hospital LoS and cost. Similarly, a Turkish study by Özer et al[17] on patients undergoing coronary artery bypass grafting reported significantly higher ICU and hospital LoS in patients with high preoperative NLR levels. On the contrary, a study by Hwang et al[18] on sepsis and septic shock patients, who referred to ICU from the emergency department, found NLR levels measured during the hospital stay to be effective in predicting the prognosis. However, no significant relationship could be found between NLR levels and ICU LoS. The present study, on the other hand, demonstrated a significant positive correlation between the ICU LoS and NLR levels of the patients who achieved recovery and were discharged from ICU.

Most of the relevant studies[16,18-23] have shown a relationship between high NLR levels and mortality. An observational cohort study conducted by Salciccioli et al[19] in surgical and medical ICUs found a significant relationship between high NLR levels and mortality. The study of Ham et al[20] investigating 1-year ICU mortality reported a significant correlation between NLR levels and mortality. Another study by Hwang et al[18] on sepsis and septic shock patients referred to ICU from the emergency department found a significant relationship between admission NLR levels and 28-day mortality. A study conducted by Fest et al[21] in Rotterdam, the Netherlands, with the participation of 8,715 volunteers showed higher NLR levels in elderly patients, patients with diabetes mellitus (DM), heart diseases, malignancies, and smokers, reporting an association between NLR levels and increased all-time mortality in the general population. Curbelo et al[22] found that the admission NLR of patients with pneumonia were significantly associated with 30-day and 90-day mortality rates. A study by Zhao et al[16] on patients followed up with acute apoplexy reported a significant relationship between NLR levels and mortality. On the other hand, a multicenter retrospective study of 428 patients by Zhou et al[23] did not show any significant difference in NLR levels of survivors and non-survivors, concluding that NLR, which was compared with APACHE II scores, procalcitonin, and CRP levels, was a relatively weaker marker[23]. The comparisons of the present study revealed a significant correlation between admission NLR and mortality. Accordingly, increased NLR values above the cut-off value of 12 were found to be significantly associated with mortality. NLR values predicted mortality with 63.54% sensitivity and 63.49% specificity.

As with RDW and NLR values, most studies[3,24-30] on the subject have demonstrated an association between CAR, prognosis, and mortality in ICU patients. One of these studies by Park et al[3] found that CAR levels measured within the first 24 hours of ICU admission were significantly associated with 28-day mortality. Another study by Oh et al[24] reported a correlation between increased CAR levels and increased 30-day mortality rates. Likewise, Mohamed and Elhawary[25] demonstrated the high predictive value of CAR levels measured at the time of pediatric ICU admission for mortality. Yilmaz and Karacan[26] found CAR to be an effective marker for both determining the urgency of patients and predicting the mortality of patients undergoing emergency and elective surgical procedures and postoperatively followed up in ICU. A study by Kim et al[27] investigating 180-day mortality in sepsis and septic shock patients reported CAR levels as an independent risk factor for 180-day mortality. A Turkish study[28] on patients followed up in ICU with acute ischemic stroke found a significant association between CAR and NLR values, and 90-day mortality. In parallel, Cirik et al[29] reported a significant relationship between serum levels of CAR and 30-day mortality in COPD patients followed up in ICU. Finally, Bender et al[30] showed high CAR values to be associated with hospital mortality in patients with acute intracranial hemorrhage. Similar to the above-mentioned studies, the results of the present study demonstrated a significant correlation between high CAR values and ICU mortality. Accordingly, a significant correlation was found between increased CAR values above the cut-off value of 40 and increased mortality. CAR levels predicted mortality with 48.49% sensitivity and 84.25% specificity. Although higher CAR levels indicate increased inflammation and increased protein loss, studies in the literature have suggested that CAR can be used as a prognostic factor for mortality, even in non-infected patients. This result could not be verified by the results of the present study since the study sample com-

prised a mixed group of patients followed up in ICU. Further, as a unique result not previously reported in the literature, a significant correlation was found between the ICU LoS and CAR levels of the survived patients.

Basile-Filho et al[31] compared the predictive values of APACHE II scores and CAR levels in patients followed up in the surgical ICU and found APACHE II scores to be more effective than CAR levels in predicting mortality. Şenyurt et al[32] reported that complete blood count parameters, in other words, MPV (mean platelet volume), RDW, NLR, and platelet-to-lymphocyte ratio (PLR), were stronger than APACHE II scores to predict mortality. Another study by Usta et al[33] on patients followed up in internal medicine and anesthesia ICUs reported significant correlations between RDW, NLR, CAR values, and APACHE II scores. Similarly, Kader et al[34] found a significant correlation between RDW levels and APACHE II scores in a mixed group of patients followed up in ICU. They concluded that RDW levels were a more cost-effective, more accessible, and more efficient marker than APACHE II scores to predict mortality and morbidity[34]. A Turkish study by Inci et al[35] investigating admission NLR and blood levels of RDW reported a significant relationship between NLR and mortality. The same study compared the prognostic power of RDW and NLR for predicting mortality and found that RDW levels were more effective in predicting mortality compared to APACHE II scores and NLR[35]. Accordingly, it was concluded that the combination of RDW with APACHE II scores could predict mortality more effectively[35]. Another study by Tutak et al[36] reported increased RDW levels as robust markers to predict mortality, concluding that RDW should be incorporated into APACHE II scores. On the other hand, the results of the present study demonstrated a significant difference between the APACHE II scores of survivors and non-survivors. A significant correlation was found between increased APACHE II scores above the cut-off value of 23 and increased mortality. The APACHE II scores predicted mortality with 75.54% sensitivity and 84.17% specificity. Moreover, the APACHE II score (AUC: 0.858) had the highest prognostic value for predicting mortality among the studied parameters within the scope of this study. In terms of prognostic value for predicting mortality, the APACHE II score was followed by RDW (AUC: 0.73), CAR (AUC: 0.716), and NLR (AUC: 0.685) in descending order. There was a weak positive correlation between APACHE II scores and ICU LoS in Group 1 but not in Group 2. On the contrary, no significant correlation was found between ICU LoS and any of the other studied three parameters, in other words, RDW, NLR, and CAR. In the APACHE II scoring system, patients are assigned a score ranging from 0 to 4 points based on different variables. There was a significant difference between Group 1 and Group 2 in terms of the studied biomarkers within the scope of this study. Several studies in the literature suggest that RDW may be incorporated into the APACHE II scoring system to more effectively predict mortality and morbidity. However, further clinical studies are needed to determine the applicability of this suggestion.

Apart from its strengths such as the large sample size, there were some limitations to this study. First, it had a retrospective design. Secondly, the parameters studied in this study, which included RDW, CAR, and NLR, were not compared with any other parameters. The study included all patients admitted to ICU and no subgroup analysis was performed.

Conclusions

The results of this study demonstrated a significant relationship between mortality and morbidity and certain biomarkers that can be easily studied using routine, inexpensive and practical blood tests. In this context, it may be feasible to combine these biomarkers, especially RDW, with existing scoring systems to more effectively predict ICU mortality. There is a need for further clinical studies to establish the methods for using these biomarkers to predict the prognosis of ICU patients.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethics Committee Approval

This study was approved by the Bolu Abant Izzet Baysal University Clinical Research Ethics Committee with Decision No.:2021/139, dated 25.05.2021.

Informed Consent

Patients' consent was not obtained due to the retrospective design of the research.

Data Availability Statement

The research data were obtained from the hospital's automation/information system and can be requested from the corresponding authors.

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Authors' Contribution

Mustafa Deniz collected the research data, wrote the main manuscript text, prepared the figures and tables, reviewed the manuscript, conducted the literature review, and did the translation work. Pınar Ozgun prepared the figures and tables, reviewed the manuscript, did the translation work, and drafted the article. Esra Ozdemir collected the research data, prepared the figures and tables, reviewed the manuscript, conducted the literature review, and did the translation work.

ORCID ID

Mustafa DENIZ: 0000-0002-1243-3028; Pınar OZGUN: 0000-0002-7639-8233; Esra OZDEMIR: 0000-0002-7328-1320.

References

1) Fernandez R, Cano S, Catalan I, Rubio O, Subira C, Masclans J, Rognoni G, Ventura L, Macharete C, Winfield L, Alcoverro JM. High red blood cell distribution width as a marker of hospital mortality after ICU discharge: a cohort study. J Intensive Care 2018; 6: 1-7.
2) Westerdijk K, Simons KS, Zegers M, Wever PC, Pickkers P, de Jager CPC. The value of the neutrophil-lymphocyte count ratio in the diagnosis of sepsis in patients admitted to the Intensive Care Unit: A retrospective cohort study. PLoS One 2019; 14: 0212861.
3) Park J, Chung K, Song J, Kim S, Kim E, Jung J, Kang Y, Park M, Kim Y, Chang J, Leem A. The C-Reactive Protein/Albumin Ratio as a Predictor of Mortality in Critically Ill Patients. J Clin Med 2018; 7: 1-10.
4) Zhang Z, Xu X, Ni H, Deng H. Red cell distribution width is associated with hospital mortality in unselected critically ill patients. J Thorac Dis 2013; 5: 730-736.
5) Kim DH, Ha EJ, Park SJ, Jhang WK. Evaluation of the usefulness of red blood cell distribution width in critically ill pediatric patients. Medicine (Baltimore) 2020; 99: 22075.
6) Doganay GE, Cırık MÖ. Is red blood cell distribution width an indicator of prognosis and mortality in respiratory intensive care unit? Eur Res J 2021; 7: 610-616.
7) Otero TMN, Canales C, Yeh DD, Hou PC, Belcher DM, Quraishi SA. Elevated red cell distribution width at initiation of critical care is associated with mortality in surgical intensive care unit patients. J Crit Care 2016; 34: 7-11.
8) Özdemir R, Mutlu NM, Özdemir M, Akçay M, Yel C, Turan IÖ. The importance of red cell distribution width (RDW) in patient follow up in intensive care unit (ICU). Acta Medica Mediterr 2016; 32: 349-354.
9) Fujita B, Franz M, Figulla HR, Pfeifer R, Kabisch B, Fritzenwanger M, Jung C. Red cell distribution width and survival in patients hospitalized on a medical ICU. Clin Biochem 2015; 48: 1048-1052.
10) Safdar S, Modi T, Sriramulu L, Shaaban H, Sison R, Modi V, Adelman M, Guron G. The role of red cell distribution width as a predictor of mortality for critically ill patients in an inner-city hospital. J Nat Sci Biol Med 2017; 8: 154.
11) Ochoa SH, Martínez MI, Carrillo RSC, Esponda PJG. Extent of erythrocyte distribution as a predictor of mortality on admission to the Intensive Care Unit of the Angeles Pedregal Hospital. Acta Med 2019; 17: 230-236.
12) Rayes HA, Vallabhajosyula S, Barsness GW, Anavekar NS, Go RS, Patnaik MS, Kashani KB, Jentzer JC. Association between anemia and hematological indices with mortality among cardiac intensive care unit patients. Clin Res Cardiol 2020; 109: 616-627.
13) Zhang L, Yu C, Guo K, Huang C, Mo L. Prognostic role of red blood cell distribution width in patients with sepsis: a systematic review and meta-analysis. BMC Immunol 2020; 21: 1-8.
14) Aydemir S, Hoşgün D. The role of serum red blood cell distribution width level in predicting the short term mortality of community-acguired pneumonia, acute attack chronic pulmonary disease, and acute pulmonary thromboembolism. Anatol Curr Med J 2021; 3: 192-197.
15) Wang L, Wang C, Wu S, Li Y, Guo W, Liu M. Red blood cell distribution width is associated with mortality after acute ischemic stroke: a cohort study and systematic review. Ann Transl Med 2020; 8: 81.
16) Zhao L, Dai Q, Chen X, Li S, Shi R, Yu S, Yang F, Xiong Y, Zhang R. Neutrophil-to-Lymphocyte Ratio Predicts Length of Stay and Acute Hospital Cost in Patients with Acute Ischemic Stroke. J Stroke Cerebrovasc Dis 2016; 25: 739-744.
17) Özer A, Mardin B, Kiliç Y, Oktar L, İriz E, Arslan M, Ünal Y, Alkan M. The effect of neutrophil-lymphocyte ratio on the postoperative course of coronary artery bypass graft surgery. Turkish J Med Sci 2018; 48: 1036-1040.
18) Hwang SY, Shin TG, Jo IJ, Jeon K, Suh GY, Lee TR, Yoon H, Cha WC, Sim MS. Neutrophil-to-lymphocyte ratio as a prognostic marker in critically-ill septic patients. Am J Emerg Med 2017; 35: 234-239.

19) Salciccioli JD, Marshall DC, Pimentel MA, Santos MD, Pollard T, Celi LA, Shalhoub J. The association between the neutrophil-to-lymphocyte ratio and mortality in critical illness: an observational cohort study. Crit Care 2015; 19: 1-8.

20) Ham SY, Yoon HJ, Nam SB, Yun BH, Eum D, Shin CS. Prognostic value of neutrophil/lymphocyte ratio and mean platelet volume/platelet ratio for 1-year mortality in critically ill patients. Sci Rep 2020; 10: 1-8.

21) Fest J, Ruiter TR, Groot Koerkamp B, Rizopoulos D, Ikram MA, van Eijck CHJ, Stricker BH. The neutrophil-to-lymphocyte ratio is associated with mortality in the general population: The Rotterdam Study. Eur J Epidemiol 2019; 34: 463-470.

22) Curbelo J, Luquero Bueno S, Galván-Román JM, Ortega-Gómez M, Rajas O, Fernández-Jiménez G, Vega-Piris L, Rodríguez-Salvanes F, Arnalich B, Díaz A, Costa R, de la Fuente H, Lancho Á, Suárez C, Ancochea J, Aspa J. Correction: Inflammation biomarkers in blood as mortality predictors in community-acquired pneumonia admitted patients: Importance of comparison with neutrophil count percentage or neutrophil-lymphocyte ratio. PLoS One 2019; 14: 0212915.

23) Zhou T, Zheng N, Li X, Zhu D, Han Y. Prognostic value of neutrophil- lymphocyte count ratio (NLCR) among adult ICU patients in comparison to APACHE II score and conventional inflammatory markers: a multi center retrospective cohort study. BMC Emerg Med 2021; 21: 1-10.

24) Oh TK, Song IA, Lee JH. Clinical usefulness of C-reactive protein to albumin ratio in predicting 30-day mortality in critically ill patients: A retrospective analysis. Sci Rep 2018; 8: 1-6.

25) Mohamed SA, Elhawary R. C-Reactive Protein/Albumin Ratio as an Independent Predictor of Mortality in Critically Ill Pediatric Patients. J Child Sci 2020; 10: 1-11.

26) Yılmaz PÖ, Karacan E. The effects of C-reactive protein/albumin ratio and hematologic parameters on predicting the prognosis for emergency surgical patients in intensive care. Ulus Travma ve Acil Cerrahi Derg 2021; 27: 67-72.

27) Kim MH, Ahn JY, Song JE, Choi H, Ann HW, Kim JK, Kim JH, Jeon YD, Kim SB, Jeong SJ, Ku NS, Han SH, Song YG, Choi JY, Kim YS, Kim JM. The C-Reactive Protein/Albumin Ratio as an Independent Predictor of Mortality in Patients with Severe Sepsis or Septic Shock Treated with Early Goal-Directed Therapy. PLoS One 2015; 10: 0132109.

28) Kocatürk M, Kocatürk Ö. Assessment of relationship between C-reactive protein to albumin ratio and 90-day mortality in patients with acute ischaemic stroke. Neurol Neurochir Pol 2019; 53: 205-211.

29) Cırık MÖ, Baldemir R, Doğanay GE, Ünver M, Avcı S. The 30-day mortality predictor role of c-reactive protein/albumin ratio in critically ill COPD patients. Crit Care Innov 2020; 3: 1-12.

30) Bender M, Haferkorn K, Friedrich M, Uhl E, Stein M. Impact of Early C-Reactive Protein/Albumin Ratio on Intra-Hospital Mortality Among Patients with Spontaneous Intracerebral Hemorrhage. J Clin Med 2020; 9: 1236.

31) Basile-Filho A, Lago AF, Menegheti MG, Nicolini EA, Rodrigues LA de B, Nunes RS, Auxiliadora-Martins M, Ferez MA. The use of APACHE II, SOFA, SAPS 3, C-reactive protein/albumin ratio, and lactate to predict mortality of surgical critically ill patients: A retrospective cohort study. Medicine (Baltimore) 2019; 98: 16204.

32) Şenyurt O, Kaygusuz K, Avcı O, İsbir AC, Özdemir Kol İ, Gürsoy S. The relation of hemogram parameters with mortality in intensive care patients. J Cardio-Vascular-Thoracic Anaesth Intensive Care Soc 2018; 24: 165-171.

33) Usta A, Gemcioglu E, Baser S, Ersoy O, Polat YH, Erden A, Izdes S. Comparison of APACHE II scores and mortality with CRP/albumin, neutrophil/lymphocyte and thrombocyte/lymphocyte ratios in patients admitted to internal medicine and anesthesia reanimation intensive care unit. Laboratoriums Medizin 2022; 46: 23-31.

34) Kader A, Islam S, Ferdoushi S, Chowdhury AA, Sultana T, Pau D, Ahmed MU, Ahmed ANN. Role of Red Blood Cell Distribution Width for Assessment of Severity of Critically Ill Patients in Intensive Care Unit and To Correlate with Acute Physiology and Chronic Health Evaluation-Ii (Apache-Ii) Score. Anaesthesia Crit Care Pain Manag 2016; 1: 7-16.

35) Inci K, Kalın BS, Türkoğlu MA. Prognostic Value of Red Cell Distribution Width and Neutrophil-Lymphocyte Ratio on Admission in Critically Ill Patients: A Retrospective Cohort Study. Egypt J Crit Care Med 2021; 7: 92-97.

36) Tutak AS, Avni Findikli H. Can RDW be Added to Intensive Care Disease Severity Scoring Systems? Arch Clin Biomed Res 2018; 2: 183-187.