Turk J Intensive Care 2022;20:86-92
DOI: 10.4274/tybd.galenos.2021.38039

ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

Burhan Sami Kalın,
İhsan Solmaz

Effects of Red Blood Cell Distribution Width on the Outcomes of Patients with Sepsis in Intensive Care Unit: A Retrospective Study

Yoğun Bakım Ünitesinde Septik Hastaların Sonuçları Üzerine Kırmızı Kan Hücresi Dağılım Genişliğinin Değerlendirilmesi: Retrospektif Bir Çalışma

Received/Geliş Tarihi : 20.12.2020
Accepted/Kabul Tarihi : 04.03.2021

Burhan Sami Kalın
University of Health Sciences Turkey, Diyarbakır Gazi Yaşargil Training and Research Hospital, Clinic of Internal Medicine, Division of Critical Care, Diyarbakır, Turkey

İhsan Solmaz
University of Health Sciences Turkey, Diyarbakır Gazi Yaşargil Training and Research Hospital, Clinic of Internal Medicine, Diyarbakır, Turkey

Burhan Sami Kalın MD (✉),
University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital, Clinic of Internal Medicine, Division of Critical Care, Diyarbakır, Turkey

E-mail : bskalin@windowslive.com
Phone : +90 538 978 71 80
ORCID ID : orcid.org/0000-0003-2624-6175

ABSTRACT *Objective:* This study aimed to determine the prognostic value of red cell distribution width (RDW) in patients with sepsis in intensive care unit (ICU).
Materials and Methods: This single centre study includes a retrospective analysis of critically ill patients with sepsis. Patients' demographic data; comorbidities; RDW values upon ICU admission, day 3 (RDW3) and day 7 (RDW7); Acute Physiology and Chronic Health Evaluation-II (APACHE-II) score; need for haemodialysis and invasive mechanical ventilation (IMV) were compared between survivors and non-survivors. In addition, patients were divided into the following two groups: high RDW (>14.5%) and normal RDW (≤14.5%). Logistic regression analysis was performed to determine independent risk factors for ICU mortality.
Results: A total of 102 patients with sepsis were included. Survivors had lower RDW than non-survivors (p<0.05 for RDW values upon ICU admission, RDW3 and RDW7). The APACHE-II score, presence of septic shock on ICU admission, need for IMV and mortality rate were higher in patients in the high RDW group than those in patients in the normal RDW group (for all p<0.05). In this study, the presence of septic shock on ICU admission, RDW3 value and need for IMV were found to be independent risk factors for mortality.
Conclusion: In this study, RDW3 value was significantly associated with mortality in critically ill patients with sepsis and has an important value in predicting the prognosis of patients with sepsis in ICU.
Keywords: Sepsis, septic shock, intensive care unit, red blood cell distribution width

ÖZ *Amaç:* Bu çalışmanın amacı yoğun bakım ünitesinde (YBÜ) bulunan septik hastalarda eritrosit dağılım genişliğinin (RDW) prognostik değerini belirlemektir.
Gereç ve Yöntem: Bu tek merkezli çalışmada, kritik olan sepsis hastalarının retrospektif bir analizi yer almaktadır. Hastaların demografik verileri, komorbiditeleri, YBÜ'ye kabuldeki RDW, 3. gün (RDW3) ve 7. gün RDW (RDW7) değerleri, Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II (APACHE-II) skoru, hemodiyaliz ve invaziv mekanik ventilasyon (IMV) ihtiyacı sağ kalanlar ve vefat edenler arasında karşılaştırıldı. Ayrıca hastalar yüksek (>%14,5) ve normal (≤%14,5) RDW olarak iki gruba ayrıldı. YBÜ mortalitesi için bağımsız risk faktörlerini belirlemek üzere lojistik regresyon analizi yapıldı.
Bulgular: Yüz iki septik hasta çalışmaya dahil edildi. Sağ kalanlar, vefat edenlere kıyasla daha düşük RDW'ye sahipti (YBÜ'ye kabuldeki RDW, RDW3 ve RDW7 değerleri, tümü için p<0,05). Yüksek RDW grubundaki hastalar normal RDW grubundaki hastalara göre daha yüksek APACHE-II skoruna, YBÜ'ye kabulde daha yüksek oranda septik şok varlığına, daha yüksek IMV ihtiyacına ve mortalite oranına sahipti (tümü için p<0,05). Bu çalışmada YBÜ'ye kabulde septik şok varlığı, RDW3 değeri ve IMV ihtiyacı mortalite için bağımsız risk faktörleri olarak bulundu.
Sonuç: Bu çalışmada RDW3 değeri, kritik septik hastalarda mortalite ile anlamlı olarak ilişkili bulunmuştur ve YBÜ septik hastalarının prognozunu öngörmede önemli bir değere sahiptir.
Anahtar Kelimeler: Sepsis, septik şok, yoğun bakım ünitesi, kırmızı kan hücresi dağılım genişliği

Introduction

Sepsis is a life-threatening organ dysfunction caused by dysregulated host response to infection and septic shock is defined as a circulatory and metabolic disorder associated with a higher risk of mortality (1,2). Sepsis and septic shock are important healthcare problems which are affecting quite a lot of people in the world (3). The progression of severity is associated with rised mortality with insufficiency in multiple organ systems and most oftenly quantified by the Acute Physiology and Chronic Health Evaluation-II (APACHE-II) score which can predict the severity and outcome depending on different organ functional status (4). It would be advantageous to identify a rapid, cheap and easily applicable biomarker associated with the severity of sepsis. Red cell distribution width (RDW) is an index of complete blood count (CBC) analysis which is commonly measured among patients. RDW is specified as a numeric percentage which is calculated as red blood cell (RBC) volume divided by the mean corpuscular volume (MCV) and multiplied by 100 (5). RDW is an indicator of anisocytosis as a part of CBC analysis to determine the heterogeneity of erythrocytes. Throughout the years, RDW has been typically utilized in combination with the MCV and mean corpuscular hemoglobin (MCH) to differentiate the etiology of anemia (6). RDW is a component of CBC which is calculated by flow cytometry machine. Normal limits of RDW is oftenly accepted between 11.5% and 14.5%. Except the assessment of anemia etiology, studies have notified that RDW may be associated with outcome in patients with heart failure, acute myocardial infarction, thrombolysis used during ischemic stroke, pulmonary thromboembolism, pneumonia and cardiopulmonary arrest (7-12). Elevation in RDW is also known to be associated with elevated inflammatory marker tests such as IL-6 and TNF-α. It is a known mechanism that proinflammatory cytokines could lead suppression on RBC maturation, which may result as an elevation in RDW. Even though there are some hypothesis, the precise pathophysiological situation underlying changes in RDW and clinical conclusions are not elucidated clearly yet (13,14). There are only few studies investigating the correlation between sepsis and RDW. The main purpose of this study was to appreciate the relation among RDW and outcome and to determine it's prognostic significance in critically septic patients.

Materials and Methods

This single center retrospective analysis was conducted in a tertiary medical intensive care unit (ICU) at hospital, Department of Internal Medicine, Division of Critical Care between January 2015 and January 2020. The study protocol was approved by the University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital Ethics Committee (decision no: 487, date: 12.06.2020). One hundred two patients older than 18 years followed up with sepsis were included in the study. The identifiaction of sepsis and/or septic shock was described according to the International Sepsis Definitions Conference criteria (1). Patients with blood product transfusion in last two weeks, active major bleeding, history of diseases which may affect RDW such as leukemia, bone marrow infiltration, transplantation, agranulocytosis, recently received chemotherapy, radiotherapy and drugs that significantly effect RDW measurements were excepted. Demographic and laboratory data were collected from hospital electronic records and patient file archives. Patient age, gender, APACHE-II score, need for invasive mechanical ventilation (IMV), lenght of stay (LOS) in ICU, comorbid conditions (cardiovascular, renal, endocrinological, respiratory and neurological diseases), need for hemodialysis, presence of septic shock on ICU admission and mortality status were recorded. APACHE-II score was calculated within the parameters of first 24 hours after admission to ICU. C-reactive protein (CRP), procalcitonin, RDW, white blood cell (WBC), hemoglobin (Hb), MCH, MCV and platelet (PLT) values were measured on ICU admission. Also, RDW3 and RDW7 values were noted. Haematological parameters were determined using analyser. The analyser calculates MCV, MCH and MCHC based on measurements of Hb. The reference range for RDW in our laboratory was 11.5-14.5%.

Statistical Analysis

Preliminarily, patients were divided in two separate groups as survivors and non-survivors, normal and high RDW values and also septic shock and non-septic shock. Continuous variables were tested using Kolmogorov-Smirnov test for normality and datas are expressed as median and interquartile range or mean ± standard deviation. Mann-Whitney U test was performed to compare distinctions for non-normally distributed variables. Student t-test was performed to compare distinctions for normally distributed variables. Categorical variables were analyzed with a

chi-square test or Fisher's Exact test and expressed as numbers (percentages). Binary logistic regression analysis was performed to determine the independent risk factors for mortality. The outcomes of the regression analyses were expressed as odds ratio (OR) and 95% confidence interval (CI). The receiver operator characteristics (ROC) curve was formed and the area under the curve (AUC) was computed to understand the strength of RDW on mortality. A p-value less than 0.05 were presumed statistically significant. Statistical analyses were carried out using the Statistical Package for the Social Sciences (SPSS), version 22.0 software (SPSS Inc.,Chicago, IL, USA).

Results

Fifty-two (51%) were female of 102 septic patients participated in this study. The median age was 72 (62-80) years. Median RDW value on admission to the ICU was 16.8 (15.3-18.8). Mortality rate was 59.8%. LOS in ICU was 6 (4-12) days. In this study, 46 (45.1%) patients had cardiovascular disease, 39 (38.2%) patients had renal disease and 25 (24.5%) patients had endocrinological disease. The frequency of comorbidities was not different between survivors and non-survivors. The need for IMV was 62 (60.8%). APACHE-II score was 20 (17-28). The number of patients undergoing hemodialysis was 49 (48%). Sixty-six (64.7%) of the patients was diagnosed as septic shock on ICU admission. Survivors had lower RDW value on admission to the ICU [15.8 (14.1-18) versus 17.4 (16.2-19.3), p=0.001], RDW3 value [15.8 (14.6-17.5) versus 17.4 (16.2-19.3), p=0.002] and RDW7 value [15.8 (14.8-17.5) versus 17.5 (16.1-19.8), p=0.003] as compared to non-survivors. The patients with RDW value >14.5% on admission to the ICU was more higher in non-survivors than in survivors and was statistically significant [56 (91.8) versus 30 (73.2), p=0.011]. Non-survivors had higher CRP [127 (82-178) versus 87 (33-188), p=0.05], procalcitonin [3.3 (1.2-8.7) versus 0.9 (0.3-2.8), p=0.001) and APACHE-II score [24 (19-32) versus 17 (15-20), p=0.001] as compared in survivors. The need for hemodialysis were higher in non-survivors than in survivors [35 (57.4) versus 14 (34.1), p=0.02]. There were no significant difference WBC, MCV, MCH, Hb and PLT values between these two groups. Detailed demographic characteristics were described in Table 1. Patients were divided in two groups as a high RDW (>14.5%) and a normal RDW (≤14.5%). The high RDW group had higher APACHE-II score [22 (17-28) versus 18 (13-23), p=0.05], septic shock rate on ICU admission [62 (72.1) versus 4 (25), p=0.001], need for hemodialysis [46 (53.5) versus 3 (18.8), p=0.011] and mortality rate [56 (65.1) versus 5 (31.3), p=0.011] as compared to normal RDW group. There were no significant difference in LOS in ICU and need for IMV between normal and high RDW groups. Detailed demographic characteristics were described in Table 2. Patients with septic shock had higher RDW value on admission to the ICU [17.3 (16-19.5) versus 15.4 (13.8-17.1), p=0.001], RDW3 value [17.3 (16.1-19.1) versus 15 (14.1-17.2), p=0.001] and RDW7 value [17.5 (16-18.8) versus 15.4 (14.2-17.2), p=0.004] as compared in patients without septic shock. Detailed demographic characteristics were described in Table 3. In the binary logistic regression analysis, presence of septic shock on ICU admission, need for IMV and RDW3 value were found to be independent risk factors for mortality [OR: 9.469 (1.964-45.646), p=0.005, OR: 9.231 (2.118-40.234), p=0.003, OR: 2.227 (1.083-4.580), p=0.029], respectively (Table 4). As shown in Figure 1, AUC of the receiver operating characteristic for prediction of mortality was 0.701 (95% CI: 0.586-0.815) for RDW3 value. Based on ROC curve for RDW3 shows a cut-off value of 16 with a sensitivity of 78.9% and a specificity of 56.1% (95% CI: 0.586-0.815, p=0.002).

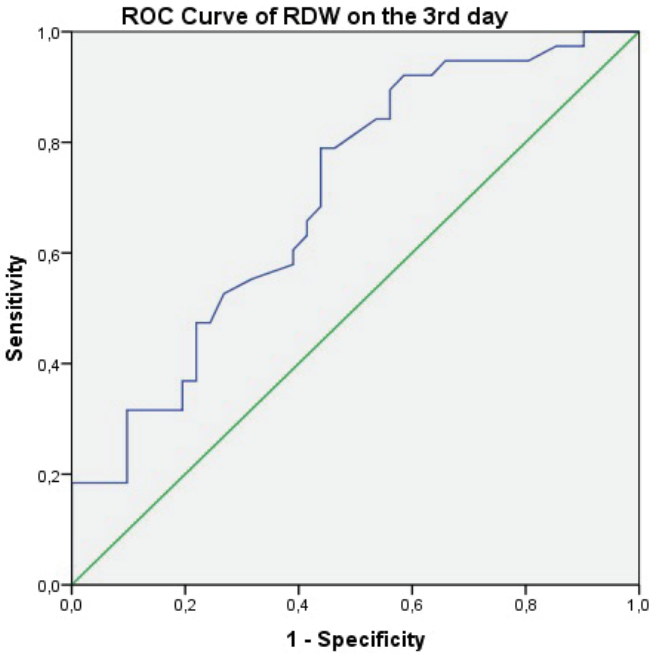

Figure 1. Receiving operator curve analysis of RDW3 value in predicting mortality
ROC: Receiver operator characteristics, RDW: red cell distribution width

Table 1. Baseline characteristics of the patients				
Variables	**Total n=102**	**Survivors n=41**	**Non-survivors n=61**	**p**
Age, (y)	72 (62-80)	69 (57-83)	72 (62-79)	0.785
Male, n (%)	50 (49)	20 (48.8)	30 (49.2)	0.968
APACHE-II score	20 (17-28)	17 (15-20)	24 (19-32)	0.001
Septic shock in ICU, n (%)	66 (64.7)	15 (36.6)	51 (83.6)	0.001
Comorbidity, n (%)				
Cardiovascular disease	46 (45.1)	19 (46.3)	27 (44.3)	0.836
Renal insufficiency	39 (38.2)	17 (41.5)	22 (36.1)	0.582
Endocrinological disease	25 (24.5)	12 (29.2)	13 (21.3)	0.379
Respiratory disease	29 (28.4)	11 (26.8)	18 (29.5)	0.769
Neurological disease	16 (15.6)	6 (14.6)	10 (16.4)	0.799
Laboratory parameters on admission				
CRP (mg/L)	109 (68-179)	87 (33-188)	127 (82-178)	0.05
Procalcitonin (ng/mL)	1.93 (0.5-5.5)	0.9 (0.3-2.8)	3.3 (1.2-8.7)	0.001
Hb (g/dL)	10.1±2.18	10.5±2.03	9.9±2.3	0.266
WBC (10^3/μL)	10.9 (7.1-16.3)	10 (7.1-15)	12 (6.8-17.3)	0.609
MCV (fL)	85.9±7.5	86.9±7.4	85.2±7.5	0.254
MCH (pg)	28 (27-30)	29 (27-30)	28 (26-29)	0.112
PLT (10^3/μL)	174±105	191±100	164±108	0.192
RDW value on admission to the ICU, %	16.8 (15.3-18.8)	15.8 (14.1-18)	17.4 (16.2-19.3)	0.001
High RDW value on admission to the ICU, n (%)	86 (84.3)	30 (73.2)	56 (91.8)	0.011
RDW3 value, %	16.8 (15-18.1)	15.8 (14.6-17.5)	17.4 (16.2-19.3)	0.002
High RDW3 value, n (%)	69 (67.6)	33 (80.5)	36 (59)	0.09
RDW7 value, %	16.4 (15.1-18.2)	15.8 (14.8-17.5)	17.5 (16.1-19.8)	0.003
High RDW7 value, n (%)	60 (58.8)	29 (70.7)	31 (50.8)	0.137
Need for hemodialysis, n (%)	49 (48)	14 (34.1)	35 (57.4)	0.02
Need for IMV, n (%)	62 (60.8)	13 (31.7)	49 (80.3)	0.001
LOS in ICU days	6 (4-12)	6 (4-10)	7 (3-15)	0.673

n: Number, y: year, p: probability, APACHE-II: Acute Physiologic and Chronic Health Evaluation-II, ICU: intensive care unit, Hb: hemoglobin, RDW: red cell distribution width, WBC: white blood cell, CRP: C-reactive protein, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, PLT: platelet, IMV: invasive mechanical ventilation, LOS: length of stay

Discussion

Sepsis is a major problem with high morbidity and mortality rates, especially for ICU patients. Most biochemical markers indicating sepsis related inflammation are expensive and not easily available, which is the point, RDW seems to have an advantage. Although RDW is not a definite indicator for sepsis, in recent years, it has been emphasized that the high RDW value is in relation with mortality in septic patients (15,16). Elevated RDW presumably reflects the presence of elevated proinflammatory cytokines in sepsis and septic shock. In a retrospective analysis of patients with sepsis and septic shock, RDW was remarkably higher in non-survivors as compared in survivors (17). In this present study, RDW was also found significantly higher in non-survivor septic patients when compared to survivors, which is compatible with literature data. In previous studies, positive association was detected between RDW and mortality rates in neonatal, pediatric and adult patient groups according to cox proportional hazards model. Ellahony et al. (18) indicated an evident association of RDW with mortality in neonatal patients (OR, 1.31; 95% CI, 1.241-1.399). Mahmood et al.

Table 2. Baseline characteristics of the patients according to RDW value

Variables	Total n=102	High RDW n=86	Normal RDW n=16	p
Age, (y)	72 (62-80)	72 (63-79)	57 (52-79)	0.665
Male, n (%)	50 (49)	39 (45.3)	11 (68.8)	0.086
APACHE-II score	20 (17-28)	22 (17-28)	18 (13-23)	0.05
Septic shock in ICU, n (%)	66 (64.7)	62 (72.1)	4 (25)	0.001
Need for hemodialysis, n (%)	49 (48)	46 (53.5)	3 (18.8)	0.011
Need for IMV, n (%)	62 (60.8)	53 (61.6)	9 (56.3)	0.686
LOS in ICU days	6 (4-12)	6 (4-12)	7 (3-12)	0.879
Mortality, n (%)	61 (59.8)	56 (65.1)	5 (31.3)	0.011

n: Number, y: year, p: probability, APACHE-II: Acute Physiologic And Chronic Health Evaluation-II, ICU: intensive care unit, RDW: red cell distribution width, IMV: invasive mechanical ventilation, LOS: length of stay

Table 3. RDW values of the patients according to situation of septic shock

Variables	Total n=102	Patients with septic shock n=66	Patients without septic shock n=36	p
RDW value on admission to the ICU, %	16.8 (15.3-18.8)	17.3 (16-19.5)	15.4 (13.8-17.1)	0.001
RDW3 value, %	16.8 (15-18.1)	17.3 (16.1-19.1)	15 (14.1-17.2)	0.001
RDW7 value, %	16.4 (15.1-18.2)	17.5 (16-18.8)	15.4 (14.2 -17.2)	0.004

n: Number, p: probability, ICU: intensive care unit, RDW: red cell distribution width

Table 4. Multivariable binary logistic regression modeling of parameters for mortality

Variables	OR (95% CI)	p
Septic shock in ICU	9.469 (1.964-45.646)	0.005
Need for IMV	9.231 (2.118-40.234)	0.003
RDW3 value, %	2.227 (1.083-4.580)	0.029
Need for hemodialysis	1.656 (0.418-9.368)	0.549
High RDW on admission to the ICU	1.287 (0.088-18.782)	0.854
APACHE-II score	0.993 (0.834-1.652)	0.798
RDW7 value, %	1.355 (0.482-1.687)	0.299
RDW value on admission to the ICU, %	0.586 (0.132-1.289)	0.134
Procalcitonin	1.095 (0.852-1.406)	0.479

OR: Odds ratio, CI: confidence interval, p: probability, ICU: intensive care unit, IMV: invasive mechanical ventilation, RDW: red cell distribution width, APACHE-II: Acute Physiologic and Chronic Health Evaluation-II

(19), demonstrated that RDW value ≥16 was an independent risk factor for mortality in the septic patients. Sadaka et al. (20) performed, RDW was assigned to be an independent risk factor for mortality occurring both in the critical care unit and hospital in patients with sepsis and septic shock. In another studies demonstrated that RDW value on admission to the ICU were valuable for predicting 28-day mortality (21). Ramby et al. (22) could not be established between mortality and RDW in pediatric septic patients. Zhang et al. (23) RDW were found to be independent risk factor for mortality in patients with severe acute pancreatitis. Similarly, in this study, RDW value on admission to the ICU and RDW7 values were not found to be independent risk factors for mortality but RDW3 value was a risk factor. Ku et al. (24) performed that 72 hours of RDW could be an indicator for all reasons mortality in patients with Gram-negative bacterial sepsis as similar to the results of this study. Severe sepsis and/or septic shock patients received massive or goal directed fluid resuscitation and appropriate empiric antibiotic therapy in the first hours of treatment and because of this reasons, the number of reported deaths in the first 24 hours was lower among our septic patients. Although the value of RDW was higher on admission to ICU, it could not be associated with mortality. Also the lack of an association between RDW value on admission to the ICU and mortality may be attributable to the relatively small number of patients, high incidence of comorbidities, life-threatening conditions of the patients on admission to ICU (such as need for hemodialysis and acute renal failure etc.), high APACHE-II score, high rate of septic shock and the increased use of IMV. Increased

mortality rate after three days with high RDW3 values were easily associated. Another study showed that RDW values on 1, 4, and 8 days were associated with prognosis in septic patients. Non-survivors septic patients had higher RDW than survivors in the first week of ICU stay and RDW during the first week was associated with mortality (25). Chan and his colleagues reported that rise in RDW values during the first 72 h after admission to hospital was associated with a higher mortality ratio in septic patients (26). In our study, non-survivor group had higher RDW values (on admission to the ICU, RDW3 and RDW7) than survivors. This result intended that dynamic observation of RDW values appeared to be more valuable than one single result in clinical practice. Also patients with septic shock had higher RDW value on admission to the ICU, RDW3 value and RDW7 value as compared in patients without septic shock (for all $p<0.05$). Lakshmi and Palanisamy (27) showed in a sepsis study as similar results to our study that the subjects with sepsis had a mean RDW of 15.92, with severe sepsis had a mean RDW of 16.73 and with septic shock had a mean RDW of 18.06. There are studies have notified that RDW may be associated a worse prognosis in patients with life-threatening illnesses such as congestive heart failure, acute myocardial infarction, thrombolysis used during ischemic stroke, pulmonary embolism, pneumonia, critical illness and cardiac arrest (7-12). The association between RDW and mortality or severity in sepsis and septic shock is uncertain. It is thought that proinflammatory cytokines may cause depression in the maturation of RBC and decrease the half-life of RBCs. Therefore, inflammatory situations could cause elevation in RDW (28). There were several limitations in our study. This was a single-center study with a small sample size. In addition, RDW may be affected by nutritional status, iron, folate, total cholesterol values, hepatic or renal dysfunction, cancer, thyroid disease, acute or chronic inflammatory response, use of some medications, albumin and vitamin B12 values. This is a retrospective analysis and we did not involve the nutritional status or any of the vitamin and hormonal values of the patients. Also, in a much wider patient population or different disease subgroups, the results related to RDW may differ.

Conclusion

Although RDW value on admission to the ICU was not a risk factor for mortality, RDW3 value was found as an independent risk factors for mortality. Accordingly the follow-up of patient's RDW value in the days after admission to the ICU can be valuable. RDW which has the low cost and universal availability can be used as an adjunct factor for predicting mortality in septic patients along with other prognostic values. Also, the RDW values (on admission to the ICU, RDW3 and RDW7) were higher especially in septic shock patients compared to sepsis patients without septic shock. Further studies are necessary to verify the act of RDW in sepsis and septic shock patients as a predictive marker in the ICU.

Ethics

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital Ethics Committee (decision no: 487, date: 12.06.2020).

Informed Consent: Patient consent was waived because no patient identifiers were disclosed and the diagnosis and management of patients would not be affected.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: B.S.K., İ.S., Design: B.S.K., İ.S., Data Collection and Process: B.S.K., İ.S., Analysis or Interpretation: B.S.K., İ.S., Literature Search: B.S.K., İ.S., Writing: B.S.K., İ.S.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Shankar-Hari M, Phillips GS, Levy ML, Seymour CW, Liu VX, Deutschman CS, et al. Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:775-87.
2. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of Clinical Criteria for Sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315:762-74.
3. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med 2001;29:1303-10.
4. Qiao Q, Lu G, Li M, Shen Y, Xu D. Prediction of outcome in critically ill elderly patients using APACHE II and SOFA scores. J Int Med Res 2012;40:1114-21.
5. Morris M, Davey FR, Henry JB. Basic examination of blood. In Clinical diagnosis and management by laboratory methods. 20th edition. Philadelphia: WB Saunders Company; 2001.
6. Demir A, Yarali N, Fisgin T, Duru F, Kara A. Most reliable indices in differentiation between thalassemia trait and iron deficiency anemia. Pediatr Int 2002;44:612-6.
7. Felker GM, Allen LA, Pocock SJ, Shaw LK, McMurray JJ, Pfeffer MA, et al. Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank. J Am Coll Cardiol 2007;50:40-7.
8. Zorlu A, Bektasoglu G, Guven FM, Dogan OT, Gucuk E, Ege MR, et al. Usefulness of admission red cell distribution width as a predictor of early mortality in patients with acute pulmonary embolism. Am J Cardiol 2012;109:128-34.
9. Dabbah S, Hammerman H, Markiewicz W, Aronson D. Relation between red cell distribution width and clinical outcomes after acute myocardial infarction. Am J Cardiol 2010;105:312-7.
10. Braun E, Domany E, Kenig Y, Mazor Y, Makhoul BF, Azzam ZS. Elevated red cell distribution width predicts poor outcome in young patients with community acquired pneumonia. Crit Care 2011;15:R194.
11. Kim J, Kim K, Lee JH, Jo YH, Rhee JE, Kim TY, et al. Red blood cell distribution width as an independent predictor of all-cause mortality in out of hospital cardiac arrest. Resuscitation 2012;83:1248-52.
12. Turcato G, Cappellari M, Follador L, Dilda A, Bonora A, Zannoni M, et al. Red Blood Cell Distribution Width Is an Independent Predictor of Outcome in Patients Undergoing Thrombolysis for Ischemic Stroke. Semin Thromb Hemost 2017;43:30-5.
13. Lippi G, Targher G, Montagnana M, Salvagno GL, Zoppini G, Guidi GC. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Arch Pathol Lab Med 2009;133:628-32.
14. Bazick HS, Chang D, Mahadevappa K, Gibbons FK, Christopher KB. Red cell distribution width and all-cause mortality in critically ill patients. Crit Care Med 2011;39:1913-21.
15. Wang F, Pan W, Pan S, Ge J, Wang S, Chen M. Red cell distribution width as a novel predictor of mortality in ICU patients. Ann Med 2011;43:40-6.
16. Hu ZD, Lippi G, Montagnana M. Diagnostic and prognostic value of red blood cell distribution width in sepsis: A narrative review. Clin Biochem 2020;77:1-6.
17. Jo YH, Kim K, Lee JH, Kang C, Kim T, Park HM, et al. Red cell distribution width is a prognostic factor in severe sepsis and septic shock. Am J Emerg Med 2013;31:545-8.
18. Ellahony DM, El-Mekkawy MS, Farag MM. A Study of Red Cell Distribution Width in Neonatal Sepsis. Pediatr Emerg Care 2017;36:378-83.
19. Mahmood NA, Mathew J, Kang B, DeBari VA, Khan MA. Broadening of the red blood cell distribution width is associated with increased severity of illness in patients with sepsis. Int J Crit Illn Inj Sci 2014;4:278-82.
20. Sadaka F, O'Brien J, Prakash S. Red cell distribution width and outcome in patients with septic shock. J Intensive Care Med 2013;28:307-13.
21. Kim YC, Song JE, Kim EJ, Choi H, Jeong WY, Jung IY, et al. A Simple Scoring System Using the Red Blood Cell Distribution Width, Delta Neutrophil Index, and Platelet Count to Predict Mortality in Patients With Severe Sepsis and Septic Shock. J Intensive Care Med 2019;34:133-9.
22. Ramby AL, Goodman DM, Wald EL, Weiss SL. Red blood cell distribution width as a pragmatic marker for outcome in pediatric critical illness. PLoS One 2015;10:e0129258.
23. Zhang FX, Li ZL, Zhang ZD, Ma XC. Prognostic value of red blood cell distribution width for severe acute pancreatitis. World J Gastroenterol 2019;25:4739-48.
24. Ku NS, Kim HW, Oh HJ, Kim YC, Kim MH, Song JE, et al. Red blood cell distribution width is an independent predictor of mortality in patients with gram-negative bacteremia. Shock 2012;38:123-7.
25. Lorente L, Martín MM, Abreu González P, Solé-Violán J, Ferreres J, Labarta L, et al. Red blood cell distribution width during the first week is associated with severity and mortality in septic patients. PloS One 2014;9:e105436.
26. Kim CH, Park JT, Kim EJ, Han JH, Han JS, Choi JY, et al. An increase in red blood cell distribution width from baseline predicts mortality in patients with severe sepsis or septic shock. Crit Care 2013;17:R282.
27. Lakshmi K, Palanisamy B. Clinical significance of red cell distribution width (rdw) and circulating neutrophil – lymphocyte count ratio (nlcr) as prognostic markers in sepsis. International Journal of Current Research 2018;10:75155-60.
28. Pierce CN, Larson DF. Inflammatory cytokine inhibition of erythropoiesis in patients implanted with a mechanical circulatory assist device. Perfusion 2005;20:83-90.