ORIGINAL PAPER

The Role of RDW in Mortality Rates of Stroke Patients

Huseyin BUYUKGOL[1], Fatma Aysen EREN[2]

Abstract

Aim: In this study, we examined the relationship between red cell distribution width (RDW) and mortality rates of the stroke patients during the input and the output of the intensive care unit (ICU). Furthermore, we aimed to show the association between RDW levels and the prognosis of the disease. **Materials And Methods:** Our study was retrospectively performed with 150 stroke patients who were followed in ICU between 01.01.2015 – 31.12.2015. The age, gender, vital parameters, GSK, NIHSS, comorbid diseases, RDW levels in the input and output of ICU, duration of their ICU stays, and mortality rates were examined. **Results:** Among all participants, 46% of them were male and the age median value was 76 years. There was no relationship between RDW values of participants ($p>0.05$) and RDW levels of excitus patients during the output from the ICU were significantly higher ($p<0.05$). In our study, we did not detect a significant difference between RDW levels of all patients and survivors ($p>0.05$). However, RDW levels of excites patients were significantly higher ($p<0.05$). RDW_{input} and RDW_{output} levels had negative correlation with GSK and positive correlation with NIHSS ($p<0.05$). There was a positive correlation between RDW_{output} levels and the duration of the hospital stay ($p<0.05$). **Discussion:** Consequently, RDW levels in stroke patients are indicators of ischemia or mortality. Furthermore, it seems that RDW levels can also be used as a parameter in the prognosis.

Keywords: Acute stroke, RDW, mortality, prognosis, intensive care.

INTRODUCTION

Ischemic stroke is the most common cause of death after cardiac pathology and malignancies. It is the most frequent cause of the mortality and morbidity among neurological diseases[1]. Ischemic stroke is classified as major vascular pathologies, lacunar infarction, and cardioembolic[1].

Patients who are admitted to the hospital due to stroke are treated and followed in the stroke unit (if there is) or in the intensive care unit (ICU). Patients who receive the thrombolytic therapy should be followed in ICU conditions at least for 24-36 hours. These clinically unstable patients should be cared in ICU. Half of the mortality (50%) during the stroke treatment occurs due to neurological complications such as brain edema or a new stroke attack. Another half of the mortality can happen due to other medical complications, particularly nosocomial infections[2,3].

Red cell distribution width (RDW) is the parameter which shows the width of the erythrocyte circulation and cell numbers in the whole blood count[4]. RDW is increased in various pathologies except anemia[5-7]. The mechanism of the increase in the RDW is not known. However, this increase is associated with the inflammatory cytokines[8-10]. Increased RDW levels are reported in stroke patients[1,11-14]. Furthermore, it has also been shown that RDW is an important determinant in mor-

[1] Department of Neurology, Faculty of Medicine, KTO Karatay University, Konya, Turkey
[2] Department of Algology, Faculty of Medicine, Istanbul University, Turkey

Corresponding author:
Huseyin BUYUKGOL, Department of Neurology, Faculty of Medicine, KTO Karatay University, Konya, Turkey.
E-mail: h_buyukgol@hotmail.com

tality[9,11,12,15]. In recent years, it has been specified that RDW levels can be used as a prognostic factor in ICU patients and patients with sepsis[8,15].

In this study, we examined the relationship between red cell distribution width (RDW) and mortality rates of the stroke patients during the input and the output of the intensive care unit (ICU). Furthermore, we aimed to show the association between RDW levels and the prognosis of the disease.

MATERIALS AND METHODS

Upon obtaining the ethical committee approval from Aksaray hospital, we conducted our study with stroke patients in the ICU of our hospital between 01.01.2015-31.12.2015. The data of the study were collected from patient follow-up documents and the hospital automation system.

We examined various features of our stroke patients such as age, gender, systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse rate, *Glasgow Coma Scale* (GCS), *National Institutes Of Health Stroke Scale Scores* (NIHSS), comorbid diseases [Hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), stroke, heart failure, atrial fibrillation (AF), valvular heart disease, chronic renal failure (CRF)], RDW levels during the input and the output of ICU, the duration of the hospital stay, and mortality rates.

In our study, we excluded some patients who were diagnosed with non-ischemic stroke, who were younger than 18 years old, who received blood transfusion in the ICU or in the last two weeks, who were admitted from other hospitals, who were pregnant, who had leukemia, myelodysplastic syndrome or tumor metastasized to the bone marrow, who had a hematological disease, whose RDW levels were not detected during the input and the output of the ICU.

The data of the study was analyzed by using SPSS Windows 15 version. Kolmogorov-Smirnov test was used to control the distribution of the variables. In case of the descriptive statistics, we used mean and standard deviation (SD) to analyze the parametric data; median and interquantile range (IQR) to analyzer the non-parametric data; and number of case(s) and percentile (%) to analyzer the qualitative data. In order to compare the parametric data, we used Student-*t* test, and the change in time of these data was shown by using Paired Samples test. Furthermore, Mann Whitney U test was used to compare the non-parametric data, and Chi Square test was used to analyze the qualitative data. The correlation between the duration of the hospital stay, NIHSS and GCS, and RDE levels were analyzed by using Spearman's correlation test. Findings were evaluated in 95% confidence interval and the significance was accepted for p values lower than 0.05 ($p<0.05$).

RESULTS

We included 150 ischemic stroke patients and their mean age was 76 years (IQR:17) and 46% of them were male. There was no relationship between the mortality and the age and the gender. Blood pressures at the time of the admission to ICU were similar to each other in both groups ($p>0.05$) whereas the heart rates of excites patients were significantly higher compared to others ($p<0.05$). GCS values of excites patients were significantly lower and NIHSS scores were significantly higher ($p<0.05$). Mean RDW value of patients was 14.3 ± 2.3 when they were accepted to ICU and mean RDW value of patients was 14.4 ± 2.5 during the output from the ICU. We did not detect any significant relationship between the RDW levels of patient during the input and the output of the ICU ($p>0.05$) whereas RDW levels of excitus patients had significantly higher during the output from the ICU ($p<0.05$). The median of the duration of the hospital stay was 12.4 days and the duration of the excitus patients was significantly longer ($p<0.05$). The most common morbid diseases determined in our patients were hypertension (HT) (74.5%) and diabetes mellitus (DM) (44.7%). The mortality rate of the patients with a stroke, heart failure, and chronic kidney failure (CKF) background was higher ($p<0.05$).

In our study, there was no significant difference between RDW levels of all patients and survivors ($p>0.05$) whereas the RDW levels of excitus patients were significantly higher (Table 2, Figure 1).

During the input of ICU, RDW levels of patients had a negative correlation with GCS and positive correlation with NIHSS ($p<0.05$). Furthermore, RDW levels did not correlate with the duration of the hospital stay ($p>0.05$). During the output from the ICU, RDW levels had a negative correlation with GCS and positive correlation with NIHSS and the duration of the hospital stay ($p<0.05$) (Table 3).

DISCUSSION

Stroke is the sudden and 24 hours long focal or global cerebral dysfunction[16]. Stroke is the status of ischemia/hypoxia development in the brain due to the deteriora-

Table 1. The comparison of the mortality rate with clinical findings and RDW levels

		All group	Excitus	Survivor	p
Age, Median (IQR)		76 (17)	78 (14.5)	75 (18.5)	0.068*
Gender	Female	81 (54)	40 (54.8)	41 (53.2)	0.960**
	Male	69 (46.0)	33 (45.2)	36 (46.8)	
SBP, Median (IQR)		160 (40)	155 (50)	160 (30)	0.386*
DBP, Median (IQR)		90 (16.3)	85 (30)	90 (10)	0.574*
Heart rate, Median (IQR)		80 (18.3)	90 (26)	78 (9)	<0.001*
HT, n(%)		11 (74.5)	54 (74.0)	58 (75.3)	0.849**
DM, n(%)		67 (44.7)	36 (49.3)	31 (40.3)	0.265**
CLD, n(%)		52 (34.7)	29 (39.7)	23 (23.3)	0.205**
Stroke history, n(%)		51 (34.0)	31 (42.5)	20 (26.0)	0.033**
Heart failure, n(%)		51 (34.0)	32 (43.8)	19 (24.7)	0.013**
AF, n(%)		34 (22.7)	17 (23.3)	17 (22.1)	0.860**
Heart valve disease, n(%)		25 (16.7)	12 (16.4)	13 (16.9)	0.942**
CKF, n(%)		20 (13.4)	16 (21.9)	4 (5.3)	0.003**
GCS, Median (IQR)		10 (5)	7 (3)	12 (3)	<0.001*
NIHSS, Median (IQR)		22 (12.3)	27 (6)	16 (8.5)	<0.001*
RDW_{input}, Mean±SD		14.3 ± 2.3	14.6±2.5	14.0 ±2.0	0.140***
RDW_{output}, Mean±SD		14.4 ± 2.5	15.4±2.7	13.6 ±1.9	<0.001***
The duration of the hospital stay, Median (IQR)		9.5 (14)	9 (22.5)	10 (12)	<0.001*

*Mann Whitney U test, **Chi Square testi, ***Student *t* test

tion of the 80% cerebral blood circulation as a result of the thromboembolism and hemorrhage[16].

Stroke is a pathology which is observed generally after the age of 60 and its incidence increases as the age interval increases[1,8,17,18]. Even though the stroke incidence in young women is lower compared to young men, the frequency of the stroke in older women exceeds the stroke frequency in older men[19]. Regenon et al. showed that 69% of their stroke patients were male and the mean age of them was 65[17]. Kıyan et al. reported that 57% of the patients were male and the mean age of them was 67.5[18]. Acar et al. also found that 51% of the patients were male and the mean age of them was 69.5[1]. Similarly, we also showed that 46% of our stroke patients were male and the mean age was 76. In our opinion, our stroke patients needed ICU health care because they were older stroke patients who were hospitalized to ICU with an acute stroke development and who had pathologies at the cellular or organ level. Increased comorbid diseases of our patients affected the vessel structures of our patients. We conducted this study with stroke patients who were followed in ICU because of their older ages which led to comorbid diseases and thus deteriorated vessels due. The protective effect of the estrogen is lost in time in females and they live longer than men. Therefore, it is possible that the frequency of female patients increase in contrast to the findings of the literature.

As a result of the ischemia occurs in the corpus striatum, it was shown that the massive release of dopamine led to increase in the blood pressure and the heart rate[16]. Furthermore, arrhythmia (especially tachycardia) and ST changes are often developed in the first 24 hours in acute stroke patients[20]. In our patients, high tension and the increase in the heart rate in our patient group is similar to the findings of the literature. We

Table 2. The effect of the clinic on RDW level changes

	RDW_{input}	RDW_{output}	p*
All group	14.3 ± 2.3	14.4 ± 2.5	0.340
Excitus	14.6±2.5	15.4±2.7	<0.001
Survivor	14.0 ±2.0	13.6 ±1.9	0.080

*Paired samples test

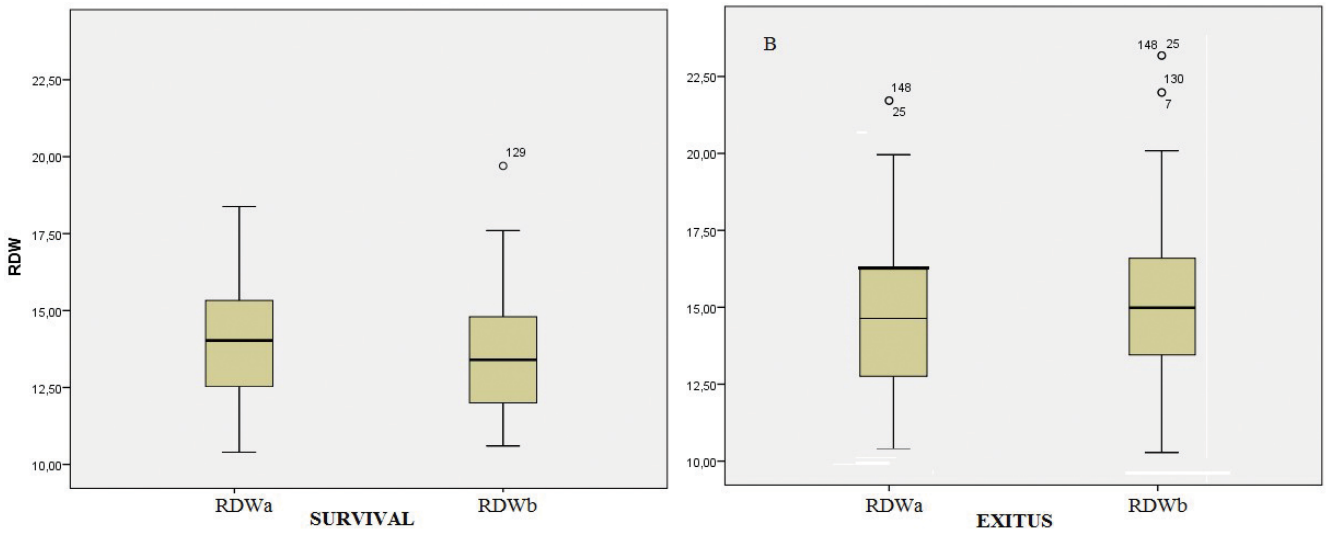

Figure 1. RDW levels of excitus patients were significantly higher.

Table 3. The relationship between the RDW levels and the GCS and NIHSS

		RDW_{Input}	RDW_{Output}
GCS	r	-0.231	-0.306
	p*	0.005	0.000
NIHSS	r	0.198	0.321
	p*	0.015	0.000
The duration of the hospital stay	r	0.076	0.242
	p*	0.356	0.003

*Spearman's rho

believe that hypertension and tachycardia frequencies were high due to the dopamine release and increased stress hormones in older ages.

In the etiology of the stroke, diseases such as HT, DM and AF have effects[21,22]. Half of the mortality (50%) during the stroke treatment occurs due to neurological complications such as brain edema or a new stroke attack. Another half of the mortality can happen due to other medical complications, particularly nosocomial infections[2,3]. In line with literature, we also showed that the frequency of hypertension and diabetes mellitus was high[21,22]. Furthermore, we detected high mortality rates in former stroke patients, heart failure patients, and CKF patients. We believe that brain edema frequency increases due to new ischemic areas that are formed near the existing ones in former stroke patients. Furthermore, we also state that mortality rates increase due to new stroke attacks. In CKF and heart failure patients, mortality rates are high because of the susceptibility to infections and the inappropriate support treatment.

In studies related to stroke, RDW values were shown to be significantly higher in patients compared to control individuals. Here are some RDW scores shown by different groups; 14.6 shown by Acar et al. 1; 14.7 shown by Kara et al.[23]; and 14.1 shown by Ntaisos et al.[24]. RDW levels are high in various pathologies. However, the underlying pathophysiology of this has not yet been explained[6]. Majercik et al. conducted a study in which they related increased RDW levels with increased inflammatory responses[9]. Montana et al. showed that increased stress led to cytokine release (TNF-α, IL-1 and IL-6), these cytokines shorten the lifespan of cells and desensitized the progenitors of the erythrocytes via affecting the bone marrow. They supported that idea that this desensitization led to anisocytosis by deteriorating the red blood cell maturation[10]. Isik et al. associated the increased RDW levels with the stress factors that were formed due to the cytokines and bleeding in patients with acute gastrointestinal bleeding[25]. Marinkovic et al. concluded that increased oxidative stress led to increment in the hemolysis and thus increased RDW levels[26]. In our study, we detected the RDW levels (14.3) in line with the findings in the literature.

RDW levels of mortal patients were high both during the input and the output of the ICU 8. The mortality of patients in the ICU was related to the increased RDW levels[12]. It was stated by Fujita that RDW levels can be used as the mortality indicator in ICU patients[27]. It was emphasized by Patel et al. that factors such as the age,

nutrition, anemia, and inflammation can influence the RDW levels and altered RDW levels can have effects on the mortality[28]. Hunziker et al. specified that RDW levels can be used as a simple physiological score for the determination of the long- and short-term mortality[29]. Vashita et al. stated that RDW can be the strong indicator of the mortality in hemodialysis patients and they associated this with anemia[30]. In our study, there was no difference between the RDW levels of groups when they were first admitted to the ICU. However, RDW levels were higher in excitus patients during the output of the ICU. In our opinion, RDW is not the mortality indicator at the time of the admission to ICU because the event occurred acutely. Acute stroke patients are immediately admitted to the hospital because of the dramatic deterioration of the clinical status of the patient. Inflammation occurs just at that time. We believe that RDW levels are higher in mortal patients because additional complications lead to further deteriorations in RDW levels.

Our study is the first one in which RDW level alterations are examined in stroke patients. According to the Meta analysis of Peta, it was shown that one unit increase in RDW levels increased the death risk as 14%[28]. Ozdemir et al. showed that RDW levels of excitus patients in ICU tended to increase whereas RDW levels of discharged patients decreased[8]. Ozdogan et al. measured RDW levels of intraabdominal sepsis patients and they observed that RDW levels decreased in survivors and RDW levels increased in mortal patients[15]. Kim et al. measured the RDW levels of sepsis patients for three days and they associated the increased RDW levels with mortality[31]. We observed that RDW levels increased in mortal patients whereas the difference in RDW levels was not significantly changed in discharged patients. We believe that ICU complications lead to stress and inflammation and thus RDW levels further increase. In case of survivors, RDW levels do not change because the red blood cell regeneration takes long time.

NIHSS and GCS scores are effective in demonstrating the general status of patients and their mortality rates[32,33]. Ntaios et al. reported that RDW levels increased as the health status of the stroke patients deteriorates[24]. We showed that there was a negative correlation between RDW levels and GCS scores whereas the negative correlation was detected between RDW levels and NIHSS scores. In other words, RDW levels increase as a result of the worsening clinical status of patients. We think that there is an intensive stimulation on the bone marrow, red blood cell production excessively accelerates, and there is an increase in the maturation of cells and/or the deterioration of the shape of cells as the clinical status of the patients deteriorates.

Bueno-Cavanillas et al. emphasized that the mortality rate increased as the duration of the hospital stay increased[34]. Wang et al. found a positive correlation between the RDW levels and the mortality time in excitus patients. Furthermore, they also showed that there was a negative correlation between the duration of ICU stay and RDW levels of survivors[12]. Even though there was no relationship between low RDW levels and the discharge time, it was shown that there was a positive correlation between the increased RDW levels and the mortality time[8]. In our study, we observed a positive relationship between the RDWoutput levels and the duration of the hospital stay. We believe that acquired complications are the most important factors which affect the duration of the ICU stay. We also state that these complications lead to an increment in RDW levels which is positively correlated with the duration of the hospital stay.

Consequently, RDW levels in stroke patients are indicators of ischemia or mortality. Furthermore, it seems that RDW levels can also be used as a parameter in the prognosis. A clinician should consider that a complication can be developed if the RDW level is high and the treatment protocol should be accordingly re-evaluated.

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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