# THE IMPORTANCE OF RED CELL DISTRIBUTION WIDTH (RDW) IN PATIENT FOLLOW UP IN INTENSIVE CARE UNIT (ICU)

Rabia Özdemir[1], Nevzat Mehmet Mutlu[2], Metin Özdemir[3], Murat Akçay[2], Cihat Yel[4], Işil Özkoçak Turan[2]
[1]Department of Anesthesiology and Reanimation, Medipol University Hospital, İstanbul - [2]Department of Intensive Care, Ankara Numune Education and Research Hospital, Ankara - [3]Department of Intensive Care, Ankara Numune Education and Research Hospital, Ankara - [4]Department of Emergency, Antakya State Hospital, Antakya, Turkey

**ABSTRACT**

*Objective: In this study we aimed to determine the effect of RDW on mortality by comparing the temporal changes in RDW level in deceased and surviving ICU patients.*

*Materials and method: This study was retrospectively conducted in 776 patients admitted to intensive care unit between 01.01.2013 and 31.12.2013. Age, sex, clinical diagnosis, comorbid conditions, RDW levels at intensive care admission and discharge, duration of intensive care stay, and mortality rate were evaluated. Kolmogorov Smirnov, student t-test, Mann Whithey u test, and Chi-square test were used for data analysis. The results were provided at a confidence interval of 95% and a significance level of p<0. 05.*

*Results: Conducted on 776 patients in Ankara Numune Hospital's general intensive care clinic 3, this study revealed a mortality rate of 38.2%. The mean age of the study population was 65.4±18.3 years, with the deceased patients having a greater mean age (p<0.05). Four hundred and thirteen (53.2%) patients were male, and there was no significant difference between the ratios of both genders (p>0.05). The deceased patients had significantly increasing RDW levels whereas the surviving patients had significantly reducing RDW levels (p<0.05). There was a significant correlation between the magnitude of RDW increment and duration of hospital stay in the deceased patients (p<0.05).*

*Conclusion: The results of this study suggest that RDW, with known association with mortality, can be used as a simple marker for patient follow-up and monitorization of effectiveness of the administered therapies in ICU.*

*Key words: RDW, intensıve care unit, mortalite.*

## Introduction

Intensive care units (ICU) are units designed for the management of both acute disorders and life-threatening complications of chronic disorders, where necessary equipment and personnel are available for close monitoring and rapid management of patients[1]. Patients admitted to ICU have an increased mortality. A study involving 12162 patients admitted to 24 ICUs found an in-hospital mortality rate of 0.91-1.34% whereas the corresponding rate for ICU was 24-41%[2].

Erythrocyte distribution width is a parameter measured in complete blood count that reflects the distribution of erythrocytes' sizes in circulation[3]. Studies have shown that RDW is not only correlated to anemia, but a variety of other pathological conditions[4-6]. RDW was found to be correlated to mortality in sepsis, trauma, cardiovascular disorders, and patients admitted to general ICUs[7-12]. Although the exact mechanism of the association of RDW with mortality is yet to be fully explained, several studies, particularly those conducted in sepsis, have implicated inflammatory cytokines in the

disease pathogenesis[7]. Studies conducted on patients with sepsis have indicated that RDW may have prognostic implications[13]. However, as these studies have only focused on patients with sepsis, no consensus has been reached as to whether it has a similar prognostic role in other conditions managed in ICU.

Herein, we aimed to analyze the temporal changes in RDW levels of patients deceased in or discharged from intensive care unit in an attempt to determine its prognostic value.

## Materials and method

After being approved by the Local Ethics Committee of Ankara Numune Training and Research Hospital, our study retrospectively examined patients managed in intensive care unit between 1.01.2013 and 31.12.2013. Patients' data were accessed from patient records and hospital's local automation system.

Age, sex, clinical diagnosis, comorbid conditions, RDW levels at intensive care admission and discharge, duration of intensive care stay, and mortality rate were evaluated.

Our study excluded patients who were below 18 years of age; who were pregnant; who had myelodysplastic syndrome, bone marrow metastases, or hematological disorders; who were transfused blood within 2 weeks; who were referred from another hospital; and patients who underwent a procedure.

Study data were analyzed in SPSS Windows 18 software package. Descriptive statistics included mean, standard deviation for parametric data; median and interquartile range (IQR) for non-parametric data; and number and percentile for categorical data. The distribution of the data was tested with Kolmogorov Smirnov test. Continuous parametric variables were compared with student t-test, and non-parametric variables were compared with Mann Whitney U test and Chi-square test. The correlation between the duration of ICU stay and RDW was tested with Pearson correlation analysis. The results were evaluated at a confidence level of 95% and a significance level of p<0.05.

## Results

Conducted in 776 patients admitted to the general ICU 3 clinic of Ankara Numune Training and Research Hospital, this study revealed a mortality rate of 38.2%. The mean age of the study population was 65.4±18.3 years, with the deceased patients having a significantly higher mean age (p<0.05). Four hundred and thirteen (53.2%) patients were male; the two groups had no significant difference with regard to the proportions of both genders (p>0.05) (Table 1).

| | | DECEASED Mean/ N(%) | SURVIVING Mean/ N(%) | Total Mean/ N(%) | p |
|---|---|---|---|---|---|
| Age | | 67.6±16.1 | 64.1±19.3 | 65.4±18.3 | 0.008* |
| Sex | Male | 160 (54.1) | 253(52.6) | 413(53.2) | |
| | Female | 136(45.9) | 227(47.4) | 363 (46.8) | 0.754** |
| | Total | 296 (100.0) | 480 (100.0) | 776 (100.0) | |

**Table 1**: Demographic characteristics of the study subjects.
* *student-t test, ** X² test*

Sepsis was the most common diagnosis among the deceased patients while pneumonia was the most frequent diagnosis among the discharged patients. In the deceased patients the rates of sepsis and acute renal failure (ARF)/electrolyte disorder were significantly higher whereas intoxication, trauma, and other disease groups were significantly more common in the surviving patients (p<0.05) (Table 2).

| | DECEASED N(%) | SURVIVING N(%) | P* |
|---|---|---|---|
| Pneumonia | 61(20.5) | 106(22.1) | 0.611 |
| Stroke | 62(20.9) | 87 (18.2) | 0.344 |
| Sepsis | 94(31.6) | 13 (2.7) | <0.001 |
| ARDS | 21(7.1) | 26 (5.4) | 0.347 |
| PTE | 8(2.7) | 6(1.3) | 0.142 |
| AMI | 6(2.0 | 13 (2.7) | 0.546 |
| ARF/Electrolyte disorder | 72(24.2) | 75 (15.7) | 0.003 |
| Intoxication | 2(0.7) | 39(8.1) | <0.001 |
| Trauma | 14(4.7) | 48 (10.0) | 0.008 |
| UTI | 23(7.7 | 26 (5.4) | 0.195 |
| Other | 13(4.4) | 57 (11.9) | <0.001 |

**Table 2**: Distribution of care unit diagnoses of the study subjects.
* *X2 test (ARDS:Acute Respiratory Distress Syndrome, PTE:Pulmonary Thromboembolism, AMI:Acute Myocardial Infarction, UTI: Urinary Tract Infection)*

The analysis of the comorbidities of the study subjects revealed that hypertension (43.1%; 37.8%) and diabetes mellitus (15.2; 17.9%) were the com-

monest comorbidities. The rates of comorbid conditions were similar in the deceased and surviving patients (p>0.05) (Table 3).

| | Deceased n(%) | Surviving n(%) | P* |
|---|---|---|---|
| HT | 128(43.1) | 181 (37.8) | 0.136 |
| DM | 45(15.2) | 86 (17.9) | 0.317 |
| COPD | 9(3.0) | 14 (2.9) | 0.928 |
| Malignancy | 58(19.5) | 122 (25.4) | 0.059 |
| Stroke, Alzheimer, Dementia | 24(8.1) | 45 (9.4) | 0.538 |
| AF | 7(2.4) | 21 (4.4) | 0.142 |
| CAD | 11(3.7) | 25 (5.2) | 0.332 |
| CRF | 8(2.7) | 11 (2.3) | 0.724 |
| Other | 10 (3.4) | 75 (15.6) | 0 |

**Table 3**: Comorbid conditions of the study subjects.
* *X2 test (HT: Hypertension; DM: Diabetes Mellitus, COPD: Chronic Obstructive Pulmonary Disease, AF: Atrial fibrillation, CAD: Coronary Artery Disease, CRF: Chronic Renal Failure).*

The median RDW level was 15.2 (IQR 3.4) at admission and 15.5 (IQR 3.5) at discharge. While the median RDW level increased from 15.8 to 17.1, it remained constant at 14.8. RDW level was significantly higher in the deceased patients at both admission and ICU discharge (p<0.05) (Table 4).

| | | N | Median (IQR) | P* |
|---|---|---|---|---|
| RDW$_{admission}$ | Deceased | 296 | 15.8 (3.65) | <0 .001 |
| | Surviving | 480 | 14.8 (2.78) | |
| | Total | 776 | 15.2 (3.4) | |
| RDW$_{final}$ | Deceased | 296 | 17.1 (3.77) | <0.001 |
| | Surviving | 480 | 14.8 (2.8) | |
| | Total | 776 | 15.5 (3.5) | |

**Table 4**: RDW levels at admission and discharge.
* *Mann Whitney-U test*

The analysis of changes in RDW levels during ICU stay revealed that it increased in 261 (87.9%) of the deceased patients and decreased in 31 (10.4%); it increased in 167 (34.8%) of the surviving patients and decreased in 281 (58.5%) (p<0.05) (Table 4).

While the median duration of ICU stay was 5 (IQR=12) days for the deceased patients, it was 6 (IQR=11) days for those who were discharged. Whereas no significant correlation was found between the duration of ICU stay and the admission, discharge RDW levels in the deceased patients (p>0.05), there was a positive correlation between the RDW increment and duration of hospital stay (p<0.05).

No significant correlation was determined between duration of ICU stay and admission, discharge RDW levels and the amount of RDW change (p>0.05).

## Discussion

Intensive care units are places where debilitated patients with poor general status in need of continuous monitoring and care are admitted and where the mortality rates are higher than that of other clinics[2]. Studies have suggested that 5% of all beds of a hospital should meet ICU standards[14,15]. Each institution flexes the criteria for ICU admission and discharge due to deficiencies in personnel and bed capacity of these units[15].

Studies have shown ICU mortality rates ranging between 24-43%[1,2,16]. In our study the mortality rate of the patients was similarly found 38.2%. We are of the opinion that mortality rate is higher in this population since patients admitted to ICUs have more advanced age, worse overall status, and more severe forms of diseases; they are also exposed to nasocomial infections at a higher rate during ICU stay. Hence, a higher age and an infection rate in the deceased patients support our hypothesis.

In a metaanalysis by Patel et al. involving 7 trials showed that the mean patient age ranged between 74 and 78 years, and that women predominated ICU populations[16]. In a domestic study by Ceylan et al. conducted on internal ICU patients, the mean age was found 63 years, and 62% of patients were male[17]. In a study by Uysal et al. the reported mean age was 53 years, and 52% of subjects was male[1].

Our study population had a mean age and gender distribution consistent with the literature reports from our country, although these figures were lower than those reported by foreign studies. The main reason of this finding may be some international differences in living standards and average life expectancies.

Altun et al. reported that the most common ICU admission indications were stroke, COPD, and sepsis, and COPD and sepsis were associated with the highest mortality rate (18) Uysal et al, in a study from our country, reported that the most common indications of ICU admission were sepsis and neu-

rological disorders, with oncological diseases having the highest mortality rates. Increased rate of nasocomial infections is a common problem of ICUs[19]. We believe that mortality is higher in these patients as a result of deteriorated general status due to infections and ARF/electrolyte disorders added on top of preexisting comorbidities. Moreover, increased nasocomial infection rate in hospitals probably led to an increase in overall infection rate. Although underlying malignancies modified the results of the study by Uysal et al, we opine that additional pathologies added onto malignancy actually led to death. Lower mortality rates found for intoxication and stroke cases support our hypothesis.

In a metaanalysis by Patel et al. comprising 11827 patients, the most common comorbidities in ICU populations were HT, DM, and malignancy[16]. We found that HT, malignancy, and DM were the most common comorbid disorders in both groups. Since the subjects enrolled in our study had an advanced mean age, the rate of comorbidities was also high. Although Patel et al.[20] and Perlstein et al.[21] reported that RDW level predicted cardiovascular death and its level increased in cancer and chronic lower respiratory rate diseases, we found no significant differences between the RDW levels of both groups, possibly as a result of similar rates of comorbidities in deceased and surviving patients.

Wang et al. reported that mortality was correlated to increased RDW level[8]. Anderson showed that RDW level was higher in patients who died as a result of cardiac pathologies[10]. Lee et al. explored 30-day mortality in patients with pneumonia and found that RDW was correlated to mortality. Jo et al. studied patients in shock and demonstrated that RDW was correlated to sepsis severity and mortality[22]. Ku et al. reported that RDW was correlated to mortality in infectious diseases[23].

Fujita et al. suggested that RDW may be used as a predictor of mortality in patients admitted to ICU[24]. Patel et al. stressed that, affected by many factors such as age, nutritional status, anemia, and inflammation, RDW independently predicted mortality[20]. Braun et al. assessed 90-day mortality in patients with pneumonia and found that patients with increased RDW level had a higher mortality[5]. The same study also found that RDW and blood urea nitrogen had a better ability to predict mortality than glucose, hypernatremia, creatinine, and white blood cell count[5].

Hunziker et al. reported that RDW can be used as a simple physiological score for determining short- and long-term mortality[25].

In the metaanalysis by Patel et al. each 1 point increment in RDW level caused a 14% increase in mortality[16]. Özdoğan et al. measured RDW serially for 7 days in patients with intraabdominal sepsis; they found that while RDW level was reduced in surviving patients, it was increased in the deceased ones[13]. Kim et al, in a study where serial daily RDW measurements were done for 3 days, found that RDW level was correlated to mortality[26]. In our study the RDW tended to increase in deceased patients whereas it had a tendency to decrease in those who were discharged. We think that enhanced inflammatory effect and impaired neurohumoral balance that result from a deterioration of the preexisting clinical condition during ICU stay suddenly accelerates erythrocyte production in bone marrow through excess levels of stimulants, with disorders in the maturation and/or morphogenesis of red blood cells, leading to increased RDW level. It is equally probable that RDW tended to decrease in patients with a tendency to convalesce thanks to an improvement of stress and neurohumoral mechanisms by administered therapies.

It is a common observation that RDW is increased independently of hemoglobin level by many pathologies, albeit by unknown mechanisms[5]. Lippi et al. showed a direct relationship between RDW and CRP[25]; Majercik et al.[9] reported that RDW increased in response to increased inflammatory milieu. Montana et al. reported that inflammatory cytokines such as TNF-α, IL-1 and IL-6 are released as a result of increased stress, and they both shorten cells' life span and affect bone marrow to desensitize erythroid progenitors which disrupt erythrocyte maturation and cause anioscytosis[28]. It was reported that increased stress causes neurohumoral changes to activate stress hormones, leading to significant changes in RDW level[29]. Marinkoviç et al. showed that increased hemolysis resulting from oxidative stress causes RDW increase[30]. Işik et al. reported that patients with gastrointestinal bleeding had increased RDW levels, and linked that increase to cytokines and bleeding-induced stress factors[31]. Vashistha et al. reported that RDW was a powerful predictor of mortality in hemodialysis patients, an association which they linked to anemia[32]. Jo et al. demonstrated that RDW may be elevated due to impaired blood flow in sepsis[7].

Several studies have indicated that mortality increases as the duration of hospital stay is prolonged[33]. Özay et al.[15] reported a duration of stay of 6.81 days; Uysal et al.[1] 3.4 days; and Ayazoğlu et al.[34] 4.7 days. The mean durations of ICU stay of both the deceased and surviving patients in our study were compatible with figures reported by other domestic studies.

Wang et al. reported that, in addition to RDW being a powerful predictor of mortality, the elevation of its levels had a positive correlation to time to mortality, while it had a negative correlation to duration of hospital stay[8]. We determined no relationship between the magnitude of the decrements in RDW level and time to discharge but found a significant correlation between the magnitude of RDW elevation and time to death. As a result of the overcrowding of our hospital's ICU, patients are transferred to regular wards as soon as they are deemed suitable for follow-up there. We are of the opinion that since time to transfer to a regular ward may sometimes be too short, RDW levels of patients discharged from ICU remain unchanged as there appears no opportunity for new erythrocytes to be produced. On the other hand, considering that 1% increments in RDW level increase mortality in deceased patients, the correlation between time to death and RDW level can be explained.

Our study concluded that RDW, which has a known association with mortality, may be used as a marker for disease monitoring and assessment of treatment efficacy.

### Limitations

As our study has a retrospective design, clinical information including general condition, APACHE scores, and vital parameters could not be accessed. In addition, the criteria for transferring patients to regular ward was not clear. Exclusion criteria were based on medical records and were not confirmed by information obtained from patients or their relatives.

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*Corresponding author*
RABIA ÖZDEMIR
Medipol Mega University Hospital
Anestesiology and Reanimation Department, Bağcilar
İstanbul
*(Turkey)*