THE ROLE OF RED CELL DISTRIBUTION WIDTH PREDICTING IN-HOSPITAL MORTALITY OF INTENSIVE CARE UNIT PATIENTS

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ABSTRACT

Introduction: Red cell distribution width (RDW) has been reported as a prognostic marker in many clinical conditions. Mortality prediction of intensive care unit (ICU) patients is challenging and in this study we aimed to assess the value of RDW in predicting mortality of adult ICU patients.

Materials and methods: RDW values and outcomes of ICU patients from former study were retrospectively collected from medical records. Acute Physiology and Chronic Health Evaluation (APACHE) II, Sequential Organ Failure Assessment (SOFA), and Simplified Acute Physiology Score (SAPS) II scores were calculated according to data obtained from medical charts.

Results: 81 patients of the former study were screened for eligibility and 58 of them were enrolled. Mean age was 69.0 ±15.42 years (95 % CI; 30-90) and 55.2 % were male. There were 26 patients in the survivor group and 32 patients were in the non-survivor group. Regression analysis showed no association between mortality and initial RDW values. However, RDW values of last ICU day showed a positive correlation with mortality. APACHE II, SOFA, and SAPS II scores were higher in non-survivor patients than survivors.

Conclusion: Whilst there was some correlation between RDW at the end of stay and mortality, RDW had no benefit over existing scoring systems. RDW value does not seem as a promising independent factor but further studies investigating its contribution to current scoring systems in specific groups can be reasonable.

Key words: Red Cell Distribution Width; Mortality; Intensive Care Unit, Count blood cell.
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Introduction

Red cell distribution width (RDW) is an index in the complete blood count and a measure of the variation of red blood cell volume(1). Although mechanisms have not been identified clearly, RDW is an emerging marker of chronic inflammation, oxidative stress, and coronary artery disease (CAD)(2-4).

Recent studies showed that RDW increase can be an independent prognostic indicator of heart failure(5-7), stable coronary diseases(8), acute myocardial infarction(9), stroke(10), pulmonary hypertension(11), sepsis(12), trauma(13), and pulmonary embolism(14). Also, it was reported that increased RDW was associated in increased mortality risk in critically ill patients(15,16).

The aim of this study is to determine whether RDW has a role in predicting mortality of intensive care unit (ICU) patients.

Materials and methods

Study design

This is a re-evaluation of a previous prospective study conducted for the value of peripheral
perfusion index (PI) predicting mortality of ICU patients\(^{(17)}\). Ethical approval of this study was obtained from local ethic committee. RDW values of the same patients of the former study were obtained from medical records retrospectively. The 58 patients, whose RDW values could be reached, were included. The previous study had been conducted in a medical intensive care unit of a university hospital between February and May 2012.

**Patient selection**

Patients who were admitted to the ICU during the study period were screened for eligibility and the patients who gave informed consent were included in the study. Exclusion criteria were: (1) patients under 18-years-old, (2) short intensive care stay (because data collection was difficult for these patients), (3) known hematologic disease such as myelodysplastic syndrome, leukemia, metastasis to bone marrow, (4) RDW value can not be found in medical records.

**Data collection**

Demographics, medical history, ICU stay, clinical diagnoses, outcomes and laboratory results (complete blood count (CBC), urea, creatinine, electrolytes, albumin, C-reactive protein (CRP), blood gas profile) of patients who met eligibility criteria were recorded from their medical charts daily.

The worst vital signs and laboratory test results were recorded daily. These data were obtained from patients’ charts. According to these records Acute Physiology and Chronic Health Evaluation (APACHE) II, Sequential Organ Failure Assessment (SOFA) and Simplified Acute Physiology Score (SAPS) II scores were calculated by internet modules for each patient\(^{(18)}\). Last Glasgow Coma Score (GCS) before sedation was recorded for sedated patients.

Fractioned oxygen percentage (\(\text{FiO}_2\)), which is required to calculate APACHE II, SOFA and SAPS II scores, was recorded directly from monitor if the patient was mechanically ventilated. If the patient was in room air, \(\text{FiO}_2\) was assumed as 21\%. The patient was classified as being vasopressor dependent if he/she is on such an agent for at least two hours.

The patients were followed for mortality status after discharge and/or transfer to other department and mortality status assumed positive if the patient died within 24 hours.

**Measurement technique**

RDW and hemoglobin values were measured with ABX Pentra XL 80 Hematology Analyzer (France) as a component of CBC. Normal range of RDW in our laboratory is between 11.7\% and 14.6\%.

**Outcomes**

Main outcome of this study was determined as the initial and last day RDW values of ICU patients in mortality predicting. Secondary outcomes were the association of RDW values with APACHE II, SOFA, and SAPS II scores.

**Statistical analysis**

Descriptive statistics are presented as frequency (percentage) for categorical variables whereas continuous data are presented as mean ± standard deviation for normally distributed data and median interquartile range (IQR) for non-normally distributed data. Statistical Package for the Social Sciences (SPSS) 15.0 (SPSS Inc., Chicago, IL) was used for statistical analysis and \(p<0.05\) considered as statistically significant.

Association between RDW and mortality, and between RDW and APACHE II, SAPS II, SOFA scores were assessed with Cox regression analysis.

Age, gender, hospitalization time, mean arterial pressure, GCS and P/F ratio were not included in multi-variate adjusted Cox regression analysis. Because, these parameters are all included in calculating APACHE II, SOFA and SAPS II scores and/or they have potential for altering results.

ROC Curve analysis have been performed in order to determine the optimal cut-off value for RDW. Specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV), positive and negative likelihood ratios (LR+, LR-) were calculated according to this value for mortality prediction of RDW.

**Results**

**Descriptive analysis**

Patients were screened for eligibility and 58 of them were enrolled (Figure 1). Mean age was 69.0 ±15.42 years (95% CI; 30-90) and 55.2\% (n=32) were male. Patient demographics are given in Table 1.

**Primary outcomes**

There were 26 patients in the survivor group.
and 32 patients were in non-survivor group. There were no significant differences between the RDW at baseline between survivors and non-survivors (p=0.086). Regression analysis showed no association between mortality and initial RDW values. (p=0.902) However, last day RDW values showed a positive correlation with mortality, (p=0.021) (Table 2).

Figure 1: Flowchart of study. All the patients hospitalized in adult ICU were screened for eligibility and included patients were analyzed in two groups.

Table 1: Demographics and diagnosis of patients. Both groups were similar in terms of age and gender.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survivor (n)</th>
<th>Non-survivor (n)</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean±SD, 95% CI)</td>
<td>61±14 (51-71)</td>
<td>60±19 (49-72)</td>
<td>60±19 (49-72)</td>
</tr>
<tr>
<td>Gender (Female/Male)</td>
<td>12/14</td>
<td>15/17</td>
<td>26/22</td>
</tr>
</tbody>
</table>

Table 2: Base line clinical and laboratory characteristics of survivor and non-survivor patients. RDW and Hb levels were not different in two groups but other parameters showed statistically significant difference.

Table 3: This table shows the odds ratios of studied variables for predicting ICU mortality.

Secondary outcomes

APACHE II, SOFA, and SAPS II scores were higher in non-survivor patients than survivors. Also hospital stay and GCS were lower in non-survivor group and it was statistically significant. There was not any difference in hemoglobin levels between these two groups (Table 2).
There was not any correlation between RDW and APACHE II, SOFA, SAPS II scores. (p=0.184, 0.054, 0.140 respectively) Last day RDW and hemoglobin level correlation was not statistically significant. (p=0.069) Higher APACHE II, SOFA, and SAPS II scores were associated with higher mortality but not for RDW (Table 3).

**Discussion**

Current study showed that, last day RDW levels have a positive correlation with mortality but initial RDW has not a value in mortality prediction of ICU patients.

Many methods were used to predict mortality in ICUs for last three decades(19-21). RDW has been studied as an emerging mortality predictor in recent literature. These studies showed conflicting results.

Bazick et al.(22) reported that RDW was a strong and independent indicator of mortality prediction in a study with larger than 50000 participants. In a retrospective study, it was shown that initial RDW value could be used as an independent variable in the prediction of in-hospital mortality beyond corrected APACHE II score according to age, mechanical ventilator, sepsis and hospital admission type in ICU patients(16). In a 17922-patient multi-centered study, Hunziker et al. found that RDW enhanced the prognostic value of SAPS score(23). However, in a single centered 602 patient study, Wang et al.(15) showed that RDW was not an independent indicator in mortality prediction but could be used in prediction of hospital stay time. To our findings, however, last day RDW values showed a positive correlation with mortality, RDW has not a value in mortality prediction of adult ICU patients.

In their study about mortality prediction of ICU patients, Wang et al. reported that RDW has a sensitivity of 51.2%, specificity of 74.7% and AUC of 0.672(15). In another study that was conducted for 28-day mortality prediction of septic patients the AUC was 0.678 (95% CI, 0.631-0.724) for RDW. This study also showed that, patients with RDW value between 14.1-15.7 % has 1.66-fold greater mortality risk than the ones whose RDW value is below 14.0%. This mortality risk increase was 2.57-fold greater for the RDW value more than 15.8%. Our findings seem to be consistent with literature and have not any promising value of RDW in mortality prediction.

In predicting mortality risk, while APACHE II was having the greatest odds ratio (23.11), SAPS and SOFA had the same value (8.25) in terms of median values were taken as upper limit. Odds ratio of RDW (2.67) was lower in case of the cut-off value was taken as upper limit. Wang et al. (15) reported odds ratio 1.78 for RDW and 4.2 for APACHE II. This discordance may result from the difference of the cut-off values.

**Limitations**

Primary limitation of this retrospective study is the small number of cases and limitations in standardization. Some cases were not included because of missing data. Patients could not be assessed for B12 and iron deficiency as a factor for high RDW values. Mental status changes of patients, different hospitalization reasons, comorbidities, continuous medications, very different therapies and/or invasive procedures were the main reasons of inadequate standardization. Limited study population restricts to generalization of these results to population but larger studies seem to be needed. Because of this study did not targeted primary to re-hospitalization or mortality patients were not followed for mortality after discharge or re-hospitalization.

**Conclusion**

The study showed that the value of RDW in predicting mortality is limited to final day of the patients during ICU stay. RDW has not an additional value to current scoring systems. **

**References**


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