The red cell distribution width prognostic significance in critical illness

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Abstract

RDW (red cell distribution width) has been reported to been associated with the prognosis of critically ill patients. However, RDW is often overlooked by clinicians in treating patients in an emergency. The objective of this review is to explore the prognostic value of RDW in different diseases in emergencies.

KeyWords:RDW, Prognosis, Review.

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Introduction.

The red cell distribution width (RDW) is a parameter for measuring variability in red blood cell size. **(1)** In critically sick patients with AKI, it was found that higher RDW was linked to an increased risk of hospital death and 30-day all-cause mortality. In addition, the high RDW was linked to an increase in mortality after controlling for factors such age, gender, albumin, haemoglobin, liver disease, renalillness, malignancy, bilirubin, WBC, BUN, APS III, SOFA, SIRS, RRT, temperature, and Elixhauser. The findings of investigation also suggested that RDW was an independent predictor of mortality in patients with AKI. Several studies have previously shown that RDW was independently related with a variety of poor outcomes (**2).**

Red Blood Cell Distribution Width as a Predictor of Stroke Occurrence and Outcome

On the basis of earlier investigations, it is known that RDW is closely related to inflammatory responses and that inflammationhas a significant impact on the development of stroke**(3)**. Increased RDW may be able to predict the incidence of stroke, according to a growing body of research about the relationship between RDW and stroke. Furthermore, a high baseline RDW level is linked to a poor outcome in stroke patients**(4).**

RDW value is influenced by demographic characteristics, such as age, gender, and race, according to recent studies. While the link between gender and RDW is still debatable, studies on healthy controls have shown that RDW increases gradually with age. According to some research, women have a somewhat higher RDW than men do, but other studies show no discernible gender-based variation in RDW values. The link between RDW and stroke is weaker in blacks than it is in whites, according to studies examining the effects of race. In this study, the results were stratified based on demographic variables using subgroup analysis. The findings showed that, regardless of age, gender, or race, higher RDW could predict the

likelihood of strokes and a poor prognosis for survival (**5).**

Both continuous and categorical (quartiles) baseline RDW factors were analyzed. For cutoff values, which ranged from 13.8 to 18.1%, the fourth quartile was frequently utilized. The pooled OR/RR of trials that used a ROC analysis to determine cutoffs, however, was more negative and the heterogeneity was lower. Additionally, combined OR/RR and 95% confidence intervals were more likely to be less when RDW was evaluated as a continuous variable. 14.6% has been set as the cutoff value. in the past, routinely used to treat anaemia**(6).** According to this study, the majority of research used cutoffs below 15%, which were associated with worse clinical results. After performing a sensitivity analysis, these results were still significant. As a result, future research may undertake individual ROC analyses, experimentally utilise 15% as a threshold number, or take stroke patients' RDW into account as a continuous variable (**7**).

It's important to note some restrictions. First, RDW can be used in conjunction with other haematological parameters to systematically and broadly reflect the inflammatory and thrombotic state. These parameters include neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and platelet distribution width (PDW). Second, there is still debate about whether calculating RDW within a specific time frame following a stroke or using an original RDW number at a specific time point would be a superior way to forecast prognosis.and (**8).**Third, no study has examined the function of RDW in foretelling the recurrence of a stroke. To further understand the relationship between RDW and stroke recurrence, long-term follow-up is advised. Because the included studies used different populations, sample times, and procedures to determine the cutoff value of RDW, there was a slight degree of variation among them(**9).**

Association Between Red Cell Distribution Width and Hospital Mortality in Patients with cardiovascular diseases

In numerous observational studies, increased red cell distribution width (RDW) has been linked to a worse prognosis in patients with heart failure (HF) and coronary heart disease (CHD)**(10).**

Red blood cell distribution width as a predictor of atrial fibrillation

According to recent research, an increased risk of developing atrial fibrillation (AF) may be linked to a greater red blood cell distribution width (RDW). We performed a thorough meta-analysis and a systematic review of the recent literature to assess the relationship between RDW and the onset of AF in light of certain contentious findings(**11).**

The term "red blood cell distribution width" (RDW) refers to a numerical indicator of the degree of size variability among circulating red blood cells. RDW is frequently included in complete blood count (CBC) examinations and is practical for usage in clinical settings. Higher RDW levels have been linked in the past to increased morbidity and death, according to research(12).

Unknown processes underlie the association between high RDW levels and suboptimal clinical results in cardiovascular illnesses.First, current research suggests that elevated RDW levels may be an indicator of an inflammatory state.It is true that the release of pro-inflammatory cytokines can inhibit erythropoietin-induced red cell maturation, and that more immature red cells can result in higher levels of RDW.Second, it was suggested that an expansion of erythrocyte life duration with a decrease in MCV and an increase in RDW would be a key response to disease.

Another explanation would be that aged erythrocytes, which are smaller and have a higher RDW due to their long-term circulation, have degraded enzyme systems and lost some of their anti-oxidative capabilities(**13).**

Additionally, it has been proposed that high RDW is not only a standalone predictor of AF incidence but also a standalone predictor of long-term unfavourable clinical outcomes in AF patients. According to **Kurt et al.**, RDW values were an independent predictor of a high CHA2DS2-VASc score and substantially linked with CHA2DS2-VASc score in nonanemic patients with AF. Furthermore, a research that included 567 individuals with paroxysmal AF found that RDW was a significant predictor for new-onset stroke after a median follow-up of 4.8 years(**14).**

Prognostic Value of Red Cell Distribution Width in Patients With Pulmonary Embolism

The goal of the current investigation is to determine clinically the prognostic significance of RDW in PE patients. The study's key finding is that rising RDW levels have the potential to be a reliable independent predictor of higher mortality in PE patients. RDW remained a reliable predictor of death in the current study even after accounting for other characteristics such as haemoglobin concentration. According to a recent study, patients with PE who were anaemic died at higher rates than PE patients with normal haemoglobin levels.Nevertheless, a meta-analysis,(**15) .**

RDW has been demonstrated to have a stronger correlation with mortality in older persons who are not anaemic than in those who are. In the current investigation, there was no discernible difference in PE mortality between individuals with and without anaemia. Haemoglobin concentrations cannot be the direct cause of pulmonary embolism death since pulmonary embolism is an acute illness process. However, the greater risk of bleeding among anaemic patients may be related to their higher mortality risk. Additionally, in PE, haemoglobin levels are typically linked to underlying illness. Therefore, rather than the haemoglobin level, it may be claimed that the mortality of PE is actually connected to these associated comorbidities. We discovered a strong correlation between RDW and death in the hospital, in contrast to Hb levels. Although the exact function of inflammation in PE is still unknown, a meta-analysis has revealed that the pathophysiology of VTE was influenced by inflammatory markers such interleukin 6 (IL-6), IL-8, and monocyte chemotactic protein.In individuals with PE, there was a strong correlation between CRP and right ventricular dysfunction.Interestingly, a randomised trial known as the JUPITER research has revealed that statins reduce the risk of VTE(**16)**.

Actually, it was reported in this study that this risk-lowering effect of statin treatment in patients with PE is not only related to its anticoagulant effect but also related to its antiinflammatory effect. In a previous study, it was found that there was a significant correlation between inflammatory cytokines (eg, IL-6) and RDW in idiopathic pulmonary hypertension. In the study significant correlations was found between CRP and RDW in patients with PE. Therefore, our data suggest the hypothesis that high RDW levels may reflect a variety of pathologic processes, such as inflammatory stress and may be potentially attributed to the poor outcomes in patients with PE.

The present study showed 364 (52%) patients with PE had high sPESI score. The RDW values were higher in those patients with higher sPESI score than the patients with lower sPESI score that was statistically significant. Venetz et al found that negative predictive value of sPESI score was 97%(**17).**

According to the current study, RDW has a 93% negative predictive value. The sPESI score, on the other hand, is based on a number of factors, including age >80 years, a history of cancer, a history of chronic cardiopulmonary disease (HF or pulmonary disease), a heart rate 110 bpm, a systolic blood pressure of 90 to 100 mm Hg, and an arterial oxyhemoglobin saturation of less than 90% as determined at the time of PE diagnosis. These PE patients may be categorised as high risk if even one criterion (such as age >80) is variable. In contrast, RDW is a straightforward, single parameter that is simple to use and was found to function similarly to sPESI score in the current investigation. Similar to this, our study's serum levels of RDW 15% exhibit significant negative predictive values (93%) for all causes of mortality (**18).**

Red Cell Distribution Width and Outcome in Patients With Septic Shock

This study demonstrates a significant graded independent association between RDW and hospital and ICU mortality in septic shock patients. Even after taking into account other variables, this link is still important. Additional research revealed that RDW accurately predicted mortality in persons over 44 with chronic lung illnesses, cancer, and cardiovascular disease.acute heart failure, acute stroke, symptomatic persistent congestive heart failure, and recently in critically ill patients in general (**19).**

This is the first study to demonstrate the strong link between RDW and death in septic shock patients. Multiple processes by which inflammation, such as that present in sepsis, can affect erythropoesis. Inhibiting erythrocyte maturation by inflammatory cytokines results in the release of immature RBCs into the circulation, which raises RDW.Additionally, inflammation can directly suppress erythroid precursors in the bone marrow, limit the formation of erythropoietin, create resistance to erythropoietin, reduce iron bioavailability, and trigger apoptosis and peripheral phagocytosis in red blood cells(**20).**

The retrospective nature of our study and the small number of patients are its principal limitations. We did not have access to longer-term outcomes, therefore our survival analyses made the assumption that patients who were discharged from the hospital alive would still be alive at subsequent time points. Our key outcome measures were hospital mortality and ICU mortality. This study also has a number of advantages. The use of mortality as an objective end point and the PI database, which has acceptable internal validity, are the study's strong points. In contrast to surrogate end points like length of stay (LOS), our study's primary endpoint is mortality (hospital and ICU), which is objective and has a far higher clinical importance (**2).**

This study demonstrates a very substantial correlation between RDW on the first day of septic shock and the likelihood of hospital and ICU mortality. The presence of proinflammatory cytokines and oxidative stress in septic shock is likely reflected by elevated RDW. The RDW is a cheap and widely used measurement used in complete blood counts. For predicting mortality, the RDW performed better than APACHE II and SOFA. RDW and APACHE II together were a better predictor of death than either one separately. Future research on the effects of combining RDW with other recognized outcome prediction scores (such APACHE II) and markers of inflammation and mortality in patients with septic shock is supported by the findings of this study. Additional study is required to understand the mechanisms underlying RDW-mortality (**2)**

HEART FAILURE

RDW has received a lot of attention in this area over the past 10 years. Appropriate and early risk classification of patients with congestive heart failure (CHF) is essential for their targeted therapy.

For the first time, RDW was shown to have a protective role in CHF patients by (**22**) They also came to the conclusion that an elevated RDW value was a reliable independent predictor of death and morbidity in these patients. The findings of a different study conducted in 2015 showed that individuals with CHF may have a longer hospital stay if their RDW values were greater at admission. RDW may serve as a marker for hospital mortality, according to Liu et al., however it performs less predictably than NT-pro BNP.Therefore, it appears that the use of RDW in conjunction with verified cardiac indicators**(23).**

MYOCARDIAL INFARCTION

Higher levels of RDW may be linked to unfavourable outcomes in myocardial infarction (MI) patients, according to recent research. The first investigation in this area was carried out by Tonelli et al., who came to the conclusion that patients with a higher RDW value had an increased risk of all-cause mortality in patients with coronary artery disease (**24**) and a completely adjusted hazard ratio for the occurrence of MI.A different study separated 329 patients with ST-elevation MI (STEMI) into two groups: high and low RDW. In individuals with a greater value of RDW, the cumulative incidence of all-cause mortality was considerably higher, according to a multivariate comparison between two groups.Recent research shows that a cutoff value of higher than 13.9 can predict the development(**25)**.

CEREBROVASCULAR ACCIDENT

25.992 people were examined for their relationship between RDW and cerebrovascular accident (CVA). This study found no evidence that RDW was linked to a higher risk of death within a year of an incident stroke or throughout the whole follow-up period (**25)** Without taking into account anaemia or the conventional atherosclerotic risk factors, red cell distribution width was linked to incident stroke in the general population. RDW was a powerful predictor of mortality and the risk of ischemic stroke, although more studies were required to assess and corroborate the correlation suggested.Furthermore, throughout the course of a 9-year period, assessed patients who had undergone IV thrombolysis for acute anterior circulation ischemic stroke. RDW may be based on their findings **(25, 26)**.

Association between red blood cell distribution width and mortality in diabetic ketoacidosis

The study's key conclusion was that RDW was independently correlated with all-cause mortality in DKA patients at 90 and 365 days after ICU admission. After correcting for age, gender, ethnicity, APSIII, SIRS, CHF, stroke, ARDS, SBP, MCV, MHC, and MCHC, the link was still statistically significant. Although earlier research has demonstrated that RDW is independently linked to a number of unfavourable outcomes, our investigation found that RDW was a standalone predictor of mortality in critically sick DKA patients(**26)**.

Elevated RDW has been linked in several observational studies to alterations in inflammatory biomarkers.Proinflammatory cytokines prevented erythrocytes from proliferating and maturing.Increased RDW could be a sign of inflammation, which has a detrimental effect on patient survival.greater RDW has also been linked to greater levels of the inflammatory marker C-reactive protein, according to reports. Additionally, it has been proposed that RDW displays the variation in circulating RBC size. The release of reticulocytes into the circulation causes an increase in RDW. The increase in smaller erythrocytes may be due to RBCs shedding more vesicles.Additionally, RDW is a marker for probable metabolic problems and is linked to endothelial function. It is primarily measured by flow-mediated dilation **(27).**

This study's RDW-mortality link may also be influenced by oxidative stress. Increased RDW may be a result of high oxidative stress, which may also enhance the release of large and small premature erythrocytes into the peripheral circulation and lower RBC survival**.** This is because heterogeneous RBCs with low oxygen carrying capacity are released into the peripheral circulation, and hypoxia might harm the local tissue's microcirculation.Immature reticulocytes may release thrombus into the bloodstream as a result of the increased RDW, albeit it is unknown how immature reticulocytes contribute to thrombosis. This connection may also be influenced by the neurohumoral response to arterial underfilling.(**28).**

The primary benefit of this study is that it is the first in-depth analysis of how RDW and mortality in DKA patients in the ICU are related. For patients admitted to the ICU with DKA, RDW appears to be a long-term prognostic indication. RDW is also readily accessible and doesn't cost the patient any extra money. Additionally, there were a lot of patients that took part in our study. We admit that this study has several other drawbacks as well. First off, our study has biases common to retrospective observational studies. Selection bias cannot be disregarded because of this. Second, the study did not look into possible long-term variations in RDW, which might contribute more prognostic data. Third, the groups had different numbers of cancer patients. **(29)**.

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