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Original Article

Study of Red Cell Distribution Width in Heart Failure Patients

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Abstract

Introduction: Red cell distribution width (RDW) is a measurement of size variability of the red blood cells and has been shown to be a powerful predictor of prognosis in heart failure (HF) in the recent years. We sought to investigate the prognostic value and longitudinal pattern of RDW in patients with concomitant HF.

Aims: This study aims to study the relationship between RDW and HF assessed by echocardiography.

Materials and Methods: This is a prospective study was done on 50 patients with clinical diagnosis of HF. HF patients both with preserved and reduced ejection fraction (EF) were included in the study. RDW was measured with the use of an analyzer on the day of admission, ECG, ECHO, and chest X-ray were done and EF was calculated. HF was classified according to NYHA classification.

Results: Fifty patients with HF were studied and advancing age and male gender had increased association with HF. The mean RDW was 52.1 and ischemic heart disease was the most common cause of HF. Mean RDW in patients with EF < 54 was 55.68 with a SD of 6.1.

Conclusion: The study emphasizes that RDW can be used as a novel biomarker in HF at a low cost. Elevated RDW is associated with advanced stage of heart disease and correlates well with echocardiography findings in HF patients with reduced EF.

Key words: Anisocytosis, Echocardiography, Ejection fraction, Heart failure, Red cell distribution width

INTRODUCTION

Red cell distribution width (RDW) is the measure of variation in the size of erythrocytes and differentiates iron deficiency anemia from thalassemia trait. It is a simple, rapid, inexpensive, and straightforward hematological parameter that reflects the degree of anisocytosis *in vivo*. An increased RDW usually correlates to iron deficiency anemia.[1,2] RDW has been recently discovered as a new marker in cardiac failure. There are studies about the association of anemia and cardiovascular outcome in patients and the findings state that an increased RDW is associated with increased morbidity and mortality in chronic heart failure (HF) patients.[3] Scientific evidence suggests that RDW assessment also predicts the risk of adverse outcomes like hospitalization for acute decompensation or worsened left ventricular function in acute and chronic HF patients and is also a significant predictor of developing HF in otherwise normal individuals. There is no definite pathophysiology explaining this association and factors such as inflammation, nutritional deficiencies, and inadequate production of erythropoietin may be responsible.[4,5]

HF is a complex clinical syndrome, characterized by dyspnea and fatigue, impaired exercise tolerance, fluid retention, pulmonary and/or splanchnic congestion, ankle swelling, peripheral edema, elevated jugular venous pressure, and pulmonary crackles.[6,7] Several cardiac biomarkers including brain natriuretic peptide, N-terminal pro-BNP, and cardiac troponins have been identified as predictors of severity of HF. RDW has been studied in

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routine complete blood count in all patients admitted with the diagnosis of HF in the recent years.[8,9]

The biological interplay between impaired hematopoiesis and cardiac dysfunction may be present in HF patients and an increased RDW contributes to the worsening of HF. Overall, the longitudinal assessment of RDW changes overtime may be an efficient measure to predict the risk of development and progression of HF. In this study, we sought to investigate the prognostic value and longitudinal pattern of RDW in patients with concomitant HF.

Aims

This study aims to establish the relationship between RDW and HF assessed by echocardiography.

MATERIALS AND METHODS

This is a prospective randomized study done on 50 patients with clinical diagnosis of HF. The study was approved by the local ethics committee and informed consent was obtained from all patients before the start of the study. HF patients both with preserved and reduced ejection fraction (EF) were included in the study. Patients with liver disease, renal disease, anemia with hemoglobin <12 g/dl, hematological malignancy, or who had blood transfusion within the past 3 months were excluded from the study. For all patients, complete blood count with RDW was measured with the use of an analyzer on the day of admission. ECG, ECHO, and Chest X-ray were also done. The patients were classified according to NYHA functional classes of HF as follows:

Class I: No symptoms and no limitation in ordinary physical activity, for example, shortness of breath when walking, climbing stairs, etc.

Class II: Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity.

Class III: Marked limitation in activity due to symptoms, even during less than ordinary activity, for example, walking short distances (20–100 m). Comfortable only at rest.

Class IV: Severe limitations. Experiences symptoms even while at rest. Mostly bedbound patients.

EF was calculated using the formula EF= (SV/EDV)* 100, where SV = Stroke volume and EDV = End-diastolic volume.

RESULTS

Of the 50 study patients, majority of the study patients (22) were of the age group 51–60 years and 6 patients were above 61 years of age. About 64% of the patients were male and 34% were female. Incidence of HF is more with increasing age and male gender, Figures 1 and 2. The etiology of HF is depicted in Figure 3. The most common cause is ischemic heart disease (46%) followed by rheumatic heart disease (16%). Other causes of HF according to our study were cor pulmonale (12%), DCM idiopathic (10%), and two cases of calcific AS/AR and RVD (4%), and one case each of alcoholic cardiomyopathy, peripartum, Eisenmenger, and myocarditis (2%). HTN, DM, dyslipidemia, smoking, alcohol, and obesity were the

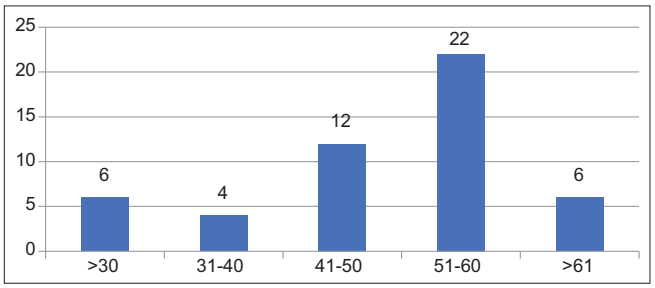

Figure 1: Age distribution

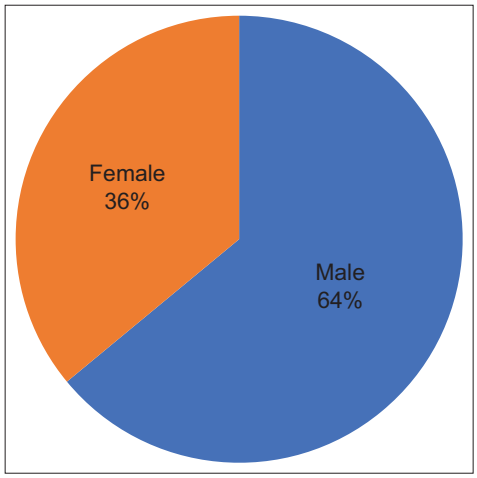

Figure 2: Gender distribution

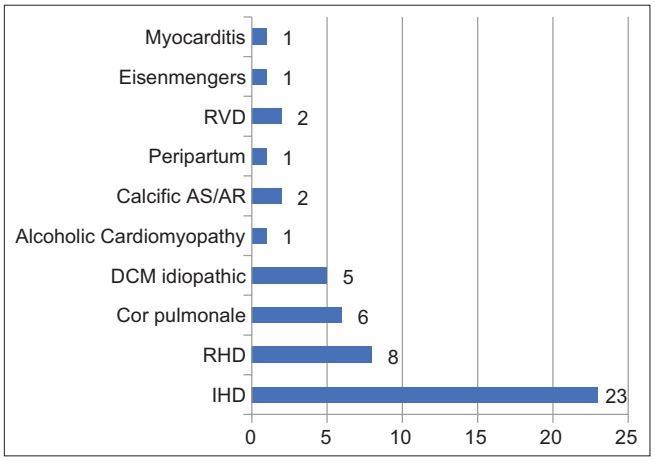

Figure 3: Etiology of heart disease

risk factors of HF as observed from our study, Figure 4. According to NYHA classification, 60% of the patients fell under Class III and 18% fell under Class IV. About 16% belonged to Class II and 6% fell under Class I classification, Figure 5. The mean RDW of each class of patients is shown in Figure 6. An increased mean RDW was observed in Class III (50.24 fL) and Class IV (62.48 fL) patients with a SD of 3.16 and 4.24, respectively (normal reference range of RDW – 39–46 fL). The total mean RDW is 52.1 with a SD of 5.14. A low EF < 54 was noticed in 66% of the patients, Figure 7. The mean RDW in patients with EF < 54 is 55.68 with a SD of 6.1, Figure 8. The findings indicate that an increased RDW is associated with low EF and high risk of HF.

DISCUSSION

Although a wide variety of biological markers have been used for morbidity and mortality prediction in patients with HF, many of them are still used only for research and not for clinical use. RDW, which is the variation in the size of erythrocytes, has been investigated as a new marker in cardiac diseases in the recent years. It can be done as a part of routine blood investigation and can reveal a lot about an underlying heart disease.[10] Conditions like impaired hematopoiesis can lead to a size heterogeneity of RBC volumes and play a role in the physiopathological interplay between anisocytosis and HF. Evidence states that both cell- and cytokine-mediated inflammatory pathways actively contribute to the development and progression of HF.[11] Inflammation is frequently associated with bone marrow dysfunction which can cause an increased production of circulating premature erythrocytes. Oxidative stress can also lead to deranged hematopoiesis by an excess reactive oxygen species production, all of which result in anisocytosis and alteration in RDW.[12,13] Impaired renal function in the elderly also can to anisocytosis and is an important determinant of adverse outcomes in patients with HF.

According to our study, advancing age and male sex are strong contributing factors for cardiac dysfunction. This finding is similar to the study findings of Lippi and Vigen who also demonstrated in their study about the association of advancing age and HF.[14] The reason for anisocytosis

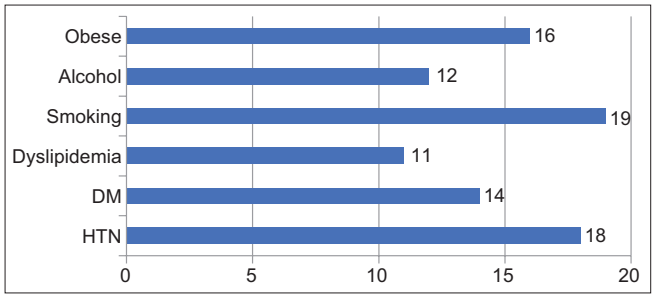

Figure 4: Distribution of risk factors

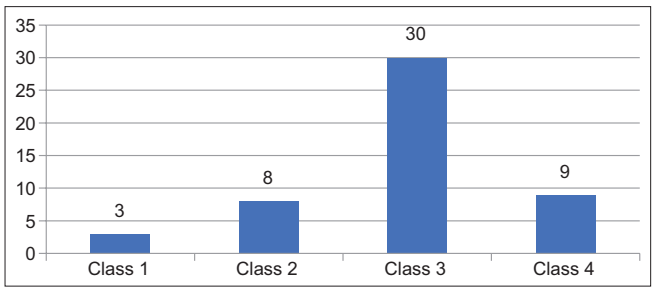

Figure 5: NYHA classification of heart disease

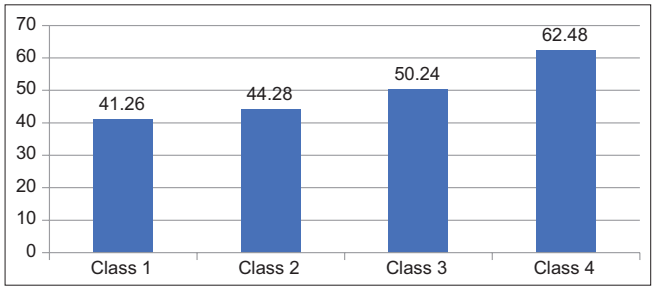

Figure 6: Mean red cell distribution width according to NYHA classification

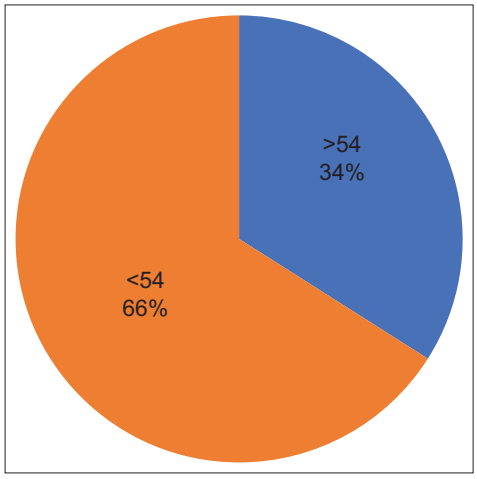

Figure 7: Percentage of ejection fraction

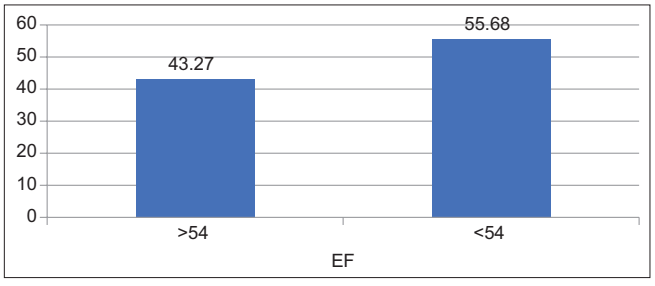

Figure 8: Elevated red cell distribution width is associated with low ejection fraction

with advancing age can be the result of multiple metabolic dysfunctions. All these conditions explain why RDW is a reliable marker of cardiac dysfunction. Anisocytosis may also play a direct role in the onset and progressive worsening of HF. The erythrocyte size heterogeneity signifies a reduced and severely impaired function of the essential corpuscular blood elements. RBCs are often characterized by lower deformability and decreased oxygen carrier capacity in conditions of high anisocytosis, contributing to reduced oxygenation of many peripheral tissues and cells (including cardiomyocytes), while abnormal erythrocytes may also actively participate in the pathogenesis of cardiac fibrosis through promotion or amplification of inflammation, cardiomyocyte stress, and apoptosis.[15]

In our study, an increased mean RDW of 50.24 and 62.48 was observed in Class III and Class IV HF patients, which indicates that altered RDW is a feature of advanced heart disease. Xanthopoulos *et al.* studied 218 patients who were admitted to the emergency department for acute HF and observed 1% increase in RDW up to 12 months after hospitalization.[16] A low EF usually signifies a LV dysfunction, cardiomyopathy, valvular defects, or cardiac muscle failure. In our study, a low EF of <54 was observed in 66% of the patients. Eroglu *et al.* in his study demonstrated that RDW was increased in patients with low EF.[17] The mean RDW of patients with EF < 54 was 55.68 in our study which indicates clearly that RDW can be a strong predictor of HF and a measure of prognostic outcome.

The limitation of this study is the small sample size and failure to assess RDW on a timely interval during the follow-up period.

CONCLUSION

RDW is reported as a component of the standard complete blood count and is significantly correlated with echo parameters for evaluation of HF. Elevated RDW is associated with advanced stage of heart disease and correlates well with echocardiography findings in HF patients with reduced EF. The study emphasizes that RDW can be used as a novel biomarker in HF. This simple test can be used as a marker of HF in the emergency room at a low cost. Further studies should be prompted for evaluating the association between RWD and outcomes of cardiac failure to improve understanding of the pathophysiology of HF. The degree of anisocytosis could also be used as an additional marker to identify these high-risk patients and improve treatment strategies in future.

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