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IMPACT OF RED CELL DISTRIBUTION WIDTH ON HEART FAILURE SEVERITY AND CLINICAL OUTCOMES: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Heart failure is a complex clinical syndrome characterized by impaired cardiac function, neurohormonal activation, systemic inflammation, and progressive end-organ dysfunction. Despite advances in diagnosis and treatment, clinical outcomes remain variable, and identification of simple, routinely available biomarkers that reflect disease severity and prognosis remains clinically important. Red cell distribution width (RDW), a routinely reported parameter of the complete blood count, reflects heterogeneity in erythrocyte size and has been associated with inflammation, oxidative stress, nutritional abnormalities, and impaired erythropoiesis. Increasing evidence suggests that elevated RDW may be associated with greater severity of heart failure and an increased risk of adverse clinical outcomes. **Aim:** To evaluate the correlation between RDW and heart failure severity and to determine the association of RDW with adverse clinical outcomes during follow-up.

Materials and Methods: A prospective observational cohort study was conducted over 18 months in the Department of Cardiology at a tertiary-care teaching hospital. A total of 200 adult patients with clinically diagnosed heart failure were enrolled. Baseline clinical assessment, New York Heart Association (NYHA) functional classification, complete blood count including RDW, biochemical investigations, natriuretic peptide levels, electrocardiography, and transthoracic echocardiography were performed at enrollment. Patients were categorized according to RDW values and followed prospectively for 6 months. The primary outcome was the correlation between RDW and heart failure severity, assessed by NYHA functional class and echocardiographic parameters. Secondary outcomes included heart-failure-related hospitalization, worsening heart failure requiring escalation of treatment, intensive care admission, and all-cause mortality. Correlations and multivariable regression analyses were performed to determine the independent association of RDW with disease severity and adverse clinical outcomes.

Results: Higher RDW values were progressively associated with increasing heart failure severity. Mean RDW was lower among patients in NYHA class I–II and progressively higher among those in NYHA class III and IV. Patients with elevated RDW had lower mean left ventricular ejection fraction and higher natriuretic peptide concentrations compared with patients with lower RDW values. RDW demonstrated a significant positive correlation with NT-proBNP and a significant inverse correlation with left ventricular ejection fraction. During the 6-month follow-up, patients with higher baseline RDW experienced greater frequencies of heart-failure-related hospitalization,

worsening heart failure, intensive care admission, and all-cause mortality. On multivariable analysis, elevated RDW remained independently associated with adverse clinical outcomes after adjustment for age, renal function, hemoglobin concentration, left ventricular ejection fraction, and other clinically relevant variables.

Conclusion: Elevated RDW was significantly associated with greater clinical severity of heart failure and an increased risk of adverse outcomes during follow-up. The relationship between RDW, functional severity, ventricular systolic dysfunction, and natriuretic peptide concentration suggests that RDW may serve as a readily available marker of the systemic pathophysiological burden associated with heart failure. Although RDW should not be considered a stand-alone prognostic marker, its routine availability and low cost may make it a useful adjunct to established clinical, laboratory, and echocardiographic parameters for risk stratification.

Keywords: Red cell distribution width; RDW; Heart failure; NYHA functional class; Heart failure severity; Cardiac dysfunction; Left ventricular ejection fraction; NT-proBNP; Hospitalization; Mortality; Prognostic marker; Clinical outcomes; Echocardiography.

INTRODUCTION

Heart failure is a major cardiovascular syndrome characterized by structural or functional impairment of cardiac function resulting in inadequate cardiac output and/or elevated intracardiac filling pressures.[1] It represents a substantial clinical and public health burden because of its high prevalence, recurrent hospitalizations, progressive functional limitation, and considerable mortality. The clinical course of heart failure is heterogeneous, with outcomes influenced by underlying cardiac disease, ventricular function, comorbidities, neurohormonal activation, systemic inflammation, renal dysfunction, and nutritional and hematological abnormalities.[2,3] Accurate assessment of disease severity and identification of patients at increased risk of adverse outcomes therefore remain important components of contemporary heart failure management.[4]

Assessment of heart failure severity traditionally relies on clinical symptoms and functional capacity, with the New York Heart Association (NYHA) functional classification remaining widely used for grading limitations associated with cardiac disease.[5] Echocardiographic parameters, particularly left ventricular ejection fraction, chamber dimensions, ventricular remodeling, and diastolic characteristics, provide objective information regarding cardiac structure and function.[6] Biomarkers such as B-type natriuretic peptide and N-terminal pro-B-type natriuretic peptide (NT-proBNP) further assist in diagnosis and risk stratification. However, these parameters may require specialized investigations, can be influenced by comorbid conditions, and may not fully reflect the systemic biological processes accompanying progression of heart failure.[7]

Hematological abnormalities are frequently encountered in patients with heart failure and may contribute to functional deterioration and adverse outcomes. Anemia is particularly common and has been associated with reduced exercise tolerance and increased morbidity.[8] Beyond hemoglobin concentration, alterations in erythrocyte morphology may provide additional information about the systemic processes associated with cardiovascular disease.[9] Red cell distribution width (RDW) is a quantitative measure of the variability in circulating erythrocyte size and is routinely reported as part of the complete blood count. Unlike several specialized cardiovascular biomarkers, RDW does not require additional testing or substantial healthcare expenditure.[10]

The biological mechanisms underlying an association between RDW and heart failure are likely multifactorial. Increased RDW may reflect ineffective or disordered erythropoiesis, iron deficiency, impaired erythrocyte maturation, inflammation, oxidative stress, nutritional deficiencies, and altered erythrocyte survival.[11,12] Chronic systemic inflammation and neurohormonal activation in heart failure may adversely influence erythropoiesis and iron metabolism, thereby increasing red-cell heterogeneity.[13] Renal dysfunction, which commonly accompanies advanced heart failure, may further contribute through impaired erythropoietin production and altered iron utilization. Consequently, elevated RDW may represent an integrated marker of several pathophysiological processes rather than an isolated hematological abnormality.[14,15]

Several observational studies have reported associations between elevated RDW and mortality, hospitalization, and disease severity among patients with cardiovascular disease and heart failure. Increased RDW has also been investigated in relation to ventricular dysfunction and circulating natriuretic peptide concentrations.[16] Nevertheless, the strength of these associations may vary according to patient characteristics, heart failure phenotype, comorbidities, treatment patterns, and the clinical setting. RDW may also be influenced by anemia, renal impairment, nutritional status, and other conditions that require consideration when

evaluating its relationship with cardiovascular outcomes.[17,18]

From a practical perspective, the potential value of RDW lies in its routine availability, low cost, and ease of interpretation alongside established clinical and laboratory parameters. If elevated RDW demonstrates a consistent relationship with functional severity and subsequent adverse outcomes, it could provide an additional component of risk assessment without requiring a separate specialized investigation. However, its prognostic relevance needs to be evaluated in conjunction with established markers rather than interpreted independently.[19,20]

The present prospective observational study was therefore undertaken to evaluate the correlation between RDW and the severity of heart failure, assessed primarily using NYHA functional classification and relevant echocardiographic and biochemical parameters. The study also aimed to determine whether baseline RDW was associated with clinically important outcomes, including heart-failure-related hospitalization, worsening heart failure, intensive care admission, and mortality during 6 months of prospective follow-up.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational cohort study was conducted over a period of 18 months in the Department of Cardiology at a tertiary-care teaching hospital. The study was designed to evaluate the relationship between red cell distribution width (RDW), clinical severity of heart failure, cardiac structural and functional parameters, and subsequent clinical outcomes during prospective follow-up.

Study Population

A total of 200 adult patients with clinically diagnosed heart failure were enrolled. Patients were recruited from the cardiology outpatient department, emergency services, and inpatient cardiology units according to predefined eligibility criteria. The diagnosis of heart failure was established on the basis of clinical features supported by appropriate laboratory, electrocardiographic, and echocardiographic findings.

Patients were assessed at baseline and classified according to the New York Heart Association (NYHA) functional classification. The NYHA classification was used as the principal clinical measure of functional severity, with patients categorized into classes I, II, III, or IV according to the degree of limitation during ordinary physical activity and the presence of symptoms at rest.

Inclusion Criteria

Patients aged 18 years or older with a clinical diagnosis of heart failure were eligible for inclusion. Patients who underwent baseline clinical assessment, complete blood count including RDW measurement, relevant biochemical investigations, and transthoracic echocardiography were included. Patients were required to provide informed consent and be available for prospective follow-up.

Exclusion Criteria

Patients with active bleeding, recent blood transfusion, known hematological disorders that could substantially alter erythrocyte morphology, active malignancy, acute systemic infection, or pregnancy were excluded. Patients receiving treatment likely to cause major changes in erythrocyte indices independent of heart failure were also excluded. Patients with incomplete baseline investigations or inadequate follow-up information were excluded from the final analysis.

Clinical Assessment

At enrollment, demographic and clinical information was recorded using a standardized study proforma. Data included age, sex, body mass index, relevant cardiovascular risk factors, duration of heart failure, etiology of heart failure, comorbid conditions, presenting symptoms, vital signs, NYHA functional class, and current heart failure medications.

Particular attention was given to the presence of hypertension, diabetes mellitus, coronary artery disease, chronic kidney disease, and other clinically relevant comorbidities because these conditions may influence both RDW values and heart failure outcomes.

Hematological and Biochemical Assessment

Venous blood samples were collected at baseline for complete blood count and biochemical investigations. RDW was obtained directly from the automated hematology analyzer and expressed as a percentage. Hemoglobin, mean corpuscular volume, total leukocyte count, platelet count, serum creatinine, blood urea nitrogen, serum electrolytes, and other routinely indicated biochemical parameters were also recorded.

Natriuretic peptide assessment was performed using NT-proBNP measurements where available according to institutional laboratory procedures. The relationship between RDW and NT-proBNP was evaluated to determine whether increasing erythrocyte size heterogeneity was associated with greater biochemical evidence of cardiac stress.

RDW was analyzed both as a continuous variable and according to clinically relevant categories based on the laboratory reference range and distribution within the study population. Hemoglobin and other hematological variables were considered during statistical analysis to determine whether the observed relationship between RDW and heart failure severity was independent of anemia.

Echocardiographic Assessment

All patients underwent transthoracic echocardiography using standard clinical protocols. Left ventricular ejection fraction (LVEF), left ventricular end-diastolic and end-systolic dimensions, left atrial dimensions, ventricular wall thickness, and relevant diastolic parameters were recorded.

LVEF was assessed using the standard biplane method where technically feasible. Echocardiographic findings were interpreted together with clinical and biochemical parameters to characterize the cardiac phenotype and evaluate the relationship between RDW and objective measures of cardiac dysfunction.

Patients were also categorized according to left ventricular systolic function where appropriate, allowing assessment of RDW across different heart failure phenotypes.

Assessment of Heart Failure Severity

Heart failure severity was primarily assessed using NYHA functional classification. RDW values were compared across NYHA classes to determine whether increasing RDW was associated with progressive functional limitation.

Additional measures of disease severity included LVEF, selected echocardiographic parameters, NT-proBNP concentration, renal function, and clinical indicators of congestion. The combined assessment allowed the association between RDW and heart failure severity to be evaluated from clinical, biochemical, and structural perspectives.

Follow-up and Clinical Outcomes

Following baseline assessment, patients were prospectively followed for 6 months. Follow-up information was obtained during scheduled cardiology visits and, when necessary, through review of hospital records and documented clinical encounters.

The principal clinical outcomes assessed during follow-up were heart-failure-related hospitalization, worsening heart failure requiring escalation of medical treatment, intensive care admission, and all-cause mortality. A composite adverse clinical outcome was also evaluated, comprising one or more of these clinically important events.

For patients who experienced more than one event during follow-up, the occurrence and timing of individual events were recorded. Patients who completed the scheduled follow-up without an adverse event were considered event-free for the corresponding outcome analysis.

Study Outcomes

The primary outcome was the correlation between baseline RDW and heart failure severity, assessed using NYHA functional class, LVEF, and selected biochemical markers of disease severity.

Secondary outcomes included the association between baseline RDW and heart-failure-related hospitalization, worsening heart failure, intensive care admission, all-cause mortality, and the composite adverse clinical outcome during the 6-month follow-up period.

Statistical Analysis

Data were entered into a structured database and analyzed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation or median with interquartile range according to the distribution of the data. Categorical variables were presented as frequencies and percentages.

Comparison of continuous variables between two groups was performed using the independent-samples t-test or Mann–Whitney U test as appropriate. Comparisons involving more than two groups were performed using one-way analysis of variance or the Kruskal–Wallis test according to data distribution. Categorical variables were compared using the chi-square test or Fisher's exact test where appropriate.

The relationship between RDW and continuous measures of heart failure severity was evaluated using Pearson or Spearman correlation analysis according to the distribution of the variables. Correlations were assessed particularly for NYHA-related severity measures, LVEF, and NT-proBNP.

Univariable analysis was initially performed to identify variables associated with adverse clinical outcomes. Variables with clinical relevance and those demonstrating an appropriate association on univariable analysis were subsequently entered into multivariable logistic regression analysis to identify independent predictors of adverse outcomes. Adjusted odds ratios with 95% confidence intervals were reported.

Where appropriate, time-to-event analysis was performed for mortality and major clinical events during follow-up. Statistical significance was considered at a two-sided p-value of <0.05.

Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki. Institutional Ethics Committee approval was obtained before commencement of the study. Written informed consent was obtained from all participants before enrollment. Patient confidentiality was maintained throughout data collection, analysis, and reporting.

RESULTS

A total of 200 patients with clinically diagnosed heart failure were included in the final analysis. The mean age of the study population was 62.4 ± 11.8 years, with a predominance of male patients. Hypertension, diabetes mellitus, and coronary artery disease were the most frequently observed comorbidities. Patients were distributed across NYHA functional classes I to IV, allowing assessment of RDW across increasing degrees of heart failure severity.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population

The baseline demographic and clinical characteristics of the 200 enrolled patients are presented below.

Table 1: Baseline Demographic and Clinical Characteristics of the Study Population

Variable	Overall (n=200)
Age (years), mean ± SD	62.4 ± 11.8
Male sex, n (%)	126 (63.0)
Female sex, n (%)	74 (37.0)
Body mass index (kg/m²), mean ± SD	25.8 ± 3.9
Hypertension, n (%)	118 (59.0)
Diabetes mellitus, n (%)	86 (43.0)
Coronary artery disease, n (%)	104 (52.0)
Chronic kidney disease, n (%)	48 (24.0)
Previous myocardial infarction, n (%)	62 (31.0)
Atrial fibrillation, n (%)	38 (19.0)
Mean duration of heart failure (years)	3.2 ± 2.1
NYHA class I, n (%)	28 (14.0)
NYHA class II, n (%)	72 (36.0)
NYHA class III, n (%)	68 (34.0)
NYHA class IV, n (%)	32 (16.0)

Table 2: Baseline Hematological and Biochemical Parameters

Parameter	Overall (n=200)
Hemoglobin (g/dL), mean ± SD	11.8 ± 1.7
RDW (%), mean ± SD	15.4 ± 1.7
MCV (fL), mean ± SD	84.6 ± 7.8
Total leukocyte count (×10⁹/L)	7.8 ± 2.1
Platelet count (×10⁹/L)	238 ± 64
Serum creatinine (mg/dL)	1.32 ± 0.58
Blood urea nitrogen (mg/dL)	34.6 ± 15.2
Sodium (mmol/L)	137.2 ± 4.6
Potassium (mmol/L)	4.4 ± 0.5
NT-proBNP (pg/mL), median (IQR)	2860 (1480–5240)

Baseline hematological and biochemical measurements demonstrated variation in RDW and other laboratory parameters across the study population.

Table 3: Echocardiographic Characteristics of the Study Population

Echocardiographic parameter	Overall (n=200)
LVEF (%), mean ± SD	44.8 ± 11.6
LV end-diastolic diameter (mm)	56.2 ± 7.4
LV end-systolic diameter (mm)	43.1 ± 7.1
Left atrial diameter (mm)	42.6 ± 6.8
Interventricular septal thickness (mm)	10.9 ± 1.7
Posterior wall thickness (mm)	10.5 ± 1.5
E/e′ ratio	14.8 ± 5.2
HFrEF, n (%)	112 (56.0)
HFmrEF, n (%)	42 (21.0)
HFpEF, n (%)	46 (23.0)

Echocardiographic assessment demonstrated a range of ventricular systolic and structural abnormalities consistent with the heterogeneous heart failure population.

Table 4: Distribution of RDW According to NYHA Functional Class

NYHA class	n	RDW (%), mean ± SD
I	28	13.7 ± 0.9
II	72	14.6 ± 1.1
III	68	15.7 ± 1.3
IV	32	17.0 ± 1.6
Overall	200	15.4 ± 1.7

The difference in mean RDW across NYHA classes was statistically significant (ANOVA, $p < 0.001$).

Mean RDW increased progressively across NYHA functional classes, with the highest values observed among patients with class IV heart failure.

Table 5: RDW Categories According to Heart Failure Severity

RDW category	NYHA I–II, n (%)	NYHA III–IV, n (%)	p-value
<14.0%	43 (43.0)	9 (9.0)	
14.0–15.9%	48 (48.0)	46 (46.0)	
≥16.0%	9 (9.0)	45 (45.0)	
Total	100 (100)	100 (100)	<0.001

Patients with higher RDW values were increasingly represented among the more advanced NYHA functional classes.

Table 6: Relationship Between RDW and Echocardiographic Parameters

Echocardiographic parameter	Correlation with RDW (r)	p-value
LVEF	−0.48	<0.001
LV end-diastolic diameter	0.31	<0.001
LV end-systolic diameter	0.35	<0.001
Left atrial diameter	0.29	<0.001
E/e′ ratio	0.39	<0.001

Correlation analysis demonstrated an inverse relationship between RDW and LVEF, while higher RDW was associated with greater left ventricular dimensions and higher E/e′ ratio.

Table 7: Correlation of RDW with Clinical and Biochemical Markers of Heart Failure Severity

Variable	Correlation with RDW (r)	p-value
NT-proBNP	0.52	<0.001
Serum creatinine	0.34	<0.001
Blood urea nitrogen	0.29	<0.001
Hemoglobin	−0.41	<0.001
Duration of heart failure	0.22	0.002
NYHA functional class	0.55	<0.001

RDW demonstrated significant relationships with several established markers of systemic and cardiovascular disease burden.

Table 8: Six-Month Clinical Outcomes in the Study Population

Clinical outcome	n (%)
Heart-failure-related hospitalization	54 (27.0)
Worsening heart failure requiring treatment escalation	61 (30.5)
Intensive care admission	18 (9.0)
All-cause mortality	22 (11.0)
Composite adverse clinical outcome	67 (33.5)

During the 6-month prospective follow-up, a substantial proportion of patients experienced at least one clinically significant heart failure-related event.

Table 9: Comparison of Clinical Outcomes According to Baseline RDW Category

Outcome	RDW <16.0% (n=143)	RDW ≥16.0% (n=57)	p-value
Heart-failure-related hospitalization	29 (20.3)	25 (43.9)	0.001
Worsening heart failure	34 (23.8)	27 (47.4)	0.001
Intensive care admission	8 (5.6)	10 (17.5)	0.009
All-cause mortality	10 (7.0)	12 (21.1)	0.004
Composite adverse outcome	38 (26.6)	29 (50.9)	0.001

Adverse outcomes occurred more frequently among patients with RDW ≥16.0% than among those with lower RDW values.

Table 10: Heart-Failure-Related Hospitalization According to RDW and Clinical Characteristics

Variable	No hospitalization (n=146)	Hospitalization (n=54)	p-value
Age (years)	61.1 ± 11.6	65.8 ± 11.7	0.010
RDW (%)	14.9 ± 1.5	16.6 ± 1.8	<0.001
Hemoglobin (g/dL)	12.0 ± 1.6	11.3 ± 1.7	0.007
LVEF (%)	46.5 ± 10.9	40.2 ± 12.1	<0.001
NT-proBNP (pg/mL)	2390 (1280–4210)	4280 (2380–7210)	<0.001
NYHA III–IV, n (%)	60 (41.1)	40 (74.1)	<0.001
Chronic kidney disease, n (%)	27 (18.5)	21 (38.9)	0.003

Patients requiring heart-failure-related hospitalization had higher baseline RDW, greater functional limitation, higher NT-proBNP concentrations, and lower LVEF than those who remained free of hospitalization during follow-up.

Table 11: Univariable and Multivariable Predictors of Composite Adverse Clinical Outcome

Predictor	Univariable OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age ≥65 years	1.82 (1.01–3.28)	0.046	1.49 (0.78–2.86)	0.229
RDW ≥16.0%	2.86 (1.54–5.30)	0.001	2.31 (1.18–4.52)	0.014
Hemoglobin <11 g/dL	2.04 (1.08–3.84)	0.028	1.51 (0.75–3.05)	0.249
LVEF <40%	2.48 (1.34–4.60)	0.004	1.94 (0.98–3.83)	0.058
NT-proBNP ≥3000 pg/mL	2.72 (1.49–4.97)	0.001	2.18 (1.11–4.28)	0.024
Chronic kidney disease	2.14 (1.10–4.16)	0.025	1.67 (0.81–3.43)	0.166
NYHA III–IV	2.93 (1.59–5.40)	<0.001	2.22 (1.13–4.37)	0.020

RDW remained significantly associated with the composite adverse outcome after adjustment for clinically relevant demographic, laboratory, functional, and echocardiographic variables.

Table 12: Independent Association of RDW with Heart Failure Severity and Clinical Outcomes

Parameter	Lower RDW	Higher RDW	Statistical significance
NYHA class	Lower	Higher	$p < 0.001$
LVEF	Higher	Lower	$p < 0.001$
NT-proBNP	Lower	Higher	$p < 0.001$
Heart-failure hospitalization	Less frequent	More frequent	$p = 0.001$
ICU admission	Less frequent	More frequent	$p = 0.009$
All-cause mortality	Less frequent	More frequent	$p = 0.004$
Composite adverse outcome	Less frequent	More frequent	$p = 0.001$
Adjusted association with composite outcome	—	OR 2.31 (95% CI 1.18–4.52)	$p = 0.014$

The overall analysis demonstrated consistent associations between elevated baseline RDW, greater functional severity, adverse cardiac parameters, and unfavorable clinical outcomes.

Tables Summary

Table 1: The study included 200 patients with a mean age of 62.4 ± 11.8 years, with males comprising 63.0% of the cohort. Hypertension, coronary artery disease, and diabetes mellitus were the predominant comorbidities. Patients were distributed across all four NYHA functional classes, with classes II and III representing the largest groups. **Table 2:** The mean baseline RDW was 15.4 ± 1.7%. Mild anemia was common, with a mean hemoglobin concentration of 11.8 ± 1.7 g/dL. Renal function and NT-proBNP values demonstrated considerable variability, reflecting the heterogeneous clinical profile of the heart failure population. **Table 3:** The mean LVEF was 44.8 ± 11.6%. HFrEF constituted the largest heart failure phenotype, followed by HFpEF and HFmrEF. Increased ventricular dimensions, left atrial enlargement, and elevated E/e′ ratios were observed across the cohort. **Table 4:** RDW increased progressively with worsening NYHA functional class, from 13.7 ± 0.9% in class I to 17.0 ± 1.6% in class IV. The difference across functional classes was highly significant, demonstrating a strong relationship between erythrocyte size variability and clinical heart failure severity. **Table 5:** Patients with advanced NYHA class III–IV disease had a substantially greater representation of RDW values ≥16.0%. Conversely, lower RDW values were predominantly observed among patients with less severe functional limitation. **Table 6:** RDW showed a significant inverse correlation with LVEF and positive correlations with left ventricular dimensions, left atrial diameter, and E/e′ ratio. These findings demonstrated that higher RDW was associated with adverse structural and functional cardiac characteristics. **Table 7:** RDW was positively correlated with NYHA class, NT-proBNP, serum creatinine, blood urea nitrogen, and duration of heart failure, while showing an inverse correlation with hemoglobin. The strongest associations were observed with NYHA class and NT-proBNP. **Table 8:** During 6 months of follow-up, 27.0% of patients experienced heart-failure-related hospitalization and 30.5% experienced worsening heart failure requiring treatment escalation. Intensive care admission occurred in 9.0%, while all-cause mortality was observed in 11.0% of patients. The composite adverse outcome occurred in 33.5%. **Table 9:** Patients with baseline RDW ≥16.0% experienced significantly more frequent hospitalization, worsening heart failure, intensive care admission, mortality, and composite adverse outcomes than patients with RDW <16.0%. **Table 10:** Patients who were hospitalized during follow-up had significantly higher RDW and NT-proBNP concentrations, lower hemoglobin and LVEF, and a greater proportion of NYHA class III–IV disease and chronic kidney disease than patients who remained free of hospitalization. **Table 11:** On multivariable analysis, RDW ≥16.0% remained independently associated with the composite adverse clinical outcome after adjustment for age, hemoglobin, LVEF, NT-proBNP, chronic kidney disease, and NYHA class. The adjusted odds ratio was 2.31 (95% CI 1.18–4.52; p=0.014). **Table 12:** The overall findings demonstrated a consistent relationship between elevated RDW and increasing heart failure severity, adverse echocardiographic and biochemical characteristics, hospitalization, intensive care admission, mortality, and the composite adverse clinical outcome.

DISCUSSION

Heart failure is characterized by complex interactions between cardiac dysfunction and systemic pathophysiological processes, including chronic inflammation, neurohormonal activation, oxidative stress, renal impairment, and altered hematopoiesis. Identification of readily available markers that can provide additional information regarding disease severity and prognosis is therefore of considerable clinical interest.[1] In the present prospective observational study involving 200 patients with heart failure, elevated red cell distribution width (RDW) was significantly associated with greater functional severity, adverse echocardiographic characteristics, higher NT-proBNP concentrations, and an increased frequency of adverse clinical outcomes during 6 months of follow-up. The findings indicate that RDW may reflect the broader systemic burden accompanying progressive heart failure.[2]

The baseline characteristics of the study population reflected the typical clinical heterogeneity encountered in patients with heart failure. The mean age was 62.4 years, and men constituted approximately two-thirds of the cohort.[3] Hypertension, coronary artery disease, and diabetes

mellitus were the predominant comorbidities, while chronic kidney disease and atrial fibrillation were also frequently present. These conditions are relevant when interpreting RDW because several of them can independently influence erythrocyte turnover, inflammation, renal erythropoietin production, and nutritional status. The presence of these potential confounders was therefore considered in the multivariable analysis.[4]

The mean baseline RDW in the study population was 15.4%, with substantial variation between patients. Importantly, RDW increased progressively with worsening NYHA functional class. Patients in NYHA class I had a mean RDW of 13.7%, compared with 17.0% among those in class IV, and the difference was statistically significant.[5] The increasing RDW across functional classes suggests that erythrocyte anisocytosis may be associated with the clinical burden of heart failure. The relationship remained evident when RDW was categorized, as patients with NYHA class III–IV disease were disproportionately represented among those with RDW ≥16%.[6]

A potential explanation for this association is that RDW integrates several biological processes that become increasingly prominent with advancing heart failure. Chronic inflammation can interfere with erythropoiesis and iron utilization, while oxidative stress may alter erythrocyte membrane integrity and survival.[7] In addition, renal dysfunction may reduce erythropoietin production and contribute to impaired red-cell maturation. Nutritional deficiencies and chronic disease-associated abnormalities in iron metabolism may further increase heterogeneity in circulating erythrocyte size. Thus, elevated RDW should not necessarily be interpreted as a direct marker of cardiac dysfunction; rather, it may represent a composite indicator of systemic physiological stress accompanying heart failure.[8]

The relationship between RDW and echocardiographic parameters further supported its association with objective measures of cardiac dysfunction. RDW demonstrated a significant inverse correlation with LVEF, with higher RDW values observed among patients with lower ventricular systolic function. Positive correlations were also observed with left ventricular end-diastolic and end-systolic dimensions, left atrial diameter, and E/e′ ratio. These findings suggest that increasing RDW was associated not only with functional limitation but also with structural remodeling and abnormal ventricular filling characteristics.[9]

The inverse association between RDW and LVEF is clinically relevant because reduced ventricular systolic function is an established determinant of morbidity in selected heart failure populations. However, LVEF alone does not comprehensively characterize heart failure severity, particularly in patients with preserved or mildly reduced ejection fraction.[10] The present study therefore used NYHA functional class as the principal clinical measure of severity and considered echocardiographic and biochemical parameters as complementary indicators. The consistent relationship between RDW and several of these parameters strengthens the observation that elevated RDW accompanies a greater overall burden of disease rather than being linked exclusively to a single echocardiographic measurement.[11]

RDW also demonstrated a significant positive correlation with NT-proBNP. Patients with higher RDW had substantially higher circulating NT-proBNP concentrations, and this association remained clinically relevant in the overall analysis. NT-proBNP reflects myocardial wall stress and is widely used in the evaluation and risk stratification of heart failure.[12] The relationship between RDW and NT-proBNP may therefore indicate that increased erythrocyte heterogeneity accompanies greater hemodynamic and systemic stress. At the same time, the two biomarkers reflect different biological domains: NT-proBNP is predominantly related to cardiac wall stress, whereas RDW may reflect systemic inflammatory, metabolic, renal, and hematological disturbances. Their association may consequently provide complementary information.[13]

An inverse relationship was observed between RDW and hemoglobin concentration. This finding is biologically plausible because anemia and abnormal erythropoiesis can increase variation in red-cell size.[6] Anemia is also common in patients with heart failure and may contribute to reduced oxygen delivery and functional limitation. Importantly, however, the association between elevated RDW and adverse outcomes persisted after adjustment for hemoglobin concentration. This suggests that the prognostic relationship of RDW was not explained solely by the presence of anemia.[1,14]

Renal dysfunction was another important factor associated with elevated RDW. RDW correlated positively with serum creatinine and blood urea nitrogen, and chronic kidney disease was more frequently observed among patients who subsequently required hospitalization. Cardiorenal interactions are well recognized in heart failure, with renal dysfunction contributing to fluid retention, neurohormonal activation, anemia, and altered erythropoiesis.[3,15] The association between RDW and renal parameters may therefore partly reflect the systemic consequences of the cardiorenal syndrome. Nevertheless, chronic kidney disease did not remain an independent predictor of the composite outcome after multivariable adjustment in the present cohort, whereas elevated RDW retained a significant association.[16]

The prospective follow-up provided additional information regarding the clinical significance of baseline RDW. During 6 months, 27.0% of patients experienced heart-failure-related hospitalization, 30.5% experienced worsening heart failure requiring treatment escalation, 9.0% required intensive care

admission, and 11.0% died. Patients with RDW ≥16.0% experienced significantly higher frequencies of all these outcomes than patients with lower RDW values. The composite adverse outcome was also substantially more frequent in the higher-RDW group.[17]

The association between RDW and hospitalization was particularly notable. Patients who were subsequently hospitalized had a mean RDW of 16.6%, compared with 14.9% among those who remained free of hospitalization. They also had lower LVEF, higher NT-proBNP concentrations, greater functional limitation, and a higher prevalence of chronic kidney disease.[8] These findings indicate that patients with elevated RDW frequently possessed several established indicators of more advanced disease. Nevertheless, the persistence of the RDW association after adjustment for major clinical and laboratory variables suggests that RDW may provide incremental information regarding risk.[18]

The multivariable analysis demonstrated that RDW ≥16.0% remained independently associated with the composite adverse clinical outcome, with an adjusted odds ratio of 2.31. NT-proBNP and advanced NYHA class also remained significant independent predictors.[12] In contrast, age, hemoglobin concentration, and chronic kidney disease were not independently associated with the composite outcome after adjustment. These findings are important because they indicate that the relationship between RDW and outcome was not simply attributable to older age, anemia, renal dysfunction, or reduced LVEF.[19]

Several mechanisms may explain why elevated RDW is associated with adverse outcomes in heart failure. Chronic systemic inflammation may suppress normal erythropoiesis and disrupt iron metabolism, while oxidative stress can alter red-cell deformability and lifespan.[10] Ineffective erythropoiesis may lead to the release of heterogeneous populations of immature and abnormal erythrocytes into the circulation.[7] In addition, hemodilution, renal dysfunction, nutritional deficiencies, and neurohormonal activation may contribute simultaneously. The resulting elevation in RDW could therefore serve as an indirect marker of cumulative systemic stress.[20]

The clinical usefulness of RDW lies partly in its routine availability. RDW is automatically reported with a complete blood count in most clinical settings and does not require a separate specialized assay. Its incorporation into routine assessment could therefore be particularly relevant in resource-constrained settings.[15] However, elevated RDW is nonspecific and may be affected by multiple non-cardiac conditions. It should consequently be interpreted in conjunction with clinical assessment, hemoglobin concentration, renal function, natriuretic peptide levels, echocardiographic findings, and other established prognostic variables rather than used as an isolated determinant of risk.[17]

The present study has several strengths. Its prospective design permitted baseline RDW measurements to be obtained before subsequent clinical outcomes occurred, reducing some of the limitations inherent to retrospective analyses. The study also incorporated clinical, hematological, biochemical, and echocardiographic assessments and followed patients systematically for 6 months. Evaluation of RDW both as a continuous variable and as a clinically relevant category further allowed assessment of both its quantitative relationship with disease severity and its association with clinically important outcomes.

Several limitations should also be considered. The study was conducted at a single tertiary-care center, which may limit the generalizability of the findings to other populations and healthcare settings. The observational design permits identification of associations but does not establish a causal relationship between elevated RDW and adverse heart failure outcomes. RDW can also be influenced by iron deficiency, vitamin deficiencies, inflammation, renal dysfunction, and other hematological conditions, despite exclusion of several major confounding conditions and adjustment for important variables. In addition, the 6-month follow-up period may not capture longer-term cardiovascular outcomes. Larger multicenter studies with longer follow-up and more detailed assessment of iron status, nutritional factors, inflammatory biomarkers, and serial RDW measurements would help determine whether changes in RDW over time provide additional prognostic information.

Overall, the findings demonstrate a consistent relationship between elevated RDW and both clinical severity and adverse outcomes in patients with heart failure. The association with NYHA class, LVEF, NT-proBNP, hospitalization, intensive care admission, and mortality suggests that RDW may function as an accessible marker of the systemic disease burden accompanying heart failure. Its greatest potential clinical value may lie in complementing established cardiovascular and laboratory markers rather than replacing them.

CONCLUSION

Elevated red cell distribution width was significantly associated with increasing heart failure severity and unfavorable clinical outcomes in this prospective observational study. RDW increased progressively across NYHA functional classes and demonstrated a significant inverse relationship with left ventricular ejection fraction and positive correlations with NT-proBNP and markers of renal dysfunction. Patients with higher RDW experienced more frequent heart-failure-related hospitalization, worsening heart failure, intensive care admission,

and all-cause mortality during 6 months of follow-up.

The independent association between elevated RDW and the composite adverse clinical outcome, even after adjustment for established clinical, hematological, renal, and cardiac parameters, suggests that RDW may provide additional prognostic information in patients with heart failure. As RDW is routinely available as part of the complete blood count and requires no additional specialized testing, it may serve as a practical adjunct to conventional clinical, biochemical, and echocardiographic assessment. However, because RDW is influenced by several systemic conditions and is not specific to heart failure, its interpretation should remain integrated with established markers of disease severity and prognosis. Further multicenter studies with larger cohorts and longer follow-up are warranted to determine the incremental prognostic value of RDW and the potential utility of serial RDW measurements in heart failure risk stratification.

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