Original Article

# The Significance of Red Blood Cell Distribution Width (RDW) in Predicting Early Readmission of Acute Heart Failure

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## Highlights

- The study evaluates red blood cell distribution width (RDW) as a prognostic marker in acute decompensated heart failure (ADHF).
- The main clinical issue is early readmission after hospitalization, which is common and associated with poor outcomes
- Admission RDW independently predicted early readmission within 30 days.
- Admission RDW also independently predicted in-hospital mortality.
- Change in RDW during hospitalization (ΔRDW) was also associated with in-hospital mortality.

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## ABSTRACT

**Background:** Hospitalizations for acute decompensated heart failure (ADHF) impose a substantial health care burden, and prognosis worsens with each readmission. Identifying patients at risk of frequent hospitalization is therefore essential. Red blood cell distribution width (RDW) has recently gained attention as a prognostic biomarker in cardiovascular disease. This study evaluated the prognostic value of baseline RDW and its in-hospital changes in patients admitted with ADHF.

**Methods:** In this retrospective observational cohort study, all adults hospitalized with ADHF between March 2022 and August 2024 were assessed. Demographic, clinical, echocardiographic, and laboratory data–including admission RDW and in-hospital RDW measurements–were extracted from the hospital information system and medical records. Early readmission for HF within 30 days after discharge was defined as the primary end point, and in-hospital mortality as the secondary end point.

**Results:** Among 1871 hospitalization records from 1409 patients (66.9% male; mean [SD] age, 59.3 [12.4] years), 984 cases with available follow-up data were analyzed. The mean length of stay (LOS) was 9.5 days, and the mean New York Heart Association (NYHA) class was 3.3. Early readmission occurred in 201 records (20.4% of admissions, 22% of patients). Baseline RDW independently predicted both outcomes: each 1-unit increase in RDW was associated with an 11% higher risk of early readmission and a 16% higher risk of in-hospital mortality. Additionally, a 1-unit increase in the change in RDW from admission to last measurement (ΔRDW) and the ratio of ΔRDW to LOS (ΔRDW/LOS) was linked to a 1.3-fold and 2.3-fold higher mortality risk, respectively.

**Conclusion:** Baseline RDW on admission is a strong, independent predictor of both early readmission and in-hospital mortality in patients with ADHF. RDW may serve as a simple and cost-effective marker for risk stratification and early intervention in this population.

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**Keywords:** Red Blood Cell Distribution Width (RDW); Acute Heart Failure; Early Readmission; In-Hospital Mortality; Risk Stratification

## Introduction

Heart failure (HF), a major cardiovascular disorder, continues to increase in both prevalence and incidence worldwide. Although advances in therapy have led to a gradual decline in overall mortality from HF, its mortality rate remains higher than that of several common malignancies, including bladder, prostate, breast, and uterine cancers.[1] While initial hospital admissions for HF have modestly decreased over recent years, rehospitalization rates have remained unchanged.[2]

Acute decompensated heart failure (ADHF) is the leading cause of hospitalization among individuals aged>65 years.[3] The marked healthcare costs associated with these hospitalizations, coupled with the progressive deterioration in prognosis with each subsequent episode, underscore the importance of identifying patients at high risk of recurrent admissions. Several clinical models and risk stratification tools have been developed, typically falling into two main categories:

1. models that predict in-hospital mortality prior to discharge, and 2. models that assess post-discharge outcomes.

Across these models, the most consistently associated predictors include advanced age, low blood pressure, elevated heart rate, increased blood urea nitrogen (BUN) and creatinine levels, and hyponatremia.[4-8]

The early post-discharge period represents a particularly vulnerable phase for ADHF patients. Reported 30-day readmission rates range between 20% and 30%, leading many investigators to define this interval as the “vulnerable period”.[9] Close clinical surveillance and targeted interventions during this time have been shown to reduce subsequent adverse events.[10]

To date, most prognostic studies in ADHF have focused on major cardiovascular outcomes, particularly short- and long-term mortality.[4-7] Moreover, existing clinical scores designed to predict mortality or adverse outcomes in HF are not optimal for estimating the risk of readmission.[1] Only a limited number of investigations have specifically evaluated independent predictors of early readmission.[11-13] Among the factors identified are left ventricular ejection fraction (LVEF), BUN, uric acid, prior device implantation, and natriuretic peptide levels.

Red cell distribution width (RDW)-a quantitative measure of variability in erythrocyte size-has recently emerged as a potential prognostic marker across several disease states, including cardiovascular disorders.[14-18] However, data regarding its relationship specifically with early readmission in ADHF remain scarce.[19]

Consequently, in the present study, we examined the prognostic significance of RDW measured at admission and its in-hospital variation (ΔRDW) in patients hospitalized with ADHF. Given the high clinical and economic impact of early readmission, our primary aim was to determine the extent to which RDW could predict early readmission in this patient population.

## Methods

### Patient Selection

The Hospital Information System (HIS) was queried for all adult patients with a diagnosis of chronic heart failure who were hospitalized for acute decompensation of heart failure (ADHF) at our cardiovascular institute, a tertiary center for cardiovascular medicine, between March 2022 and August 2024.

Patients with acute de novo heart failure, acute myocardial infarction, those undergoing heart transplantation or LVAD implantation during hospitalization, and those undergoing cardiac surgery or coronary or valvular interventions were excluded.

Demographic and clinical characteristics, including readmission, in-hospital mortality, length of stay (LOS), echocardiography, laboratory variables, and medications at discharge, were extracted from the patients' HIS and hospital records. For those patients who did not have any further records in terms of early readmission in our HIS system, follow-up was conducted by phone. The unit of analysis was the hospitalization (admission)-level record. Because some patients contributed more than one hospitalization, an analysis restricted to the first hospitalization per patient was performed.

## Study Design, Variables, and Definition of Endpoints

The study was retrospectively designed as an observational cohort of hospitalizations for ADHF. Each eligible hospitalization (admission-level) was followed for the occurrence of predefined outcomes. For the primary endpoint, hospitalizations that were followed by early readmission for heart failure within 30 days of discharge were classified as admissions with events, and those without early readmission were classified as admissions without events. For the secondary endpoint, hospitalizations that resulted in in-hospital death were classified as admissions with events, and those with survival to discharge were classified as admissions without events.

The independent variables of this study were the raw RDW value and changes in RDW during the index hospitalization. RDW at admission was defined as the first laboratory measurement within 24 hours. The second RDW was the last value prior to discharge or death. ΔRDW was also normalized by length of stay in a supplementary analysis.

In the analysis of the relationship between RDW and early readmission, hospitalization records that resulted in in-hospital mortality and records with uncertain outcomes regarding early readmission were excluded to enable a correct comparison between records with and without events (Figure 1).

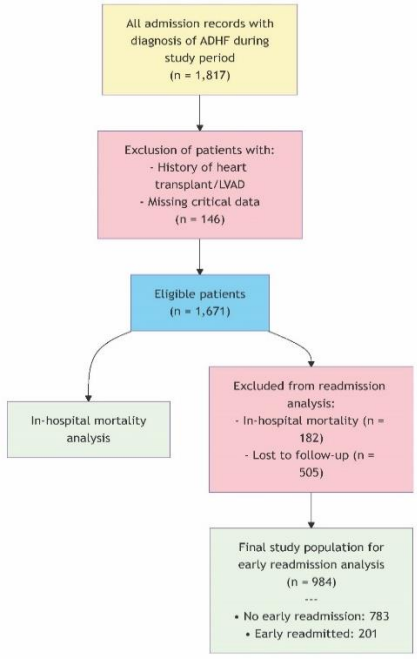


**Figure 1.** study population.

## Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki. The study was approved by the Institutional Research and Ethics Committee of our institute under ethics code number IR.RHC.REC.1403.079, and written informed consent was obtained from all patients.

## Statistical Methods

The one-sample Kolmogorov-Smirnov test was used to assess the normal distribution of the variables. Continuous variables were expressed as mean [standard deviation (SD)] or median [interquartile range (IQR)]. Categorical data were presented as numbers and percentages.

The independent t-test, Mann-Whitney U test, and univariate logistic regression were used to compare quantitative variables after analysing the equality of variances to obtain the odds ratio. The chi-square test and Fisher's exact test (if needed) were used to determine the relationship between qualitative variables. To determine the relative independent effect of RDW on early readmission, we used multivariable logistic regression with a model including indicators identified in recent or previous studies, using a stepwise entry method to eliminate the confounding effect of other factors.

## Statistical Software

All analyses were performed using IBM SPSS Statistics for Windows, Version 24.0 (IBM Corp., Armonk, NY, USA). Analyses were performed with a significance level of 5 percent.

We did not employ any artificial intelligence-assisted technologies in our study.

## Results

During the study period, 1,871 hospitalization records (from 1,409 patients) were extracted. One hundred and forty-six records were excluded due to missing follow-up or missing data. The mean age, length of stay, and New York Heart Association (NYHA) functional class were 59.3 years, 9.5 days, and 3.3, respectively. Most patients were male (66.9%) and had a non-ischemic etiology (55.1%). Regarding the category of heart failure (HF) in terms of LVEF, 146 patients were diagnosed with HF with preserved EF, 87

with HF with mildly reduced EF, and the remainder with HF with reduced EF. On admission, patients had a mean systolic blood pressure, mean diastolic blood pressure, and mean pulse rate of 112.5 mmHg, 74.6 mmHg, and 84 per minute, respectively.

Two hundred and one records with early readmission were included in the early readmission analysis (20.4% of referral records and 22% of patients), along with 783 records without early readmission. The remaining 687 records either had missing data or resulted in the patient's death (182 cases of in-hospital mortality; 10% of records and 13% of patients).

To assess the uniformity of the study population and potential selection bias due to a high rate of loss to follow-up, we compared all baseline variables between patients with and without known readmission status. After this preliminary analysis, only the length of hospital stay showed a statistically significant difference. Importantly, there was no significant difference in the primary study variable, RDW, between the two groups (P=0.49). This analysis suggests that the potential for selection bias was substantially mitigated. But this potential could not be fully eliminated due to retrospective nature of study design.

Among the demographic, clinical, and echocardiographic data, a shorter length of stay, higher NYHA functional class, lower LVEF, and lower systolic blood pressure on admission were significantly correlated with early readmission. For in-hospital mortality, a longer length of stay, higher NYHA functional class, and lower systolic blood pressure on admission were significantly correlated with this outcome, with length of stay and NYHA functional class showing a strong statistical correlation (Table 1).

The univariable analysis of the correlation between laboratory markers and study outcomes is shown in (Table 2).

The table indicates that sodium and uric acid have a strong correlation with the primary endpoint, with hyponatraemia and hyperuricaemia identified as risk factors for early readmission. Except for serum iron, all markers examined (BUN, serum creatinine, serum pro-BNP, serum haemoglobin, serum sodium, serum uric acid, serum ferritin, serum WBC, and serum C-reactive protein) had a statistically strong association with in-hospital mortality as a secondary endpoint. Both baseline RDW and ΔRDW showed a very weak but significant negative correlation with serum iron levels (Pearson's Rho=-0.1, P=0.001 for RDW; Pearson's Rho=-0.08, P=0.006 for ΔRDW). Baseline RDW was also negatively correlated with ferritin levels (Pearson's Rho=-0.1, P=0.001), but no correlation was found between ΔRDW and ferritin levels.

The relationship between the main independent variables and the study outcomes is presented in (Table 3).

**Table 1.** Clinical and demographic characteristics of patients in relation to outcomes

| variable | | Early re-admission | | | | In-hospital mortality | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Positive (201 records) | Negative (783 records) | P | RR * (1st status/2nd status) | Positive (186 records) | Negative (1485 records) | P | RR * (1st status/2nd status |
| Age(y) (mean±st. deviation) | | 56.1±18.1 | 58.6±15.8 | 0.07 | 0.99 | 60.8±19.7 | 59±16.2 | 0.24 | 1.007 |
| Gender (%) | male | 67.7 | 65.6 | 0.58 | 1.07 | 69.7 | 66.5 | 0.4 | 1.14 |
| | female | 32.3 | 34.4 | | | 30.3 | 33.5 | | |
| Length of stay(days) (mean±st. deviation) | | 7.9(6.2) | 9.3(9.7) | 0.01 | 0.979 | 17.2(19.1) | 8.4(9.2) | <0.001 | 1.049 |
| NYHA FC (%) | 1 | 0.5 | 1 | 0.019 | | 0 | 1 | <0.001 | |
| | 2 | 8.2 | 12.1 | | | 6.2 | 11.4 | | |
| | 3 | 42.6 | 50.8 | | | 12.3 | 49.4 | | |
| | 4 | 48.6 | 36.2 | | | 81.5 | 38.1 | | |
| AF rhythm at admission (%) | Positive | 20.4 | 21.1 | 0.82 | 0.96 | 21.6 | 18.5 | 0.29 | 1.19 |
| | negative | 79.6 | 78.9 | | | 78.4 | 81.5 | | |
| Etiology of heart failure (%) | Ischemic | 44.9 | 43 | 0.66 | 1.06 | 44.3 | 45 | 0.88 | 0.97 |
| | Non-ischemic | 55.1 | 57 | | | 55.7 | 55 | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| SBP at admission(mm.hg) (mean±st. deviation) | 106.4±27.3 | 116.1±31.5 | 0.017 | 0.99 | 100.2±31.1 | 116.6±31.5 | 0.004 | 0.986 |
| DBP at admission(mm.hg) (mean±st. deviation) | 70.7±20.3 | 76.2±23.8 | 0.07 | 0.99 | 68.7±25.7 | 75.9±23.2 | 0.09 | 0.987 |
| PR at admission (Per min) | 85.9±26.3 | 83.5±23.8 | 0.45 | 1.004 | 88.9±30.4 | 84.3±24 | 0.3 | 1.008 |
| LVEF (mean±st. deviation) | 22.3±13.7 | 24.8±13.6 | 0.036 | 0.986 | 23.6±13.8 | 24.6±13.7 | 0.37 | 0.995 |

**Abbreviations:** SD, standard deviation; IQR, interquartile range; NYHA, New York Heart Association
*In the case of quantitative variables these columns present odds ratio

**Table 2.** Laboratory characteristics in relation to primary and secondary outcomes

| Laboratory marker | Early re-admission | | P | OR | In-hospital mortality | | P |
|---|---|---|---|---|---|---|---|
| | Positive (201 records) | Negative (783 records) | | | Positive (186 records) | Negative (1485 records) | |
| BUN,mg/dlmean (SD) | 31.2±19.4 | 28.5±16.9 | 0.05 | 1.008 | 43.8±24 | 29.2±17.6 | <0.001 |
| Creatinine,mean (SD) | 1.78±0.88 | 1.65±0.94 | 0.08 | 1.14 | 2.35±1.26 | 1.68±0.99 | <0.001 |
| Pro-BNP,median (IQR) | 5250(2487-10971) | 4359(1882-8719) | 0.14 | 1 | 14956(6236-21974) | 4642(1864-9448) | <0.001 |
| Hgb | 12.5±2.2 | 12.5±2.4 | 0.09 | 1.003 | 11.5±2.5 | 12.4±2.3 | <0.001 |
| Na | 135±5.1 | 136.9±4.9 | <0.001 | 0.93 | 134.7±7 | 136.6±4.9 | 0.001 |
| Uric acid | 9±2.8 | 8.2±2.7 | 0.001 | 1.11 | 8.9±3.5 | 8.3±2.8 | 0.03 |
| Ferritin,median (IQR) | 99(45-239) | 105(52-208) | 0.86 | 1 | 246(96-438) | 112(51-223) | 0.007 |
| Serum iron, median (IQR) | 55(36-87) | 56(34-82) | 0.3 | 1.001 | 45.5(24-74) | 55(34-82) | 0.23 |
| WBC | 8589±3845 | 8353±3236 | 0.37 | 1 | 11401±6274 | 8433±3265 | <0.001 |
| C-Reactive Protein | 23±26.3 | 20.1±31.6 | 0.26 | 1.003 | 40.36±54.2 | 21.3±30 | <0.001 |

**Abbreviations:** BUN, blood urea nitrogen; SD, standard deviation; IQR, interquartile range; Pro-BNP, pro-brain natriuretic peptide; Hgb, hemoglobin; Na, sodium; WBC, white blood cell count

**Table 3.** Relationship of RDW with study outcomes

| Variable | Early re-admission | | | | | In-hospital mortality | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Positive (201 records) | Negative (783 records) | P value | OR | CI | Positive (186 records) | Negative (1485 records) | P value | OR | CI |
| RDW ((mean±st. deviation) | 16.73±2.83 | 15.84±2.66 | <0.001 | 1.11 | 1.059-1.179 | 17.38±3.39 | 15.91±2.7 | <0.001 | 1.16 | 1.115-1.226 |
| ΔRDW (mean±st. deviation) | 0.16±3.97 | 0.08±1.54 | 0.65 | 1.01 | 0.952-1.081 | 1.19±2.58 | 1±1.97 | <0.001 | 1.3 | 1.2-1.417 |
| ΔRDW/LOS (mean±st. deviation) | 0.02±0.66 | -0.005±0.19 | 0.3 | 1.23 | 0.81-1.8 | 0.08±0.22 | 0.002±0.3 | 0.016 | 2.3 | 1.17-4.66 |

**Abbreviations:** RDW, red blood cell distribution width; ΔRDW, change in RDW from admission to last measurement during hospitalization; OR, odds ratio; CI, confidence interval

The raw RDW value predicted both study outcomes with high statistical power. This relationship was persistent after repeating the main analyses with restricted dataset to the first eligible hospitalization per patient (P value<0.001, 95% CI=1.07-1.2 for early re-admission; P value<0.001 ,95% CI=1.11-1.22 for in-hospital mortality). An increase of one unit in RDW raised the probability of early readmission and in-hospital mortality by 11% and 16%, respectively. The ΔRDW (normalized by length of stay (LOS) in a supplementary analysis), defined as the difference between the last available RDW in each hospitalization record and the RDW at admission, was associated with in-hospital mortality but not with early readmission. A one-unit increase in ΔRDW and ΔRDW/LOS increased the probability of death by 1.3 and 2.3 times respectively.

Variables shown to have an independent effect in this study and in previous studies were reviewed for inclusion in multivariable logistic regression to determine their independent predictive power for outcome. Due to the strong correlation between NYHA functional class, pro-BNP, sodium, and BUN with the main independent variable of the study (i.e., RDW), we first constructed a baseline

multivariable logistic regression model including RDW, uric acid (indicating volume status), LVEF (indicating LV function), and length of stay (demographic finding) – variables representing different domains of heart failure severity.(Table 4) shows that multivariable regression, in a baseline model including LVEF, uric acid, length of stay, and RDW, demonstrated that all these variables could independently predict early readmission.

**Table 4.** Multivariable Regression Analysis of Predictors for Early Readmission

| variable | Multivariate logistic regression | | |
|---|---|---|---|
| | OR | CI (95%) | P |
| RDW | 1.085 | 1.021-1.153 | 0.009 |
| Uric acid | 1.095 | 1.025-1.171 | 0.007 |
| LVEF | 0.982 | 0.096-0.99 | 0.015 |
| Length of stay | 0.974 | 0.95-0.999 | 0.045 |

**Abbreviations:** OR, odds ratio; CI, confidence interval; RDW, red blood cell distribution width; LVEF, left ventricular ejection fraction

To assess the robustness of RDW as a predictor, we then performed a sensitivity analysis by adding four clinically established predictors of readmission (NYHA class, BUN, serum sodium, and pro-BNP) one at a time to the baseline model, as well as simultaneously, and observed whether the association between RDW and early readmission remained statistically significant after each adjustment (Supplementary Table 1). When BUN was added, RDW remained significant (OR: 1.08, 95% CI: 1.01–1.1, P=0.02). Similarly, after adjustment for NYHA class, RDW also remained significant (OR: 1.07, 95% CI: 1.005–1.15, P=0.03). However, when serum sodium or pro-BNP was added separately, the association between RDW and early readmission was no longer statistically significant at the α=0.05 level (P=0.07 and P=0.35, respectively). In the fully adjusted model containing all four variables simultaneously, the OR for RDW was 1.02 (95% CI: 0.89–1.18, P=0.7).

These results indicate that the prognostic value of RDW is not fully independent; rather, it is largely mediated through or shared with hyponatremia and elevated pro-BNP – markers of neurohormonal activation and hemodynamic congestion. In contrast, RDW provides information beyond BUN and NYHA class."

## Discussion

### Relation of RDW with Study Outcomes

In this study, we observed an early readmission rate of 20% among patients admitted with decompensated heart failure. The absence of any significant difference during the preliminary analysis in RDW values between patients with and without known readmission status (P=0.49) suggests that selection bias due to loss to follow up was minimal.

The baseline RDW value showed a significant association with early readmission in univariate and baseline multivariable analyses, with an 11% increase in risk per 1% rise in RDW (Figure 2). However, sensitivity analyses revealed that this association was no longer statistically significant after adjustment for serum sodium or pro-BNP, whereas it remained significant after adjustment for BUN or NYHA class. In contrast, RDW appears to provide independent information beyond simple measures of renal congestion (BUN) or subjective functional class (NYHA).

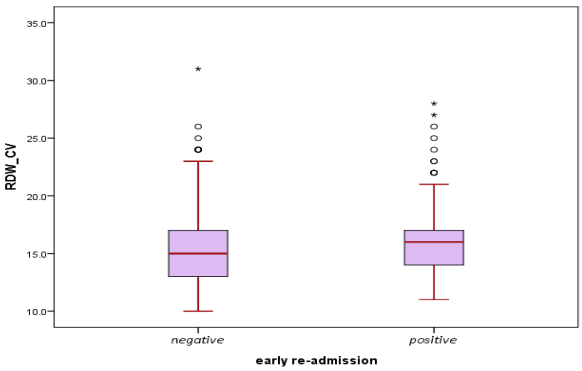


**Figure 2.** Box plot of the association of RDW and early readmission

RDW should not be viewed as a replacement for established predictors such as pro-BNP or sodium, but rather as a complementary, readily available biomarker that can raise suspicion of higher risk in patients presenting with acute heart failure.

In contrast, changes in RDW during hospitalization (ΔRDW) were not associated with early readmission. This statistical relationship appears distinctive within the current literature; only the study by Muhlestein et al. reported comparable results.[19] Consistent with previous studies (Zhang et al., Dai et al., Xanthopoulos et al., Uemura et al. and Ji et al.), RDW demonstrated a strong association with in-hospital mortality.[16,20-23] Each one-unit increase in RDW or ΔRDW was linked to a 16% and 30% higher risk of in-hospital death, respectively. It is important to say that ΔRDW is influenced by both the intensity of clinical events and the duration of hospitalization. So, we

produced a rate-normalized ΔRDW as ΔRDW divided by length of stay in days (ΔRDW/LOS) and examined its association with both outcomes. ΔRDW/LOS remained significantly associated with in-hospital mortality but not with early readmission, consistent with our original findings for absolute ΔRDW. Thus, we can conclude that ΔRDW prognostic role may primarily reflect short-term in-hospital risk rather than early post-discharge readmission.

The association between elevated RDW and heart failure readmission can likely be attributed to several mechanisms:

1. Chronic inflammation: Elevated RDW often reflects persistent inflammatory activity, which disrupts erythropoiesis and increases variability in red blood cell size. Inflammatory cytokines not only impair erythroid maturation but also worsen myocardial and vascular function, thereby increasing the likelihood of decompensation and rehospitalization.[21,24]

2. Anemia and nutrient deficiencies: Anemia-frequently observed in heart failure-results from impaired erythropoiesis, iron deficiency, or deficiencies of vitamin B12 and folate and can be contribute to increased RDW. These deficits raise cardiac workload, exacerbate symptoms, and predispose to early readmission.[21,24] Nutrient malabsorption due to gastrointestinal congestion or diuretic-induced loss of water-soluble vitamins may further aggravate this process.

3. Iron metabolism disturbances: Iron deficiency, whether absolute (low ferritin) or functional (normal/high ferritin with low transferrin saturation), is prevalent in heart failure and contributes to increased RDW. Because ferritin is an acute-phase reactant, elevated levels may mask true iron deficiency. Thus, a combination of high RDW and low ferritin may identify patients likely to benefit from iron supplementation, which is known to improve functional capacity and quality of life.

In our study, serum iron, ferritin, and RDW were significantly associated; however, ferritin was not associated to early readmission, supporting a ferritin-independent relationship between RDW and readmission risk. Conversely, ferritin was a strong predictor of in-hospital mortality, possibly reflecting the impact of severe inflammation. Given that most patients at this tertiary heart failure center had their iron status corrected according to guideline-recommended therapy, higher ferritin levels may mark patients with systemic inflammatory activation and poorer prognosis. Further studies are warranted to clarify this observation.

4. Oxidative stress: Elevated RDW may also mirror enhanced oxidative stress, which damages erythrocytes, endothelium, and myocardium, contributing to disease progression and increased hospitalizations.[21,24]

5. Comorbidities and volume status: Chronic conditions such as chronic kidney disease, diabetes, and COPD can elevate RDW and complicate heart failure management, predisposing to recurrent admissions.[21] Moreover, fluctuations in fluid volume may influence erythrocyte morphology and RDW, indirectly signaling hemodynamic instability and worsening cardiac function.

## Factors Associated with Early Readmission (Other than RDW)

The early readmission rate observed in our study is comparable to that reported by García Gutierrez et al. and Xexemeku et al.[25,26] yet higher than rates seen in large multicenter trials such as ASCEND HF, EVEREST, and TRUE HF.[27-29] This discrepancy likely reflects differences in study design, as those trials were conducted under controlled conditions, whereas our study represents real world data from a tertiary referral center. With respect to in hospital mortality, our rate was almost double that reported in studies conducted in Canada (Lee et al.), Europe (EHFS II), and Japan (ATTEND)[30-32], and higher than that observed in studies from the Arab region and the Indian subcontinent.[33] The most plausible explanation is the referral bias inherent in tertiary centers, where patients typically present with more advanced and complex forms of acute heart failure (AHF).

Interestingly, patients who were readmitted early had a shorter initial hospital stay, a finding that emphasizes the importance of achieving complete decongestion and optimizing therapy before discharge, consistent with previous studies.[26] Moreover, a higher NYHA functional class at admission was associated with increased readmission risk. However, given the inherently

subjective nature of NYHA classification and its potential overlap with other variables, establishing an independent effect requires larger samples and subgroup analyses. Additionally, each 1 mg/dL increase in serum uric acid was associated with an 11% increase in early readmission risk, suggesting that hyperuricemia may reflect persistent congestion and more severe disease.

Overall, the predictors of early readmission in this study-namely elevated uric acid, hyponatremia, higher NYHA class, low systolic blood pressure, and reduced left ventricular ejection fraction (LVEF)-are consistent with prior reports.[2,8,26] These variables primarily reflect systemic or cardiac congestion and advanced left ventricular dysfunction. Thus, the strong association between RDW and readmission appears biologically plausible: elevated RDW may serve as a surrogate for these underlying adverse conditions, indicating the need for closer monitoring and more aggressive post discharge management. Failure to address mechanisms linked to increased RDW could lead to incomplete stabilization and higher readmission rates.

Improving decongestion strategies and addressing the pathophysiological processes reflected by elevated RDW may help clinicians enhance disease control, reduce hospital readmissions, and improve outcomes in patients with acute heart failure.

## Factors Related to In-Hospital Mortality (Other than RDW)

Consistent with the findings of Naderi et al.[13], our study identified a strong correlation between length of stay (LOS) and in hospital mortality. Unlike the early rehospitalization group, patients who died during hospitalization had longer LOS, likely reflecting greater disease severity or treatment complexity.

Similar to early readmission, in hospital mortality was associated with higher NYHA functional class, lower systolic blood pressure, elevated blood urea nitrogen (BUN) and creatinine, decreased serum sodium, and increased RDW. These results align with previous investigations across different populations, reaffirming the prognostic significance of both congestive markers and renal dysfunction in acute heart failure.

## Limitations of the Study

Although the relatively large sample size could be considered a strength, the limitations of the retrospective design should be acknowledged.

This study is limited by the loss to follow up of a subset of patients who were not included in the final analysis. Such attrition may introduce selection bias and could affect the representativeness of the study population. Nevertheless, about 1,000 patients were successfully analyzed. The observed 20% incidence of the primary endpoint among these participants and the absence of any significant difference during the preliminary analysis in RDW values between patients with and without known readmission status suggests that the findings are likely to be reliable and reflect the true trend in the target population. But this does not eliminate the risk of selection bias from unmeasured confounders (such as socioeconomic status, distance from the hospital, etc.). So Future prospective studies with complete follow-up are needed to validate our results.

Furthermore, our sensitivity analyses showed that the association between RDW and early readmission was attenuated and lost statistical significance after adjustment for serum sodium or pro-BNP, two established markers of congestion and neurohormonal activation. This raises the possibility that RDW does not provide independent prognostic information beyond these variables. However, given that RDW remained significant after adjustment for BUN and NYHA class, and that the fully adjusted model had limited power (event-to-variable ratio), we cannot definitively conclude that RDW lacks independent value. Larger prospective studies with pre-specified power calculations and head-to-head comparisons with natriuretic peptides are needed to clarify the incremental role of RDW in readmission risk stratification

Most patients in our study population had heart failure with reduced ejection fraction (HFrEF); therefore, the generalizability of these findings to the broader heart failure population, including those with preserved or mildly reduced ejection fraction, is limited. Furthermore, although optimal medical therapies were applied to the entire study cohort, recruitment from a tertiary care center likely led to overrepresentation of patients with

more advanced or complex disease and specific etiologies of heart failure. Consequently, the results may not be fully applicable to centers managing patients at earlier stages or in less specialized settings. Comparison of our findings with data from community based or secondary care populations may help to mitigate this limitation.

The present study did not explore the underlying pathophysiological mechanisms linking red cell distribution width (RDW) with clinical outcomes, which warrants further basic and translational research.

## Conclusions

This study showed that RDW at admission is significantly associated with early readmission and in-hospital mortality in ADHF patients, and this relationship remains significant for early readmission after adjusting for confounding factors.

Our study also showed that RDW changes during hospitalization due to ADHF are directly related to in-hospital mortality.

The results of this and similar studies can help physicians to better triage and risk-stratify patients, choose appropriate approaches for acute and chronic treatment, and properly plan the long-term follow-up and rehabilitation of these patients. They can also be a step towards developing a clinical score for ADHF readmission.

## Disclosures

The authors disclose that this study have no any relationship with industry and financial associations and no competing interest has been declared.

We did not employ any artificial intelligence-assisted technologies in our study.

## Declarations:

## Ethical Approval

Ethical approval for this study was obtained from the Institutional Research and Ethics Committee of our institute under ethics code number IR.RHC.REC.1403.079, and written informed consent was obtained from all patients.

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## Conflict of Interest

The authors declare that they have no conflicts of interest relevant to the content of this manuscript.

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