RDW Change in Heart Failure

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Red blood cell distribution width (RDW) is an integral parameter of the complete blood count (CBC), which has been traditionally used for the classification of several types of anemia. It has been defined either as the standard deviation (SD) of erythrocyte volumes (RDW-SD), which is measured by calculating the width at the 20% height level of the red blood cell (RBC) size distribution histogram; or, as the coefficient of variation (RDW-CV) of erythrocyte volumes by dividing the standard deviation (SD) of the red blood cell volume (RBCs) by the mean corpuscular volume (MCV) multiplied by 100 (SD/MCV × 100), and expressing the variability in size of circulating erythrocytes (anisocytosis). The normal reference ranges of RDW-SD and RDW-CV are typically 39–46 fL and 11.5–15%, respectively, but often vary depending on the method of RDW calculation and the available hematological analyzers used.

red blood cell distribution width | heart failure | prognosis | mechanisms

1. RDW in Incident Heart Failure

Several studies have demonstrated that red blood cell distribution width (RDW) is an independent predictor of incident HF. In a retrospective population-based cohort analysis including 26,784 middle-aged subjects without history of myocardial infarction, stroke or HF, who participated in the Malmo Diet and Cancer study (1991–1996) and were followed up for up to 15 years, a higher RDW was found to be associated with higher long-term incidence of first hospitalization due to HF (Hazard Ratio (HR): 1.47, 95% Confidence Interval (CI): 1.14–1.89, in the top compared with the bottom quartile of RDW), after adjusting for history of coronary revascularization, biological, lifestyle and socio-economic factors [1]. Emans et al. reported that RDW levels were associated with an increased risk of incidence of HF utilizing data from 17,533 participants from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk cohort [2]. Among them, 640 participants developed HF during a follow-up of 11.2 ± 2.2 years and authors observed that there was a non-linear increase in HF risk as RDW values were increasing [2].

2. RDW in Chronic HF

The RDW is associated with indices of cardiac function and/or disease severity in HF including the natriuretic peptides [3][4], peak oxygen consumption [5][6], left ventricular end diastolic pressure (LVEDP) [7] and left ventricular deformation [8][9].

The first study examining the predictive value of RDW in chronic HF was conducted by Felker et al. back in 2007 [10]. The authors found that RDW exhibited the strongest association with cardiovascular death or HF hospitalization (adjusted HR 1.17 per 1-SD increase, 95% CI: 1.10–1.25, $p < 0.001$) among 36 laboratory parameters in a cohort of 2679 symptomatic chronic HF patients from the North American CHARM (Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity) program. Similar were the findings in the Study of Anemia in a Heart Failure Population (STAMINA-HFP) [11][12], as well as in patients post myocardial infarction (MI) [13]. In this regard, it has been proposed that RDW may be a better predictor of outcomes in HF patients than several echocardiographic parameters [14]. It is noteworthy that no association was observed between RDW and HF due to valvular heart disease [15]. A recent study reported an independent association between a low hemoglobin/RDW ratio and the risk of death as well as the combined endpoint of death or cardiovascular hospitalization in a cohort of 6888 HF patients. Interestingly, this association was observed over the whole spectrum of HF types, including HFrEF and HFpEF [16].

3. RDW in Acute HF

Increased RDW may be associated with a slower diuretic response [17], and elevated LV filling pressure (E/E') [18], and has been shown to predict early mortality in patients presenting with acute dyspnea at the emergency department (ED), irrespective of its etiology [19]. Notably, the addition of RDW to conventional laboratory tests (B-type natriuretic peptide, creatinine, sodium and chloride) may significantly improve the 30-day prognostic assessment (for all-cause mortality) of acute HF patients presenting in the ED [20].

The prognostic value of RDW in acute HF was initially reported in a Spanish study, which included 628 consecutive patients [21]. Pascual-Figal et al. collected clinical, echocardiographic and laboratory variables at discharge and followed up with patients for ~2½ years. RDW was found to be a strong and independent marker of all-cause mortality (p = 0.004, HR 1.072, 95% CI 1.023–1.124), regardless of anemia status (p for interaction > 0.1 for the entire population). Therefore, this study demonstrated that RDW may be used as an early predictor of adverse outcomes in non-anemic HF patients. Subsequently, it was demonstrated that RDW provided additional prognostic information to natriuretic peptides [22][23][24][25][26], that it may also be useful in the elderly [27] and that it may be a better predictor of outcome in patients with a preserved, than in those with reduced, left ventricular ejection fraction (LVEF) [28][29]. Patients with high RDW and N-terminal pro b-type natriuretic peptide (NT-proBNP) values exhibit the highest mortality rates, whereas those with low RDW and NT-proBNP exhibit the most favorable outcomes. Finally, a significant interaction between diabetes and RDW longitudinal changes from the patient's admission to 1-year post discharge has been reported [30].

4. RDW in Advanced HF

A retrospective analysis of 367 consecutive patients with advanced HF (New York Heart Association class III-IV) and concomitant diabetes mellitus revealed RDW as an independent predictor of all-cause mortality during the long term follow up [31].

RDW may be useful in risk stratification of patients selected for implantable cardioverter defibrillator (ICD) therapy as it predicts death and appropriate therapy [32]. In patients with advanced HF undergoing cardiac resynchronization therapy (CRT), it has been reported that elevated RDW is associated with lower rates of "positive response" to CRT (defined as a reduction in LV end-systolic volume (LVESV) ≥15% or a relative increase in LVEF ≥ 15%) [33][34], and that elevated the RDW level before and after CRT implantation is independently associated with all-cause mortality [35].

A retrospective single center analysis of 188 continuous flow left ventricular assist devices (LVADs) implanted from 2004 to June 2014, revealed an independent association between higher pre-implant RDW values and mortality in a more than 1 year follow up [36]. Similarly, in the study by Truby et al. RDW was independently predictive of 90-day mortality (Odds Ratio (OR), 1.16 for 1% increase; CI, 1.04–1.31; $p = 0.010$) in a population of 409 continuous-flow LVADs [37]. Notably, mechanical unloading with continuous-flow LVADs was associated with a reduction in RDW levels. On the contrary, Ahmad et al. reported no change in RDW values, at a median of 135 days after LVAD placement [38]. Poglajen et al. proceeded to a 5-day bone narrow stimulation with granulocyte colony stimulating factor (G-CSF) in 44 patients with advanced HF [39]. On the fifth day, a full blood count and a peripheral blood CD34+ cell count were performed. On a multivariable analysis, RDW turned out to be a sole independent predictor of poor stem cell mobilization (HR 8.64, 95% CI: 1.242–60.021, $p = 0.01$). Although the underlying mechanisms are not clearly defined, it appears that RDW may represent a useful tool to improve the selection of candidates for stem cell therapy in this population of patients [39]. Lastly, increased RDW in advanced HF patients immediately before orthotopic heart transplantation is an independent predictor of post-operative mortality during an average follow-up of 45.5 months [40].

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