

Progress in Red Blood Cell Distribution width And Cardiovascular Diseases]

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Abstract : *The red blood cell (RBC) distribution width (RDW) is a term used to describe the heterogeneity of the peripheral blood erythrocyte (i.e., Anisocytosis) volume hematology indexes of anemia in the etiology diagnosis, especially the thalassemia anemia and has important value in the differential diagnosis of iron deficiency anemia. Recently accumulated studies have found that RDW plays an important role in the diagnosis, risk stratification and prognosis of cardiovascular diseases. This review article explains the relationships between red blood cell distribution width and heart failure, acute myocardial infarction and acute coronary syndrome.*

Keywords: *Red blood cell Distribution Width (RDW), Heart Failure (HF), Acute Myocardial Infarction (AMI), Acute Coronary Syndrome (ACS)*

I. Introduction

The RDW is a measurement of the size variation as well as an index of heterogeneity of the erythrocytes, which is typically used in combination with the main corpuscular volume to troubleshoot the cause of an underlying anemia. Reliable data emerged from a variety of clinical studies have, however, disclosed a new and un predictable scenario in the clinical usefulness of this measure, supporting the hypothesis that RDW might be a useful parameter for gathering meaning clinical information, either diagnostic or prognostic, on a variety of cardiovascular and thrombotic disorders. Highly significant associations have been described between RDW value and all-cause, cardiac and non-cardiac mortality in patients with Coronary artery diseases, a cute and chronic heart failure, acute myocardial infarction, acute coronary syndrome and peripheral artery disease. It is however still unclear whether erythrocytes may be the cause, or a simple epiphenomenon of an underlying disease, such as impaired renal function, inflammation, oxidative damage, undernutrition, or perhaps an element of both. Nevertheless, RDW is an easy inexpensive, routinely reported test, whose assessment might allow the acquisition of significant diagnostic and prognostic information in patients with cardiovascular disorders.

II. Subjects

2.1 RDW And Heart Failure (HF)

In 2007, Felker [1] first reported RDW is associated with the prognosis of heart failure, also to study the relationship between RDW and cardiovascular disease to upsurge [2]. The object of the research included two groups queue, respectively people from the CHARM trial and DUKE DATABANK. Researchers found in the two groups, RDW the higher the prognosis of patients with the worse, performance for the patients of cardiovascular disease mortality and all-cause mortality increased significantly. RDW every one standard deviation increase, patients with all-cause mortality risk increased 1.29 times. Since then, several dozens of studies [3-18] reported a relationship between RDW and prognosis of heart failure, shows that the higher the RDW, the worse the prognosis of patients with heart failure. It is noteworthy that, in addition to its discovery RDW prognosis of patients with heart failure on admission, there are found changes RDW during hospitalization cases [7], as well as discharge RDW test results [13,16] and also the prognosis of heart failure related. These studies were meta-analysis [19] showed that: RDW increased per unit (ie 1%), patients with all-cause mortality risk increased 1.1 times, but there are between existing research publication bias, indicating the existing research may exaggerate RDW prognostic value in heart failure. In addition to heart failure as a prognostic factor, RDW can also serve as a risk factor for heart failure. For example Borné et al [20] of 26 784 community residents for more than 10 years of follow-up, observed the research object of baseline RDW and the relationship between the cardiovascular events in the future. The researchers found that the correction of blood pressure, smoking, lipoprotein and other known risk factors for cardiovascular disease, RDW still closely related to the occurrence of heart failure risk, the higher performance for baseline RDW, the individual risk of future heart failure also higher. Tonelli et al [21] of 4111 patients with CHD were 6 years of follow-up found that in patients with coronary heart disease, RDW prompted increased risk in patients with heart failure increased.

2.2 Rdw And Acute Coronary Syndrome, Acute Myocardial Infarction

Considering the mechanism of occurrence and development of various cardiovascular diseases have many similarities, so clearly the RDW and the prognosis of heart failure at the same time, scholars have gradually begun to explore the relationship between the RDW and acute myocardial infarction. Early studies in chest pain crowd [22] found that patients with acute coronary syndromes of RDW level are not much higher in patients with acute coronary syndromes, thus, can be used as a diagnostic indicator of acute coronary syndrome, Although the area under the receiver-operating characteristic curve of only 0.71, but it can make up for the lack of troponin, increased troponin in the diagnosis of acute coronary syndrome diagnostic sensitivity. The Follow-up study [23] found that in coronary atherosclerotic heart disease, RDW increased gradually along with the progress of the disease. On the one hand, prompt RDW may be acute myocardial infarction or acute coronary syndrome risk factors, on the other hand also explains why RDW is well useful markers of diagnosis of the acute coronary syndrome.

Several studies have found that the RDW is acute myocardial infarction or recent prognostic factor in patients with acute coronary syndromes. Such as Sangoi et al [24] in 109 cases of patients with acute myocardial infarction after research found that RDW hospitalization in patients with acute myocardial infarction (mi) is an independent risk factor for death. Domestic scholars [25] with 28 deaths as the end point, RDW also found that the higher the risk of death in patients with acute myocardial infarction is also higher. A study of 1, 654 patients with acute coronary syndromes was analyzed and found that the higher RDW, in patients with heart failure, cardiovascular-related deaths as well as the risk of recurrence of acute myocardial infarction [26].

RDW is also a risk factor for the long-term prognosis of acute myocardial infarction and acute coronary syndrome. South Korean scholars [27] on 1 596 patients with acute myocardial infarction for the 1 year of follow-up, found that patients with onset of RDW and 1 year later is closely related to the major adverse cardiovascular events. The study also found that the RDW system into the prognosis of myocardial infarction, and help to improve the accuracy of acute myocardial infarction prognosis. Vaya et al [28] on 119 patients with acute myocardial infarction in the 2-year follow-up, also found higher RDW patients, the risk of cardiovascular disease recurrence was also higher. Azab et al [29] of 619 non-ST elevation myocardial infarction (NSTEMI) patients with four years of follow-up also found that RDW every one unit increases the risk of death in patients with increased 1.1 times. In addition, there are a number of studies [30-34] analyzed the RDW and acute myocardial infarction, the relationship between the prognosis of acute coronary syndrome, despite the different subjects in these studies observed (ST-segment elevation / non-ST-segment elevation, acute myocardial infarction, acute coronary syndrome), endpoint (cardiovascular death, heart failure, all-cause mortality, etc.), the correction of confounding factors and follow-up time was different, but almost all are found RDW prognostic factors of acute myocardial infarction and acute coronary syndrome. Unfortunately, there is no meta-analysis of studies in this area are aggregated and evaluated to prove the relationship between RDW and acute myocardial infarction and acute coronary syndrome between the terms of evidence-based medicine.

RDW is also acute myocardial infarction and acute coronary syndrome risk factors. Skjelbakken et al [35] conducted a total of 25 612 patients into the research object, the object of study in has not been entered the study acute myocardial infarction, in the study were followed up to 16 years or so later, a total of 1 779 subjects with acute myocardial infarction occurred. Statistical analysis showed that the correction of the more conventional risk factors after acute myocardial infarction, RDW is still closely associated with the occurrence of acute myocardial infarction, Characterized by increased RDW per one unit, Patients had a 13% increased risk of acute myocardial infarction. Borne study [36] is similar Skjelbakken studies, but the end of its observation of acute coronary events, (Mainly acute coronary syndrome) and the risk of death after acute coronary events. The researchers found that the higher RDW, risk of acute coronary events in patients with the higher, and the prognosis after acute coronary events are poorer.

2.3. Rdw And Reasons Associated With Cardiovascular Disease.

In addition to acute myocardial infarction, heart failure, and the risk of acute coronary syndrome, RDW is also working with a variety of closely related to the occurrence, development and prognosis of cardiovascular disease. For example, studies have found that RDW is associated with the prognosis of pulmonary embolism (37-38), healthy individuals RDW and risk of Atrial fibrillation-related [39]; Coronary heart disease (CHD) in patients with RDW is closely related to the incidence of cardiovascular events and mortality [40].

Although RDW with a variety of cardiovascular diseases has close ties, the internal mechanism is poorly understood. Now that, RDW may be an indicator of inflammation, because it was found RDW and inflammatory biomarkers such as C-reactive protein, erythrocyte sedimentation rate was positively correlated [41] in the unselected outpatients. Furthermore, in healthy individuals, also found that the inflammatory marker above RDW was positively correlated [42]. So, presumably, in the process of chronic inflammation, persistent inflammation cause changes in the hematopoietic microenvironment, Cause red blood cell morphology changes,

and ultimately lead to increased RDW [43]. It is worth noting that studies have found that renal function associated with the RDW, the worse the kidney function, the higher the RDW [44].

Due to the occurrence and development of cardiovascular disease is closely related to the kidney, the renal damage will affect the body's multiple systems, including hematopoietic microenvironment, and the kidney itself secrete hormones such as erythropoietin, and regulate the production of red blood cells. Therefore, RDW relationship with cardiovascular disease may be partially mediated by renal function.

III. Conclusions

Although the Red blood cell distribution width and cardiovascular disease occurrence, development and prognosis of many research reports confirmed that RDW is an easy, inexpensive, routinely reported test, whose assessment might allow the acquisition of significant diagnostic and prognostic information in patients with cardiovascular diseases. Even though the mechanism of an association between RDW and cardiovascular disease is still not clear, however, most studies have found RDW can compensate for the lack of conventional cardiovascular biomarkers, and therefore have a wide clinical application. We believe that with further research relationship between RDW and cardiovascular disease will become more clear, which provides a new way for the prevention and treatment of cardiovascular diseases.

References

- [1]. Felker GM, Allen LA, Pocock SJ, et al. Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank[J]. *J Am Coll Cardiol*, 2007, 50(1):40-47.
- [2]. Lippi G, Plebani M. Red blood cell distribution width (RDW) and human pathology. One size fits all[J]. *Clin Chem Lab Med*, 2014,52(9): 1247-1249.
- [3]. Allen LA, Felker GM, Mehra MR, et al. Validation and potential mechanisms of red cell distribution width as a prognostic marker in heart failure[J]. *J Card Fail*, 2010, 16(3): 230-238.
- [4]. Al-Najjar Y, Goode KM, Zhang J, et al. Red cell distribution width: an inexpensive and powerful prognostic marker in heart failure[J]. *Eur J Heart Fail*, 2009, 11(12): 1155-1162.
- [5]. Aung N, Ling HZ, Cheng AS, et al. Expansion of the red cell distribution width and evolving iron deficiency as predictors of poor outcome in chronic heart failure[J]. *Int J Cardiol*, 2013, 168(3): 1997-2002.
- [6]. Bonaque JC, Pascual-Figal DA, Manzano-Fernández S, et al. Red blood cell distribution width adds prognostic value for outpatients with chronic heart failure[J]. *Rev Esp Cardiol (Engl Ed)*, 2012,65(7): 606-612.
- [7]. Cauthen CA1, Tong W, Jain A, et al. Progressive rise in red cell distribution width is associated with disease progression in ambulatory patients with chronic heart failure[J]. *J Card Fail*, 2012, 18(2): 146-152.
- [8]. Förhécz Z, Gombos T, Borgulya G, et al. Red cell distribution width in heart failure: prediction of clinical events and relationship with markers of ineffective erythropoiesis, inflammation, renal function, and nutritional state[J]. *Am Heart J*, 2009, 158(4): 659-666.
- [9]. Jackson CE, Dalzell JR, Bezlyak V, et al. Red cell distribution width has incremental prognostic value to B-type natriuretic peptide in acute heart failure[J]. *Eur J Heart Fail*, 2009, 11(12): 1152-1154.
- [10]. Jung C, Fujita B, Lauten A, et al. Red blood cell distribution width as a useful tool to predict long-term mortality in patients with chronic heart failure[J]. *Int J Cardiol*, 2011, 152(3): 417-418.
- [11]. Makhoul BF, Khourieh A, Kaplan M, et al. Relation between changes in red cell distribution width and clinical outcomes in acute decompensated heart failure [J]. *Int J Cardiol*, 2013, 167(4): 1412-1416.
- [12]. Oh J, Kang SM, Won H, et al. Prognostic value of change in red cell distribution width 1 month after discharge in acute decompensated heart failure patients[J]. *Circ J*, 2012, 76(1): 109-116.
- [13]. Pascual-Figal DA, Bonaque JC, Redondo B, et al. Red blood cell distribution width predicts long-term outcome regardless of anemia status in acute heart failure patients[J]. *Eur J Heart Fail*, 2009, 11(9):840-846.
- [14]. Rickard J, Kumbhani DJ, Gorodeski EZ, et al. Elevated Red Cell Distribution Width Is Associated With Impaired Reverse Ventricular Remodeling and Increased Mortality in Patients Undergoing Cardiac Resynchronization Therapy[J]. *Congest Heart Fail*, 2012, 18(2): 79-84.
- [15]. van Kimmenade RR, Mohammed AA, Uthamalingam S, et al. Red blood cell distribution width and 1-year mortality in acute heart failure[J]. *Eur J Heart Fail*, 2010, 12(2): 129-136.
- [16]. Zalawadiya SK, Zmily H, Farah J, et al. Red cell distribution width and mortality in predominantly African-American population with decompensated heart failure[J]. *J Card Fail*, 2011, 17(4): 292-298.
- [17]. Holmström A, Sigurjonsdottir R, Hammarsten O. An integrated multiple marker modality is superior to NT-proBNP alone in prognostic prediction in all-cause mortality in a prospective cohort of elderly heart failure patients[J]. *Eur Geriatr Med*, 2013, 6(4): 365-371.
- [18]. Simbaqueba C, Shrestha K, Patarroyo M, et al. Prognostic implications of relative hypochromia in ambulatory patients with chronic systolic heart failure[J]. *Congest Heart Fail*, 2013, 19(4): 180-185.
- [19]. Huang YL, Hu ZD, Liu SJ, et al. Prognostic value of red blood cell distribution width for patients with heart failure: a systematic review and meta-analysis of cohort studies [J]. *PLoS One*, 2014, 9(8):e104861.
- [20]. Borné Y, Smith JG, Melander O, et al. Red cell distribution width and risk for first hospitalization due to heart failure: a population-based cohort study[J]. *Eur J Heart Fail*, 2011, 13(12): 1355-1361.
- [21]. Tonelli M, Sacks F, Arnold M, et al. Relation Between Red Blood Cell Distribution Width and Cardiovascular Event Rate in People With Coronary Disease[J]. *Circulation*, 2008, 117(2): 163-168.
- [22]. Lippi G, Filippozzi L, Montagnana M, et al. Clinical usefulness of measuring red blood cell distribution width on admission in patients with acute coronary syndromes[J]. *Clin Chem Lab Med*, 2009, 47(3):353-357.
- [23]. Ma FL, Li S, Li XL, et al. Correlation of red cell distribution width with the severity of coronary artery disease: a large Chinese cohort study from a single center[J]. *Chin Med J (Engl)*, 2013, 126(6): 1053-1057.
- [24]. Sangoi MB, Guarda Ndos S, Rödel AP, et al. Prognostic value of red blood cell distribution width in the prediction of in-hospital mortality in patients with acute myocardial infarction[J]. *Clin Lab*, 2014, 60(8):1351-1356.

- [25]. QIN Qin, WANG Huaizhou, HU Zhide, et al. Predictive value of red blood cell wide distribution on the 28-day mortality of acute myocardial infarction[J]. *Chin J Clin Lab Sci*, 2012, 30(7): 515-517.
- [26]. Wang YL, Hua Q, Bai CR, et al. Relationship between red cell distribution width and short-term outcomes in acute coronary syndrome in a Chinese population[J]. *Intern Med*, 2011, 50(24):2941-2945.
- [27]. Lee JH, Yang DH, Jang SY, et al. Incremental predictive value of red cell distribution width for 12-month clinical outcome after acute myocardial infarction[J]. *Clin Cardiol*, 2013, 36(6): 336-341.
- [28]. Vaya A, Hernández JL, Zorio E, et al. Association between red blood cell distribution width and the risk of future cardiovascular events[J]. *Clin Hemorheol Microcirc*, 2012, 50(3): 221-225.
- [29]. Azab B, Torbey E, Hatoum H, et al. Usefulness of red cell distribution width in predicting all-cause long-term mortality after non-ST-elevation myocardial infarction[J]. *Cardiology*, 2011, 119(2): 72-80.
- [30]. Dabbah S, Hammerman H, Markiewicz W, et al. Relation between red cell distribution width and clinical outcomes after acute myocardial infarction[J]. *Am J Cardiol*, 2010, 105(3): 312-317.
- [31]. Sangoi MB, Da Silva SH, da Silva JE, et al. Relation between red blood cell distribution width and mortality after acute myocardial infarction[J]. *Int J Cardiol*, 2011, 146(2): 278-280.
- [32]. Uyarel H, Ergelen M, Cicek G, et al. Red cell distribution width as a novel prognostic marker in patients undergoing primary angioplasty for acute myocardial infarction[J]. *Coron Artery Dis*, 2011, 22(3): 138-144.
- [33]. Gul M1, Uyarel H, Ergelen M, et al. The relationship between red blood cell distribution width and the clinical outcomes in non-ST elevation myocardial infarction and unstable angina pectoris: a 3-year follow-up[J]. *Coron Artery Dis*, 2012, 23(5): 330-336.
- [34]. Arbel Y, Shacham Y, Finkelstein A, et al. Red blood cell distribution width (RDW) and long-term survival in patients with ST elevation myocardial infarction[J]. *Thromb Res*, 2014, 134(5): 976-979.
- [35]. Skjelbakken T, Lappégård J, Ellingsen TS, et al. Red cell distribution width is associated with incident myocardial infarction in a general population: the Tromsø Study[J]. *J Am Heart Assoc*, 2014, 3(4). pii: e001109.
- [36]. Borne Y, Smith JG, Melander O, et al. Red cell distribution width in relation to incidence of coronary events and case fatality rates: a population-based cohort study[J]. *Heart*, 2014, 100(14): 1110-1124.
- [37]. Ozsü S, Abul Y, Gunaydin S, et al. Prognostic value of red cell distribution width in patients with pulmonary embolism[J]. *Clin Appl Thromb Hemost*, 2014, 20(4): 365-370.
- [38]. Zorlu A, Bektasoglu G, Guven FM, et al. Usefulness of admission red cell distribution width as a predictor of early mortality in patients with acute pulmonary embolism[J]. *Am J Cardiol*, 2012, 109(1): 128-134.
- [39]. Adamsson Eryd S, Borné Y, Melander O, et al. Red blood cell distribution width is associated with incidence of atrial fibrillation[J]. *J Intern Med*, 2014, 275(1): 84-92.
- [40]. Su C, Liao LZ, Song Y, et al. The role of red blood cell distribution width in mortality and cardiovascular risk among patients with coronary artery diseases: a systematic review and meta-analysis[J]. *J Thromb Dis*, 2014, 6(10): 1429-1440.
- [41]. Lippi G, Targher G, Montagnana M, et al. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients[J]. *Arch Pathol Lab Med*, 2009, 133(4): 628-632.
- [42]. Vayá A, Sarnago A, Fuster O, et al. Influence of inflammatory and lipidic parameters on red blood cell distribution width in a healthy population[J]. *Clin Hemorheol Microcirc*, 2014. [Epub ahead of print].
- [43]. Pierce CN, Larson DF. Inflammatory cytokine inhibition of erythropoiesis in patients implanted with a mechanical circulatory assist device [J]. *Perfusion*, 2005, 20(2): 83-90.
- [44]. Lippi G, Targher G, Montagnana M, et al. Relationship between red blood cell distribution width and kidney function tests in a large cohort of unselected outpatients [J]. *Scand J Clin Lab Invest*, 2008, 68(8):745-748.