International Journal of Research in Medical Sciences
Abdinur MA et al. Int J Res Med Sci. 2017 Jun;5(6):2293-2300
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20172106

Original Research Article

Study of the correlation between red blood cell parameters in the patients with coronary heart disease and heart failure

Mohamed Abdirahman Abdinur, Xie Yong*, Kong Lingcai, Farah Abdidahir Mohamud, Jamac Abdidahir Mohamud, Sami Ullahi

Department of Cardiology, Northern Jiangsu People's Hospital, Clinical Medical College of Yangzhou University, Yangzhou, Jiangsu, China

Received: 14 April 2017
Accepted: 08 May 2017

***Correspondence:**
Dr. Xie Yong,
E-mail: xieyong@medmail.com.cn

ABSTRACT

Background: An increase of red blood cell distribution width (RDW) may have a certain effect to predict and evaluate the incidence and prognosis of coronary heart disease or chronic heart failure.
Methods: Our retrospective study covered a total of 230 patients that were included due to a variety of indications for coronary angiography. Patients were defined into 2 categories; CAG (-) group (n=100), and CAG (+) group (n=130). The 2 groups were compared in order to investigate the differences between their RDW and other factors related and then further were sub-dived into 4 groups according to the NYHA functional class.
Results: We observed that the patients in CAG (-) group 12.78±0.90; CAG (+) group 12.90±1.10 and had no significant difference in RDW. However higher RDW in patients with HF on all-cause was detected, 13.50±1.12 of group CAG (-)/NYHA II-IV and 13.39±1.31 of group CAG (+)/NYHA II-IV and there is statistical difference compared to group CAG (-)/NYHAI and group CAG (+)/NYHA I which were 12.80±0.47 and 12.87±0.69 respectively (P<0.001). There has no difference between the HF groups CAG (-)/NYHA II-IV and CAG (+)/NYHA II-IV group with (P=0.920), and no difference between groups without heart failure of (P=0.979).
Conclusions: Although RDW had no predictive ability of coronary heart disease, but the elevation of RDW was highly and independently associated with chronic HF. Therefore, RDW can be clinically used as a parameter in risk stratification of patients with HF.

Keywords: Coronary Heart Disease, Heart failure, Red blood cell distribution width

INTRODUCTION

Heart failure (HF) is a clinical condition where the heart is not able to meet the tissue need for oxygen delivery. Many definitions have been utilized the last decades. Current definition from European Society of Cardiology states that HF is a syndrome in which the patients should have symptoms of HF, typically shortness of breath and/or fatigue, signs of fluid retention and objective evidence of an abnormality of structure or function of the heart at rest.[1] The term chronic HF is applied for patients with persistent abnormalities of heart structure or function, Coronary heart disease is the most common cause of HF and accounts for the majority of patients.[2] Other important causes include valvular disease, cardiomyopathy, and hypertension. Chronic HF is a major public health issue with a prevalence of more than 23 million worldwide and is associated with significant morbidity and mortality.[3,4] The incidence increases with age. Prevalence in the developed world is found to be about 1% in the general population in persons aged around 50, rising to about 10% in persons aged above 80.

At 55 years of age, the lifetime risk of HF is estimated to 33% for men and 29% for women.[5] Despite the improvement in treatment options the last decades, the prognosis remains poor with 5-year mortality rates reported as high as 65%.[5]

Coronary heart disease and Chronic HF are a major public health concern in the world; each year, both of them causes a huge number of direct and indirect economic losses for many developed and developing countries, which is the ultimate outcome of disease progression in all patients with cardiovascular disease, is even greater for clinical and public investments in patients with HF. In the United States every 1000 people over the age of 65 in 10 patients with chronic HF, Projections display that by 2030, the entire cost of HF will rise almost 127% to $69.7 billion for every US adult. The costs related to treating HF comorbidities and HF exacerbations in youths are significant, totaling nearly $1 billion in inpatient costs, and may be rising.[6,7] Even today's progress in medical technology and the development of medicine, the prognosis of patients with HF variability is more serious. Therefore, it is extremely important to classify the risk stratification accurately and to distinguish the high-risk population and start effective evidence-based medical treatment according to the patient's condition. On the other hand, in improving the stratification of risk factors, identify new prognostic factors for further understanding of the pathophysiology of HF and find an effective treatment of great benefit. Clinicians must determine the condition of patients with HF and evaluate the prognosis, in order to evaluate the course of treatment.

Red cell distribution width is a measure of the variability in size of the circulation erythrocytes and could be looked at as the electronic equivalent to the anisocytosis judged from a peripheral blood smear. It gives the coefficient-of-variation of the RDW in percentage and thereby expresses the width of the volume curve. Traditionally, the measure was used in the differential diagnosis of anemia.[8] Due to fact that RDW turns into improved earlier than blood indicators, it is also helpful for early diagnosis of nutritional deficiency. Folic acid and B12 deficiencies will often present with high values of both MCV and RDW, while an iron deficiency anemia is characterized by a high RDW and low MCV. If blood cells are fragmented, agglutinated or dimorphic, this may also cause an elevation in RDW, and blood samples with elevated levels might need to be examined in a peripheral smear.

Over the last years, RDW has been associated with a vast number of diseases and both cause-specific and overall mortality. Associations include conditions affecting almost all parts of the body. The relation to chronic HF has also been described in an increasing fashion over the last few years. Felker GM and other relevant data in the analysis of the CHARM study found that RDW and chronic HF in patients with mortality and re-admission risk independent positive correlation; another set of data from the CARE study found that RDW was associated with the incidence of cardiovascular events in patients with CHF.[9,10] Subsequently, a number of related studies have been conducted to further research the relationship between RDW and cardiovascular disease.[11,12] The aim of this study was a preliminary understanding of the relationship between RDW and coronary heart disease and HF, and similarly, discusses the correlation between them and the associated mechanism.

METHODS

This study was conducted at Northern Jiangsu people's Hospital during the period from January 2015 to December 2016, which covered a total of 230 patients that were included due to a variety of indications for coronary angiography.

Grouping criteria

First, the patients were defined into 2 groups according to coronary angiography results as group CAG (-) and group CAG (+) (i.e. Coronary Heart Disease Group and Non-Coronary Heart Disease group); then, the 2 groups were further separated according to clinical manifestations, laboratory evaluations, echocardiography, and (NYHA functional class); the patients with CAG (-) and CAG (+) were further divided into 4 groups: cardiac functional Class I and cardiac functional Class II-IV group. Which are CAG (-)/NYHAI, CAG (-)/NYHAII-IV, CAG (+)/NYHAI and CAG (+)/NYHAII-IV (According to the WHO diagnostic standard; coronary angiography results suggest one or more major vascular stenosis), ≥50% for the CAG (+) group. whereas coronary angiography showed no stenosis or stenosis <50% for CAG (-) group. Chronic HF: according to the WHO diagnostic criteria, with relevant clinical manifestations, combined with laboratory evaluations and echocardiography).

Inclusion criteria

All patients who were admitted in the Department of Cardiology at Northern Jiangsu people's Hospital during in between January 2015 to December 2016 due to a variety of indications for coronary angiography, chronic HF ≥6 months, age ≥18 years old, <85 years old, within 24 hours after admission were conducted blood routine test, all individuals have been fluent in Chinese, and they are residents of Yangzhou city, China. Verbal consents have been acquired from all patients before the research procedures.

Exclusion criteria

- Any clinical data which was not complete (especially routine blood test, echocardiography, biochemical laboratory tests and other indicators of a serious missing).

- Patients a prior diagnosis of hematological diseases, such as aplastic anemia.
- Patients with severe liver dysfunction or malnutrition.
- Chronic renal insufficiency (uremia patients), the need for hemodialysis.
- History of malignant tumors, chemotherapy, radiotherapy and organ transplantation.
- Patients nearly 1 year, had history G.I. bleeding or hemorrhagic anemia;
- Patients nearly a month, had severe infections;
- Patients nearly three months had surgery operation;
- Patients nearly half a year have received a blood transfusion or blood donors.

Material collection

The results of routine blood and biochemical tests were received within 24 hours after admission. (Sample collection by the professional staff in accordance with the standard practice; and send to the laboratory in accordance with the routine procedures). Heart failure was categorized as (NYHA functional class) I-IV based on symptoms during varying activities. LVEF and LEVD were examined by an echocardiography, results are taken in one week before or after admission either in our hospital outpatients or inpatients (If the patient had multiple results, we used the data with the date of the closest result).

Observation parameters

Red blood cell distribution width (RDW, normal range 11.8-14.6%); hemoglobin concentration (Hb), hematocrit (HCT), mean corpuscular volume (MCV), NT-ProBNP; serum creatinine, BUN, total bilirubin, protein, albumin; left ventricular ejection fraction (LVEF), left atrial diameter (LAD) and left ventricular end-diastolic diameter (LEVDD).

Statistical analysis

SPSS 16.0 statistical software was used to analyze the data, the continuous data were expressed as mean±standard deviation (x±s), and categorical data were expressed as frequency and percentage (%), also, between the two groups of data, continuous data has used the t-test to compare differences between mean.

Classification data were utilized Chi-squared test, (χ^2 test) or Fisher's exact probability method to compare the difference between the composition ratios. Analysis of variance (ANOVA) was used to compare the difference of mean values between multiple groups; comparison between the two variables was used linear correlation analysis; screening of independently related factors was used multivariate, stepwise logistic regression analysis. P-value<0.05 was considered statistically significant.

RESULTS

The case characteristics

A total of 230 patients (Table 1) were enrolled in this study, including (155 i.e. 67.4%) patients were males and (75 i.e.32.6%) patients were females with an average age over 60 years. 100 Patients, among them, 55 participants were male and 45 patients were female, that have been ruled out from CHD after performed a CAG (-) group, and 130 participants, among them, 100 were male patients and 30 were female patients that were diagnosed as CHD after performed a CAG (+) group, There was no significant difference of RDW found between CAG (-) group and CAG (+) group, which were 12.78±0.90 and 12.90±1.10 respectively (P=0.376).

Table 1: Clinical data analysis of two hundred and thirty patients.

Parameters	Total (n=230)	CAG (-)		CAG (+)		P value
Cardiac functional class		**(NYHA I)**	**(NYHA Ⅱ-Ⅳ)**	**(NYHA I)**	**(NYHA Ⅱ-Ⅳ)**	
Selected cases (M/F)	230(155/75)	100(55/45)		130(100/30)		
RDW%	12.84±1.02	12.78±0.90		12.90±1.10		0.376
Number of cases(n)	230	50 (21.7)	50(21.7)	55(24)	75(32.6)	
Male n (%)	155 (67.4)	26(16.7)	29(18.7)	43(27.7)	57(36.8)	0.001
Female n (%)	75(32.6)	24 (32)	21(28)	12(16)	18(24)	
Age year	61.70±9.21	58.20±8.05	61.51±8.43	61.90±8.99	65.20±9.03	<0.023
DCM n%	10(4.3)	0(0)	10.(4.3)	0	0	
VHD n (%)	29(12.6)	1(0.4)	29(12.6)	0	0	
Other OHD n%	7(3.0)	2(0.8)	6(2.6)	0	0	
Hypertension n (%)	146 (63.5)	27(18.5)	26 (17.8)	37(25.3)	56(38.4)	0.006
DM n (%)	53(23.0)	4(1.7)	14(6.1)	15(6.5)	20(8.7)	0.118
Hyperlipidaemia n (%)	23(10)	6(2.6)	3(l.3)	7(3.1)	7(3.0)	0.825
Smoking history n (%)	77 (33.5)	15(6.5)	16(7)	18(7.8)	28 (12.2)	0.573

Abbreviations: DCM=Dilated Cardiomyopathy; VHD=Valvular Heart Disease; Other OHD=Other Organic Heart Disease.

Table 2: 230 cases of patients with their echocardiography and laboratory examination data.

Parameters	Total	CAG (-)		CAG (+)		P value
NYHA Class		NYHA I	NYHA Ⅱ-Ⅳ	NYHA I	NYHA Ⅱ-Ⅳ	
LVEF %	60.86±12.22	67.95±6.31	52.98±11.80	66.41±8.87	57.01±12.50	<0.05
LVEDD	52.93±8.28	47.14±4.78	59.60±8.70	47.89±4.79	52.30±7.81	<0.05
LAD mm	41.43±8.21	36.36±4.99	51.03±9.48	38.50±4.41	40.79±5.70	<0.05
NT-ProBNP pg/ml	966.87±2689.56	110.49±143.23	2276.86±3380.64	224.85±630.28	1255.28±616.07	<0.05
RBC*10"12/L	4.44±0.48	4.51±0.49	4.41±0.48	4.51±0.49	4.32±0.46	0.631
Hb g/dl	133.40±16.50	134.41±13.58	132.40±19.03	133.93±17.63	132.87±15.28	0.795
RDW %	13.14±0.98	12.80±0.47	13.50±1.12	12.87±0.69	13.39±1.31	0.001
MCV fl	90.50±4.20	90.36±3.19	91.59±3.89	89.51±4.60	90.55±4.49	0.434
HCT %	40.27±3.78	41.19±3.71	41.54±3.86	39.23±3.45	39.12±4.27	0.820
TB μmol/L	10.95±589	10. 48±7. 44	13.29±7.35	9.69±3.36	10.33±4.80	0.029
Pro g/L	69.52±7.61	69.91±5.99	69.31±7.16	69.89±7.25	68.95±8.78	0.441
Alb g/L	40.90±3.86	41.75±3.38	39.90±3.85	41.60±3.76	40.36±4.12	0.200
BUN mmol/L	6.36±2.08	5.61±1.64	7.15±2.03	5.98±1.71	6.71±2.48	<0.001
Cr μmol/L	83.13±39.15	73.74±17.41	90.21±53.89	82.79±4.81	85.78±36.49	0.059
UA μmol/L	360.75±112.93	339.99±106.99	400.22±129.14	336.90±100.81	368.53±114.81	0.003
ALT U/L	25.5±16.53	26.37±20.14	24.46±14.81	25.73±13.51	25.56±17.66	0.714
AST U/L	23.49±11.06	23.74±12.40	24.51±12.66	22.30±7.91	23.41±11.17	0.3915

Abbreviations: LVEF = Left ventricular ejection fraction; LVEDD = Left ventricular end-diastolic diameter; LAD = Left atrial diameter; RBC = Red blood cell; Hb = haemoglobin; RDW = Red blood cell distribution width; MCV = mean corpuscular volume; HCT = hematocrit; TB=total bilirubin; BUN = blood urea nitrogen; Cr = Creatinine; UA = uric acid; ALT = Alanine aminotransferase; AST = Aspartate aminotransferase.

Table 3: Differences between RDW in each case group.

	Groups	P value	95% CI	
			Lower bound	Upper bound
CAG (-)/NYHA I	CAG (-)/NYHAII-IV	0.000	-1.214	-0.354
	CAG (+)/NYHAI	0.979	-0.371	0.221
	CAG (+)/NYHAI I-IV	0.002	-1.009	-0.187
CAG (-)/NYHAII-IV	CAG (-)/NYHA I	0.000	0.414	1.216
	CAG (+)/NYHAI	0.000	0.230	1.181
	CAG (+)/NYHAI I-IV	0.920	-0.358	0.759

Case group 1 for the CAG (-)/NYHAI group a total of (50 i.e. 21.7%) patients, among them, (26 i.e.16.7%) patients were males and (24 i.e. 32%) patients were females, Case group 2 for the CAG (-)/NYHAII-IV group a total of (50 i.e.21.7%) patients, among them, (29 i.e.18.7%) patients were males and (21 i.e.28%) patients were females, Case group 3 for the CAG (+) /NYHA I a total of (55 i.e.24%) patients, among them, (43 i.e. 27.7%) patients were males and (12 i.e. 16%) patients were female, and Case group 4 for the CAG (+)/NYHAII-IV a total of (75 i.e. 32.6%) patients, among them, (57 i.e. 36.8%) patients were males and (18 i.e. 24) patients were females (Table 1). Continuous data were expressed as mean±standard deviation (x±s). There were statistically significant differences in gender, age among the groups. The male patients were significantly more than the female patients. The average age of the patients with HF was over 60 years (Table 1).

Table 2 shows that hemoglobin in CAG (-)/NYHAII-IV and CAG (+)/NYHAII-IV is lower than that of CAG (-)/NYHAI and CAG (+)/NYHAI, even the overall mean is lower, but the difference was not statistically significant (P>0.05). The LVEF of patients with Chronic HF was 52.98±11.80 and 57.01±12.50, respectively, which was significantly lower than that of CAG (-)/NYHAI 67.95±6.31 and CAG (+)/NYHAI group 66.41±8.87 with P<0.05). In addition, there were significant differences in LVEDD, LAD, NTpro-BNP, TB, BUN, and UA in patients with cardiac insufficiency (P<0.01) (Table 2).

Through one way ANOVA (Table 3), the RDW in CAG (-)/NYHAII-IV group and CAG (+)/NYHAII-IV group was significantly higher than that in patients without Cardiac insufficiency CAG (-)/NYHAI and CAG (+)/NYHAI (P<0.01). Among them, CAG (-)/NYHA I and CAG (-)/NYHA II-IV group and CAG (+)/NYHA II-IV, all had a significant differences (P<0.01), but, there were no difference between CAG(+)/NYHA I (P=0.979); While CAG (-)/NYHA II-IV group, CAG (-)/NYHA I and CAG(+)/NYHA I were significant difference (P<0.01), but there was no difference in CAG

(+)/NYHAII-IV with (P=0.920); RDW of each group shown in (Table 2). The correlation between Erythrocyte distribution width and Hb showed that the increase of RDW was negatively correlated with Hb (r=-0.261, P<0.02). RDW was also negatively correlated with LVEF, Pro, Alb (P<0.01). And NT-ProBNP, TB, BUN, UA, LVEDD, LAD were positively correlated (P<0.01). In our study, there was no statistically significant difference in the elevation of RDW and creatine (P<0.05) (Table 4).

Table 4: Correlation analysis of RDW with LVEF, Hb, HCT, MCV, NT-ProBNP, TB, CB, Pro, Alb, BUN, UA, LVEDD, and LAD.

Indicators	Pearson correlation coefficient (r)	P value	Indicators	Pearson correlation coefficient (r)	P value
LVEF	-0.211	0.001	Pro	-0.297	0.000
Hb	-0.261	0.001	Alb	-0.185	0.003
HCT	-0.149	0.019	BUN	0.223	0.000
MCV	-0.200	0.001	UA	0.168	0.008
NT-ProBNP	0.280	0.000	LVEDD	0.303	0.000
TB	0.163	0.010	LAD	0.281	0.000
CB	0.191	0.002			

See Table 2 for abbreviation.

Table 5: Independent factors such as age, LVEF, Hb, RDW, UA and Alb that associated with cardiac insufficiency.

Independent factors	Regression coefficient	Wald value	P value	OR value	95% CI for OR
Age	0.047	4.159	0.043	1.048	1.001-1.092
LVEF	-0.106	24.549	<0.001	0.901	0.869-0.939
LAD	0.132	14.971	<0.001	1.139	1.069-1.232
Hb	0.027	4.403	0.037	1.026	1.003-1.059
RDW	0.880	9.544	0.003	2.411	1.380-4.206
UA	0.213	4.772	0.030	1.240	1.021-1.505
Alb	-0.160	9.245	0.02	0.852	0.770-0.947

Taking NYHA I group as control group.

Since our study was different in CAG (-)/NYHA I and CAG (+)/NYHA I and CAG (-)/NYHA II-IV and CAG (+)/NYHA II-IV only in patients with coronary heart disease, Therefore, multivariate statistical analysis of cardiac insufficiency can be considered as the homogeneous whole of cardiac insufficiency. So in the case of multiple linear regression analysis, we grouped the 4 groups into NYHA functional class I and NYHAII-IV 2 groups for statistical (Table 5). After adjustment for other predictor and prognostic factors of HF such as, Age, Hb, LVEF, L AD, Alb and UA, Red blood cell distribution width still remains an independent factor that associated with chronic HF (regression coefficient=0.880, OR=2.411, P<0.01).

DISCUSSION

Cardiovascular disease, without a doubt, is an important public health problem; with Ischemic heart disease and stroke on top of the WHOs cause of death statistics.[13] Prevention and early intervention are crucial to decreasing these numbers. Except for genetic predisposition, gender, and age, many of the commonly known risk factors for cardiovascular diseases are modifiable. Such risk factors include smoking, physical activity, alcohol consumption, diet, overweight, hyperglycemia, hyperlipidemia and hypertension.[14,15] These can be controlled and treated with medication and/or by alteration of lifestyle. Identification of new risk factors is also an important step in the prevention of CHD and HF. Biomarkers able to predict cardiovascular outcomes can aid identification of subjects in need for early intervention, and thereby prevent fatal events. One such biomarker is red blood cell distribution width, which is a measure of the variability in size of the circulation erythrocytes. Over the last few years, the association between RDW and various disease outcomes has been studied broadly. Especially the association between RDW and cardiovascular diseases is described in detail. However, little is known with regard to the underlying mechanism for this observed relationship.

Heart failure is the ultimate outcome of cardiovascular disease such as coronary heart disease, cardiomyopathy, hypertension, valvular heart disease, etc. As the increasing incidence of cardiovascular diseases, the diagnosis and treatment of patients with HF have become a problem of a wider concern. Including how to accurately assess the risk stratification and prognosis of patients with heart failure, it is very important for clinicians and patients, to distinguish between high-risk

groups and to provide an effective treatment. Red blood cell distribution width is an inherent parameter in the routine blood test, traditionally; the measure is only used in the diagnosis and differential diagnosis of Anemia. In recent years, it has been found that it has great potential as a prognostic factor and risk stratification index for heart failure.[8,9] This research revealed that the increase of RDW is not related to the occurrence of coronary heart disease, so it cannot be used as a predictor of coronary heart disease and risk stratification indicators; In addition, our findings revealed that RDW increased with a variety of causes of heart failure was positively correlated, at the same time, similar to the CHARM and Duke studies, our correlation analysis also suggested that red blood cell distribution width and hemoglobin in was negatively correlated, and after adjustment of haemoglobin in the control group, RDW still remains an independent factor that associated with heart failure. In addition, present research results also revealed that red blood cell distribution width is also an independent maker currently accepted heart failure prognosis and stratification-related factors such as Age, EF value, left atrial diameter, haemoglobin, blood urea nitrogen and serum albumin. Moreover, combined with a prospective study of international databases.[6,16-19] We believe that RDW is associated with the progression of heart failure and can be used as a risk stratification and prognostic indicator for patients with HF.

The change of RDW reflects the heterogeneity of the red blood cell cycle; increased RDW may indicate that erythrocyte damage in the body, such as hemolytic or nutritional status, such as iron, folic acid, vitamin B12 deficiency, lack of erythropoietin production when renal insufficiency.[2,8] However, RDW in the case of the MCV is still in the normal range first reflects the size of the red blood cell volume and size vary significantly. So far, the exact mechanism of RDW and cardiovascular disease is not clear, the body's inflammatory state, iron metabolism disorders, oxidative stress, erythropoietin (EPO) deficiency and other factors can affect RDW. Therefore, the red blood cell distribution width may comprehensively reflect the development of the disease in a series of the pathophysiology of a variety of integrated mechanisms, including malnutrition, renal failure, liver congestion, inflammation response and so on.

Anemia-related mechanisms

In recent years, the relationship between anemia and the incidence of adverse events in cardiovascular disease is a hot topic in cardiovascular research, a series of hypotheses related to anemia and heart failure have been proposed, generally recognized, including oxidative stress, malnutrition, erythropoietin formation, etc. and the combined effects of the above mechanisms.[20] Red blood cells are rich in antioxidant factors, an increase in oxidative stress during anemia may lead to the release of antioxidant factors, resulting in a large number of free radicals in myocardial cell damage, thereby increasing the progress of HF. In addition, activation of the neuroendocrine system in patients with chronic heart failure leads to increased levels of norepinephrine, angiotensin II, arginine vasopressin, endothelin, thromboxane A2 and prostaglandin F in the blood vessels, vasoconstriction leads to renal ischemia, resulting in decreased erythropoietin synthesis, therefore reduced erythropoiesis eventually cause anemia.[21] And renal insufficiency eventually leads to Anemia caused by a decrease in EPO, and also we found that in RDW in patients with CHF is more closely associated with Glomerular filtration rate.[22]

The role of inflammatory factors

Inflammatory factors are prognostic factors for chronic heart failure, which may affect bone marrow hematopoiesis and Iron metabolism in vivo.[23,24] So the increase in RDW may reflect the inflammatory factor inhibition of the EPO-mediated mature red blood cells of the pathological process. Either it's through hemolysis, bleeding, anemia or some other condition causing a hypoxic state, the body will respond by producing/releasing erythropoietin. Normally, about 90% is synthesized in peritubular interstitial cells of the kidneys, and 10% is made in the liver. The hormone is produced in response to oxygen tension in the kidneys. Hypoxia leads to increased EPO production. EPO is considered the principle regulator of red blood cell production.[25] It is crucial for the final step in maturation erythroid cells.[25] EPO stimulates many steps in the maturation from stem cell to erythrocyte, including the late CFU GEMM (colony forming unit-granulocyte, erythroid, monocytes, and megakaryocyte) and BFU E (burst-forming unit erythroid), the pronormoblasts and the normoblasts.

The erythropoiesis is an important topic in understanding why the RDW differs both Intra-and inter-individually. Everything affecting the synthesis or function of the EPO will have some sort of impact on RDW. So will other factors affecting the erythropoiesis. The RDW measures the variation in the size of the circulating red blood cells but does not differentiate between mature erythrocytes and reticulocytes. Thereby, an increased release of reticulocytes will lead to an increased RDW due to the reticulocytes being larger in size than the mature erythrocytes. A reduced release of reticulocytes will have the opposite effect, by increasing the proportion of evenly-sized mature cells. All factors affecting the erythropoiesis, through EPO synthesis, affinity, or through other mechanisms, will have the potential to change RDW.

The pathophysiological mechanism of hepatic congestion in heart failure

Liver function damage is one of the complications of HF and is closely related to the poor prognosis of heart

failure.[26,27] Hepatic congestion is a part of the development process of heart failure disease, and in the liver congestion at the same time patients often accompanied by varying degrees of digestion and absorption dysfunction caused by Megaloblastic anemia or microcytic anemia, RDW rise may reflect liver congestion caused by Iron metabolism in the body, Folic acid, Vitamin Bl2 and other hematopoietic factors resulting Anisocytosis. In addition, the further development of late-stage hepatic congestion may be associated with hypersplenism, so that the destruction of red blood cells in the Spleen accelerates and morphological changes occur. Meanwhile, the spleen hyperthyroidism will make bone marrow immature red blood cell proliferation and differentiations are inhibited, resulting in circulatory red blood cell volume heterogeneity increased. Any of the above factors or a combination of multiple factors can affect the red blood cell volume distribution width. At the same time, RDW may also be more effective than hemoglobin directly reflects the relationship between the above mechanism and Heart failure, allowing clinicians can more accurately determine and evaluate the prognosis of patients, and then adjust the treatment plan. The routine blood test is the current clinical application widely used laboratory test index, which is simple, and inexpensive, routinely reported test and the application of RDW in the blood test parameters, this index was used preliminary evaluation prognosis of CHF, and also use a wide range of development and its advantages can be extensively accepted by the patients.

Present study had several limitations, first, this study was a retrospective case analysis and sample size was relatively small. Second, there are many influencing factors. Therefore we could not observe the causal link between the two, while chronic HF has many influencing factors, including age, ejection fraction, total bilirubin, lymphocyte count, creatinine, uric acid, type 2 diabetes, body mass index (MBI) and diastolic blood pressure increase correlates with poor prognosis of heart failure. Because there is no confrontation of all the mixed factors one by one comparison analysis, it is inevitable there is a certain bias. However, we hope to reduce the impact of bias by expanding the sample content and multiple stratification analysis, but the retrospective analysis of the study itself for the causal inference argument strength is low, Therefore, more large-scale prospective studies are needed to further clarify the evaluation and prediction of the RDW in chronic HF. Finally, the future research direction should be devoted to further understanding the pathophysiological mechanisms of red blood cell distribution width associated with chronic HF, the incidence and development of disease in patients with chronic heart failure have a better understanding.

CONCLUSION

Present findings suggest, that there was no correlation found between the changes of RDW and the development of coronary heart disease, but the increase of erythrocyte distribution width was highly correlated with chronic HF patients. Therefore, these finding agrees with previous researchers that the red blood cell distribution is a firm independent predictor of risk factors in patients with chronic HF and suggest an increased RDW may reveal an inflammatory stress and other factors. Meanwhile, after adjustment of other predictor and prognostic factors of Heart failure such as, Age, Hb, LVEF, LAD, Alb and UA; RDW still remained an independent factor that associated with chronic HF (regression coefficient=0.880, OR=2.411, P<0.01). However, little is known with regard to the underlying mechanism for this observed relationship. In addition, further observations of how and why this indicator relates to chronic HF and study of related-mechanism will allow us to understand better the pathophysiology of heart failure.

ACKNOWLEDGEMENTS

Authors would like to express sincere thanks to all the doctors and nurses of Cardiology department for their constructive suggestions and appropriate guidance during in this study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Abdinur MA, Yong X, Lingcai K, Mohamud FA, Mohamud JA, Ullahi S. Study of the correlation between red blood cell parameters in the patients with coronary heart disease and heart failure. Int J Res Med Sci 2017;5:2293-300.