Correlation between Red Blood Cell Distribution Width (RDW) andDegrees of Severity in Coroner Heart Disease (CHD) Patients Based on Syntax I Score

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Abstract

Coronary heart disease (CHD) is one of the most common causes of death in the world. CHD is caused by the narrowing of the arteries of the heart due to a buildup of fat on the vessel walls (atherosclerosis), therefore inhibiting blood flow to organs. Red blood cell distribution width (RDW) represents the variability of red blood cell size and has been shown to correlate with the incidence of atherosclerosis. RDW is also often used to identify diseases associated with heart failure. The aim of this study was to assess the relationship between the level of RDW and the severity in CHD patients. A cross-sectional study was carried out on 62 patients from July to December 2020 at Dr. Zainoel Abidin Hospital, Banda Aceh. RDW level was obtained from the patient's medical record and divided into two categories (group $1 < 13.0295$ and group $2 > 13.029\%$). Severity of CHD patients was calculated using the SYNTAX I score and divided into three categories (low, moderate, and high). The correlation between the baseline characteristics, laboratory results, RDW level, and severity of CHD was assessed statistically at a 95% confidence level. The majority of patients with CHD were men aged 56-65 years and had BMI obesity I and hypertension. Patient baseline characteristics (gender, age, body mass index, history of hypertension and diabetes) and laboratory results did not have a significant relationship with the RDW level and the severity of CHD ($p > 0.05$). The correlation value between RDW level and severity of CHD is $p = 0.435$ which indicated no significant relationship between them.

Keywords: Coronary heart disease, red blood cell distribution width, CHD, RDW, SYNTAX I score

1. Introduction

Coronary heart disease (CHD) is the leading cause of death in the world and increased since 1970, with a mortality rate of one in five for men and one in six for women. CHD is one of the leading causes of death from cardiovascular disease in the United States (45.1%), followed by stroke (16.5%), heart failure (8.5%), hypertension, high blood pressure (9.1%), arterial disease (3.2%), and other cardiovascular diseases [1]. In Indonesia, according to the Basic Health Research (RISKESDAS), CHD is the third leading cause of death after stroke and hypertension [2].

CHD occurs when the arteries narrow and harden due to the accumulation of fat/plaque on the walls of blood vessels (atherosclerosis) [3]. Atherosclerosis causes disturbances in the blood circulation system to organs or tissues and causes endothelial cell damage [4]. CHD risk factors are determined by modifiable factors such as smoking, physical activity, diet, dyslipidemia, obesity, hypertension and diabetes mellitus and non-modifiable factors as age and heredity [1]. The red blood cell distribution width (RDW) represents the variability of red blood cell size and is routinely evaluated as part of an automated full blood count [5]. The role of RDW has been widely recognized in screening for iron deficiency anemia, but currently RDW is known to be able to predict mortality in other clinical conditions such as coronary artery disease, heart failure, acute pancreatitis, infective endocarditis and peritoneal dialysis [6].

Several studies reported that RDW level are significantly associated with stable heart disease and used as an identification of further risks in patient [3, 7, 8]. Sensitive biomarker is important to diagnosis or prognose the diseases [9-16]. High RDW level can increase the atherosclerosis incidence which is the main cause of CHD [17]. However, the relationship between RDW level and CHD is still very limited. The aim of the present study was to prospectively investigate the potential correlation of RDW level and severity of CHD in Indonesia populations.

2. Methods

A cross-sectional study was conducted among CHD patients at Dr Zainoel Abidin Hospital, Banda Aceh, from January to November 2018. The patients aged over or equal to 18 years and diagnosed with CHD based on

angiography and electrocardiography (ECG) results were included in the study. On the other hand, the patients diagnosed with anemia, chronic kidney failure, autoimmune, congestive heart failure, and three months of blood transfusion record were excluded. This study has ethical approval from the Institutional Review Board of the Faculty of Medicine, Universitas Syiah Kuala/Dr Zainoel Abidin Hospital Banda Aceh (02/EA/FK- RSUDZA/2019).

There were two variables used in this study: independent (severity of CHD) and dependent (Red blood cell width (RDW). CHD patients were sampled using the consecutive sampling method. Baseline characteristic such as gender, age, body mass index (BMI), hypertension, and diabetes record was collected and assessed. RDW level was measured using a hematology analyzer with a mean level of RDW divided into two groups (1. <13.0295 and 2. >13.029%). The degree of severity in CHD patients was measured using Synergy between percutaneous coronary intervention with taxus and cardiac surgery I (SYNTAX I) score and categorized into: low (SYNTAX I score: <22), moderate (SYNTAX I score: 23-32) and high (SYNTAX I score: > 32)[18].

Data analysis was performed using SPSS software. Relationship between age, gender and BMI with RDW level and severity of CHD was assessed using fisher exact test and the relationship between hypertension and diabetes with RDW level and severity of CHD was assessed using chi-square test. Relationship between laboratory test result and RDW level was assessed using independent sample t test (normal distribution data) and Mann-Whitney test (abnormal distribution data). Relationship between laboratory test result and severity of CHD was assessed using ANOVA test (normal distribution data) and Kruskal-Wallis H test (abnormal distribution data). RDW level and severity of CHD correlation was assessed using Spearman rank correlation test with a 95% confidence level.

3. Results

In table 1, the distribution of patients in RDW group 2 (55.6%) was more than RDW group 1 (44.4%) for male patients, while more female patients were in RDW group 1 (62.5%). More than half of CHD patients aged >55 years, 52.5% of them had RDW group 1. In the BMI variable, patients were generally categorized as obese 1 with RDW group 1 (52.1%), and only one patient had a low BMI and was included in RDW group 2. CHD patients had more history of hypertension, and 47.6% of them were in RDW group 1, and the others (52.4%) belonged to group 2. more CHD patients did not have a history of diabetes with RDW group 2. In addition, only 13 patients had a history of diabetes, and 8 had an RDW group 2. Based on the Fisher and Chi-square test, the baseline characteristics of the patients did not have a significant relationship with the RDW category ($p > 0.05$). Most of the CHD patients in the study had a low severity, and only patients with category II obesity were more dominant with moderate and high severity. Based on Fisher's exact test and chi-square test, baseline characteristics also did not significantly correlate with the severity of CHD ($p>0.05$).

Table 1. Relationship between baseline characteristic, RDW value, and SYNTAX I score

| Variable | RDW n (%) | | | SYNTAX I score n (%) | | | |
	Group 1 (<13.029)	Group 2 (>13.029)	P-value	Low	Moderate	High	P-value
Gender n			0.456[a]				0.880[a]
Male	24 (44.4)	30 (55.6)		29 (53.7)	16 (29.6)	9 (16.7)	
Female	5 (62.5)	3 (37.5)		4 (50)	3 (37.5)	1 (12.5)	
Age			0.616[a]				0.793[a]
< 55 years	8 (36.4)	14 (63.6)		14 (63.7)	6 (27.3)	2 (9)	
> 55 years	21 (52.5)	19 (47.5)		19 (47.5)	13 (32.5)	8 (20)	
BMI (Kg/m^2)			0.654[a]				0.092[a]
Low	0 (0)	1 (100)		1 (100)	0 (0)	0 (0)	
Normal	7 (43.8)	9 (56.3)		10 (62.5)	5 (31.3)	1 (6.3)	
High	9 (52.9)	8 (47.1)		8 (47.1)	3 (17.6)	6 (35.3)	
Obesity I	12 (52.1)	11 (47.8)		13 (56.5)	9 (39.1)	1 (4.3)	
Obesity II	1 (20)	4 (80)		1 (20)	2 (40)	2 (40)	
Hypertension			0.847[b]				0.406[b]
No	9 (45)	11 (55)		10 (50)	5 (25)	5 (25)	
Yes	20 (47.6)	22 (52.4)		23 (54.8)	14 (33.3)	5 (11.9)	
Diabetes			0.499[b]				0.703[b]
No	24 (49)	25 (51)		27 (55.1)	15 (30.6)	7 (14.3)	
Yes	5 (38.5)	8 (61.5)		6 (46.3)	4 (21.1)	3 (23.1)	

[a] Fisher exact test, [b] Chi-Square test

Based on table 2, all laboratory variables except MCH had no significant difference between RDW groups 1 and 2 as indicated by p-value (p>0.05), while the MCH variable had p=0.02. In severity of CHD, all laboratory variables had p-values greater than 0.05. The result showed laboratory variables did not have a significant correlation to the low, medium, and high severity categories

Table 2. Relationship between laboratory test result, RDW value, and SYNTAX I score

Variable	RDW (Mean ± SD)		P-value	SYNTAX I score (Mean ± SD)			P-value
	Group 1 (<13,029)	Group 2 (≥13,029)		Low	Moderate	High	
HGB (g/dL)	14.24 ± 1.11	14.32 ± 0.97	0.755[a]	14.41 ± 1.09	14.02 ± 1.01	14.37 ± 0.82	0.395[c]
HCT (%)	41.52 ± 3.10	42.26 ± 2.92	0.333[a]	42.23 ± 2.91	41.21 ± 3.38	42.20 ± 2.62	0.479[c]
RBC (10^6/mm³)	4.83 ± 0.44	5.03 ± 0.47	0.092[a]	4.93 ± 0.41	4.92 ± 0.52	4.97 ± 0.56	0.957[c]
WBC (10^3/mm³)	8.86 ± 2.30	9.00 ± 2.73	0.955[b]	9.04 ± 2.86	8.72 ± 2.00	9.00 ± 2.40	0.989[d]
PLT (10^3/mm³)	244.17 ± 54.84	274.33 ± 139.32	0.320[b]	243.27 ± 52.96	297.58 ± 177.03	245.20 ± 55.02	0.425[d]
MCV (fl)	86.10 ± 4.27	82.94 ± 10.91	0.245[b]	85.64 ± 3.07	81.83 ± 14.17	85.30 ± 6.43	0.717[d]
MCH (pg)	29.62 ± 1.56	28.63± 1.67	0.020[a]	29.27 ± 1.40	28.69 ± 1.67	29.30 ± 2.50	0.409[d]
MCHC (g/dL)	34.47 ± 1.38	34.15 ± 1.06	0.219[b]	34.36 ± 1.11	34.14 ± 1.50	34.40 ± 1.07	0.692[d]
MPV (fl)	9.58 ± 1.14	9.78 ± 0.72	0.631[b]	9.70 ± 0.87	9.59 ± 1.22	9.82 ± 0.44	0.552[d]
Creatinine (mg/dL)	1.05 ± 0.25	1.15 ± 0.33	0.196[a]	1.08 ± 0.32	1.16 ± 0.27	1.08 ± 0.28	0.637[c]
Random Blood Sugar (RBS) (mg/dL)	151.10 ± 49.05	159.79 ± 79.68	0.582[b]	146.42 ± 59.74	165.37 ± 73.49	168.10 ± 77.56	0.440[d]

[a] Independent sample t test, [b] Mann-Whitney test, [c] Anova test, [d] Kruskal-Wallis test

The distribution of CHD patients based on RDW level and CHD severity is presented in Table 3. A total of 33 (53.2%) CHD patients in this study had low severity, 19 (30.6%) moderate, and ten (16.1%) high. Meanwhile, based on the RDW level, 29 patients (46.8%) were in the RDW group 1, and 33 patients (53.2%) were in group 2. The correlation between the RDW level and the severity of CHD was measured using the Spearman test, and a correlation value of 0.101 was obtained with p=0.435 (Table 3). These results showed a positive but insignificant correlation value (p> 0.05).

Table 3. Relationship between RDW and SYNTAX I score

Variable		RDW n (%)		Correlation Value	P-value
		Group 1 (<13.029)	Group 2 (<13.029)		
SYNTAX I score	Low	17 (27.4)	16 (25.8)	0.101	0.435
	Moderate	8 (12.9)	11 (17.7)		
	High	4 (6.5)	6 (9.7)		

4. Discussion

In this study, there were more male CHD patients than women, with the majority being elderly (56-65 years). Based on previous reports, in 2010, men aged 40-70 years were more at risk for CHD than women [19]. Patients also had more hypertension which is a major risk factor for CHD. Patients without cardiovascular disease generally had low systolic pressure (down to 90-114 mmHg) and low diastolic pressure (down to 60-74 mmHg) [20]. Diabetes is another factor that affects CHD patients and occurs in patients with old age (≥65 years)[21]. However, the study showed inconsistent results because the population under 65 years was observed. Obesity is also an independent

factor in the development of CHD [1]. More than 50% of patients with CHD were overweight or obese. Weight loss can reduce the number of major risk factors, such as hypertension, dyslipidemia, and diabetes mellitus [22]

In general, the baseline characteristics of the patients in this study did not have a significant correlation with the RDW level. An independent sample t-test was applied to assess the significant relationship between RDW level and gender. It was found that there was no significant correlation between them (p>0.05) [23]. Other study also reported that BMI and diabetes did not significantly correlate with the RDW level [24]. However, an analysis of hypertension and age with RDW level contrasted results with previous studies. The different results of this study are due to the number of samples being smaller and different categories of age group [23, 25, 26]

The relationship between the severities of CHD and the patient's baseline characteristics also did not show a significant relationship. Previous studies showed that age, BMI, and diabetes potentially caused CHD but were not correlated with severity [27, 28]. In contrast to other studies, hypertension and age did not show a correlation with the severity of CHD [27]. This difference in results is due to differences in patient severity groupings and a larger patient population with a more diverse age range. Currently, there is no research that links gender to the severity of CHD. This study showed men had a higher severity than women. Cases of death in male CHD patients are more than in females. Men dealing with stressful events are less adaptive physiologically, behaviorally, and emotionally which contributes to an increase in the severity of CHD[29].

Overall, laboratory variables did not show a correlation between RDW level and the severity of CHD. RDW is a numerical measurement of variations in the size of erythrocytes. RDW is a routine parameter of the complete blood count (CBC) used to diagnose anemia [5]. A previous study showed results different from our findings. Higher levels of RDW (>14.4%) showed a significant correlation with laboratory variables [30]. In this study, the grouping of RDW level was in the range of 12%-14%, which may be a factor in the results' difference. The RDW is useful when determining microcytic anemia, particularly iron deficiency anemia (high RDW, normal to low MCV) [6].

The final result of this study was no significant correlation between RDW level and the severity of CHD patients. This study was contrary to other studies where 6737 respondents showed a relationship between RDW and CHD patients [31]. A high level of RDW is a risk for heart failure, cardiovascular events, and causes of death in patients with previous myocardial infarction [2]. Our study used an observed RDW level of <15%, whereas patients prone to chronic CHD disease had a mean RDW level of >15%. The role of RDW in cardiovascular disease is associated with decreased red blood cell turnover. A high RDW level causes the red blood cell size to decrease gradually and reduces the turnover of red blood cells in circulation [32].

5. Conclusion

Our findings found no significant correlation between baseline patient characteristics and laboratory results on RDW and the severity of CHD. In addition, the Spearman rank correlation test showed that RDW did not significantly correlate with the severity of CHD. For further research, it is expected to use a larger number of samples and a wider distribution of samples for each degree of severity and level of RDW to ensure the results are more representative.

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References

1. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das SR, Deo R, de Ferranti SD, Floyd J, Fornage M, Gillespie C et al: Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. Circulation 2017, 135(10):e146-e603.
2. Hussain MA, Al Mamun A, Peters SA, Woodward M, Huxley RR: The Burden of Cardiovascular Disease Attributable to Major Modifiable Risk Factors in Indonesia. J Epidemiol 2016, 26(10):515-521.
3. Nagula P, Karumuri S, Otikunta AN, Yerrabandi SRV: "Correlation of red blood cell distribution width with the severity of coronary artery disease-A single center study". Indian Heart J 2017, 69(6):757-761.
4. Davignon J, Ganz P: Role of endothelial dysfunction in atherosclerosis. Circulation 2004, 109(23 Suppl 1):III27-32.
5. Tonelli M, Sacks F, Arnold M, Moye L, Davis B, Pfeffer M, for the C, Recurrent Events Trial I: Relation Between Red Blood Cell Distribution Width and Cardiovascular Event Rate in People With Coronary Disease. Circulation 2008, 117(2):163-168.

6. Lippi G, Targher G, Montagnana M, Salvagno GL, Zoppini G, Guidi GC: Relationship between red blood cell distribution width and kidney function tests in a large cohort of unselected outpatients. Scand J Clin Lab Invest 2008, 68(8):745-748.

7. Felker GM, Allen LA, Pocock SJ, Shaw LK, McMurray JJ, Pfeffer MA, Swedberg K, Wang D, Yusuf S, Michelson EL et al: Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank. J Am Coll Cardiol 2007, 50(1):40-47.

8. Akin F, Kose N, Ayca B, Katkat F, Duran M, Uysal OK, Arinc H: Relation between red cell distribution width and severity of coronary artery disease in patients with acute myocardial infarction. Angiology 2013, 64(8):592-596.

9. Sarengat R, Islam MS, Ardhi MS: Correlation of neutrophil-to-lymphocyte ratio and clinical outcome of acute thrombotic stroke in patients with COVID-19. Narra J 2021, 1(3):e50.

10. Mahmud AA, Anu UH, Foysal KA, Hasan M, Sazib SM, Ragib AA, Taher AB, Hossain MS, Islam MS, Hossain MS: Elevated serum malondialdehyde (MDA), insulin, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and thyroid-stimulating hormone (TSH), and reduced antioxidant vitamins in polycystic ovarian syndrome patients. Narra J 2022, 2(1).

11. Zahra Z, Ramadhani CT, Mamfaluti T, Pamungkas SR, Firdausa S: Association between depression and HbA1c levels in the elderly population with type 2 diabetes mellitus during COVID-19 pandemic. Narra J 2022, 2(1).

12. Lorena C, Hamzah H, Maulydia M: Accuracy Comparison of Endotracheal Tube (ETT) Placement Using Chula Formula With Manubrium Sternal Joint (MSJ) Formula. Indonesian Journal of Anesthesiology and Reanimation 2021, 3(2):54-61.

13. Mudatsir M, Fajar JK, Wulandari L, Soegiarto G, Ilmawan M, Purnamasari Y, Mahdi BA, Jayanto GD, Suhendra S, Setianingsih YA: Predictors of COVID-19 severity: a systematic review and meta-analysis. F1000Research 2020, 9.

14. Harapan H, Fajar JK, Supriono S, Soegiarto G, Wulandari L, Seratin F, Prayudi NG, Dewi DP, Monica Elsina MT, Atamou L: The prevalence, predictors and outcomes of acute liver injury among patients with COVID-19: A systematic review and meta-analysis. Reviews in Medical Virology 2022, 32(3):e2304.

15. Al-Farabi MJ, Nugraha RA, Marsudi BA, Azmi Y: Biomarkers of endothelial dysfunction and outcomes in coronavirus disease 2019 (COVID-19) patients: A systematic review and meta-analysis. Microvascular research 2021, 138:104224.

16. Witarto AP, Witarto BS, Putra AJE, Pramudito SL, Rosyid AN: Serum Krebs von den Lungen-6 for Predicting the Severity of COVID-19 Lung Injury: A Systematic Review and Meta-Analysis. Iranian Biomedical Journal 2021, 25(6):381.

17. Soderholm M, Borne Y, Hedblad B, Persson M, Engstrom G: Red cell distribution width in relation to incidence of stroke and carotid atherosclerosis: a population-based cohort study. PLoS One 2015, 10(5):e0124957.

18. Ong AT, Serruys PW, Mohr FW, Morice MC, Kappetein AP, Holmes DR, Jr., Mack MJ, van den Brand M, Morel MA, van Es GA et al: The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery (SYNTAX) study: design, rationale, and run-in phase. Am Heart J 2006, 151(6):1194-1204.

19. Writing Group M, Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, Ferguson TB, Ford E, Furie K et al: Heart disease and stroke statistics--2010 update: a report from the American Heart Association. Circulation 2010, 121(7):e46-e215.

20. Weber T, Lang I, Zweiker R, Horn S, Wenzel RR, Watschinger B, Slany J, Eber B, Roithinger FX, Metzler B: Hypertension and coronary artery disease: epidemiology, physiology, effects of treatment, and recommendations : A joint scientific statement from the Austrian Society of Cardiology and the Austrian Society of Hypertension. Wien Klin Wochenschr 2016, 128(13-14):467-479.

21. Carnethon MR, Biggs ML, Barzilay J, Kuller LH, Mozaffarian D, Mukamal K, Smith NL, Siscovick D: Diabetes and coronary heart disease as risk factors for mortality in older adults. Am J Med 2010, 123(6):556 e551-559.

22. Ades PA, Savage PD: Obesity in coronary heart disease: An unaddressed behavioral risk factor. Prev Med 2017, 104:117-119.

23. Bilal A, Farooq JH, Kiani I, Assad S, Ghazanfar H, Ahmed I: Importance of Mean Red Cell Distribution Width in Hypertensive Patients. Cureus 2016, 8(11):e902.

24. Ferreira IB, Lima E, da Silva NC, Prestes IV, Pena GDG: Combination of red blood cell distribution width and body mass index (COR-BMI) predicts in-hospital mortality in patients with different diagnoses? PLoS One 2019, 14(7):e0219549.

25. Hoffmann JJ, Nabbe KC, van den Broek NM: Effect of age and gender on reference intervals of red blood cell distribution width (RDW) and mean red cell volume (MCV). Clin Chem Lab Med 2015, 53(12):2015-2019.

26. Zheng LH, Liu SY, Hu F, Hu ZC, Shen LS, Wu LM, Yao Y: Relationship between red blood cell distribution width levels and atrial fibrillation in hypertensive patients. J Geriatr Cardiol 2020, 17(8):486-494.

27. Canat L, Cicek G, Atis G, Gurbuz C, Caskurlu T: Is there a relationship between severity of coronary artery disease and severity of erectile dysfunction? Int Braz J Urol 2013, 39(4):465-473.

28. Niraj A, Pradhan J, Fakhry H, Veeranna V, Afonso L: Severity of coronary artery disease in obese patients undergoing coronary angiography: "obesity paradox" revisited. Clin Cardiol 2007, 30(8):391-396.

29. Weidner G: Why do men get more heart disease than women? An international perspective. J Am Coll Health 2000, 48(6):291-294.

30. Li J, Yang X, Ma J, Gong F, Chen Q: Relationship of Red Blood Cell Distribution Width with Cancer Mortality in Hospital. Biomed Res Int 2018, 2018:8914617.

31. Akın F, Köse N, Ayça B, Katkat F, Duran M, Uysal OK, Arinc H: Relation between red cell distribution width and severity of coronary artery disease in patients with acute myocardial infarction. Angiology 2013, 64(8):592-596.

32. Danese E, Lippi G, Montagnana M: Red blood cell distribution width and cardiovascular diseases. J Thorac Dis 2015, 7(10):E402-411.