THE ASSOCIATION BETWEEN INCREASE RED BLOOD CELL DISTRIBUTION WIDTH VALUE AND INCREASE NUMBER OF CORONARY ARTERY LESIONS IN SANGLAH GENERAL HOSPITAL, BALI

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Abstract

Background : Coronary Artery Disease (CAD) is leading cause of death worldwide. In 2013 there were approximately 54 million deaths globally and 32% of these deaths were attributable to cardiovascular disease (CVD). The majority of these CVD deaths were either CAD or cerebrovascular disease. There are extensive researches on inflammatory biomarkers to predict the severity of CAD by looking at the number of coronary artery lesions which correlated with high mortality and morbidity. Red blood cel distribution width (RDW) is routinely assessed as one of the component of complete blood count and can also act as inflammatory biomarker. This study was aimed to investigate the potential association between RDW and increase number of coronary artery lesions.

Method : This research is an analytic study with cross-sectional design. Secondary data were taken from medical record at Sanglah General Hospital, Bali in 2016. A total sample of 196 patients with CAD had RDW measured at baseline examination and the vessel score was assessed during coronary angiography. The vessel score was categorized into single vessel disease and multi vessel disease (≥ 2 significant coronary artery lesions). Data were analyzed using univariate, bivariate, and multivariate analysis.

Result : From total of 196 samples, 87.2% were males with age range between 34 and 79 years old. We used median as the cut-off point of RDW (median: 12.27±1.36). Among 196 CAD patients, 49% patients have high RDW value (>12.27%). We found a significant correlation between high RDW value and increase number of vessel score with OR 3.4 (95% CI from 1.294 to 8.940). In multivariate analysis, RDW was a predictor of increase number of coronary artery lesions (p=0.013) with adjusted OR 3.115 (95% CI from 1.174 to 8.253).

Conclusion : Increase baseline of RDW is a strong and independent predictor of increase coronary artery lesions in patients with CAD. Therefore, RDW may be used for the prediction and identification of cardiac risks in CAD patients.

Keywords : red blood cell distribution width (RDW), coronary artery disease, vessel score, coronary artery lesions

Introduction

Cardiovascular disease (CVD) is one of the most cause of death worldwide. In 2015, there was a sharp increase in mortality rate of CVD to more than 30% deaths in which 17.7 million of 57 million global deaths were caused by CVD and 7.4 million deaths were attributable to coronary artery disease (CAD).[1] In Indonesia alone, CVD is the number one cause of death in non-communicable disease. Based on Basic Health Research (RISKESDAS)'s data in 2013, approximately 2.650.340 people suffers from CAD. [2]

CAD is charaterized by necrosis and myocardiocal ischemia which is caused by atherosclerotic plaque formation. This atherosclerotic plaque will then lead to imbalance of between the need for oxygen and blood supply to the heart. Risk factos such as dyslipidemia, diabetes mellitus and smoking cause endothelial inflammatory process.[3] Endothelial dysfunction and persistent inflammatory process will result in migration of low density lipoprotein (LDL) into the intima of coronary artery and cause blockage.[4] Several blockage in coronary artery results in poorer prognosis of the patients.

Because of the inflammatory nature of CAD, extensive researches are conducted to find a sensitive yet spesific biomarker to predict morbidity and mortality. Unfortunately, some of those biomarkers are expensive and not widely available. Therefore, there is a need to find an accurate yet cheaper inflammatory biomarkers. One of those inflammatory biomakers is red blood cell distribution width (RDW) value. In previous studies, higher RDW level is associated with poorer prognosis in patient with heart failure, cancer and even respiratory failure.[5, 6, 7] RDW is a measure of variability of circulatory erythrocytes. Increased in RDW is equivalent to anysocytosis in peripheral blood smear.[7] Both severity and complexity of CAD had been linked to higher RDW levels.

Method

In this analytical observational study with cross sectional approach, a total 196 patients who presented with AMI and had underwent PCI and had complete blood count measured at admission between January 2016 until December 2016 in Integrated Heart Service in Sanglah General Hospital, Bali were included in this study. The inclusion criteria were: presented within 12 hours from the onset of typical chest pain, had ST-segment elevation 1 mm or greater in two contiguous electrocardiographic leads, had primary percutaneous coronary intervention (PCI), had complete medical record which consists of age, hypertension, gender, complete blood count, diabetes mellitus history and coronary angiography result. If patients' data failed to meet the inclusion criteria, they would be excluded. Complete blood count was measured at first admission and vessel score from coronary angiography data was categorized into single vessel and multiple vessel disease if patients had ≥2 more occluded vessels.

Data were then analyzed using IBM SPSS Statistics version 25. For bivariate analysis, data were analyzed using Mann-Whitney test to see the correlation between independent variables and vessel score. Data which showed significant correlation were then categorized into high and low group based on their respective median. Afterwards, Pearson-chi square was used to determine the odds ratio (OR), p value and 95% confidence interval (CI) between independent variable, control variable and dependent variable. In multivariate analysis, logistic regression test was conducted to obtain the adjusted OR for significant variables which associated with vessel score.

Result

The demographic charactheristics of patients are displayed in Table 1.

Table 1. Research Subjects Characteristics

	Total	
	n (196)	**%**
Age (mean ± SD)	58.12 ± 8.923	
Male >45 y.o, Female >55 y.o	176	89.8
Male <45 y.o, Female <55 y.o	20	10.2
Gender		
Male	171	87.2
Female	25	12.8
Hypertension		
Yes	110	56.1
No	86	43.9
Diabetes Mellitus		
Yes	23	11.7
No	173	88.3
Smoking		
Yes	99	50.5
No	97	49.5
Vessel Score		
Single vessel disease	25	12.8
Multiple vessel disease	171	87.2

Table 2. Bivariate Analysis on CBC data and other risk factors on increase of vessel score

	Normal Value	Single Vessel **n = 25**	Multiple Vessel **n = 171**	P value
Age		56 (34-71)	59 (36-79)	0.041*
Gender				0.447
Male		23	148	
Female		2	23	
Hypertension				0.382
Yes		12	98	
No		13	73	
Diabetes Mellitus				0.536
Yes		2	21	
No		23	150	
Smoking				0.016*
Yes		7	92	
No		18	79	
WBC (10μ/μL)	4.1 – 11.0	7.59 (5.2-16.4)	8.13 (4.4-18.7)	0.382
Neutrophil (10μ/μL)	2.50 – 7.50	4.2 (2.4-14.24)	4.9 (2.1-14.3)	0.391
Basophil (10μ/μL)	0.0 – 0.1	0.07 (0.03-0.23)	0.07 (0.02-0.15)	0.975
Eosinophil (10μ/μL)	0.0 – 0.5	0.21 (0.0-1.41)	0.29 (0-2.81)	0.047*
Lymphocyte (10μ/μL)	1.0 – 4.0	2.31 (0.92-3.4)	2.12 (0.4-5)	0.708
Monocyte (10μ/μL)	0.1 – 1.2	0.58 (0.4-1.0)	0.6 (0.2-6.15)	0.994
Erythrocyte (10^6/μL)	4.0 – 5.2	5.3 (0.1-6.3)	5 (0.41-42.33)	0.098
Hemoglobin (g/dL)	12.0 – 16.0	14.85 (11 – 17.2)	14 (3-18.3)	0.034*
Hematocrit (%)	36.0 – 46.0	47.3 (35.3-53.6)	44.7 (30.9-59.2)	0.078
Mean corpuscular volume (fL)	80.0 – 100.0	87.7 (81.4-97.1)	89.78 (72.5-111)	0.066
Mean corpuscular hemoglobin (pg)	26.0 – 34.0	27.8 (24.4-31.1)	28 (20.3-35.4)	0.659
Mean corpuscular hemoglobin concentration (g/dL)	31 – 36	31.6 (29.3-34.2)	31 (27.3-35.7)	0.039*
Red blood cell distribution width (%)	11.6 – 14.8	11.8 (10.8-16.7)	12.3 (10.4-19.5)	0.034*

Most of subject in this study was male with the age range between 34 and 79 years old. In bivarite analysis using Mann-whitney test only age (p=0.041), smoking (0=0.016), eosinophil (p=0.047), hemoglobin (p=0.034), mean corpuscular hemoglobin concentration (MCHC) (p=0.039) and RDW (p=0.034) showed significant correlation with multiple vessel disease (**Table 2**). The CBC parameters which showed significant correlation were then categorized into high and low value groups based on their median as their cut-off points. The median for esoniphil, Hb, RDW and MCHC are 0.29 (0.0-2.81), 14.12 (3.03-18.30), 12.27 (10.43-19.49), 31.11 (27.32-35.71) respectively. In chi-square test, high vessel score only had statisticaly significant correlation with RDW [p=0.017, OR=3.401 (1.294-8.940)] while hypertension [p=0.381, OR=0.688 (0.297-1.594)], smoking [p=0.016, OR=0.334 (0.133-0.841)], eosinophil [p=0.045, OR=2.511 (0.997-6.326)], Hb [p=0.126, OR=0.418 (0.214-1.222)], and MCHC [p=0.05, OR=0.418 (0.171-1.021)] failed to show any correlation (**Table 3**).

Table 3. Bivariate Analysis (Chi-square test) of the variables that have significant relationship with increase vessel score

	p value	OR	95% CI	
			Lower	Upper
Hypertension	0.381	0.688	0.297	1.594
Smoking	0.016	0.334	0.133	0.841
Eosinophil	0.045	2.511	0.997	6.326
Hemoglobin	0.126	0.511	0.214	1.222
MCHC	0.05	0.418	0.171	1.021
RDW	0.017*	3.401	1.294	8.940

The statistically significant variables in the bivariate were then assessed by multiple logistic regression analysis to determine the independent predictors. In multiple logistic regression, RDW [p=0.022, adjusted OR=3.115 (1.174-8.263)] were revealed as independent predictor of multiple vessel disease (**Table 4**). **Discussion**

Table 4. Multivariate Analysis on of the variables that have significant relationship with increase vessel score

	p value	Adjusted OR	95% CI	
			Lower	Upper
Age	0.060	1.050	0.998	1.106
RDW	0.022	3.115	1.174	8.263

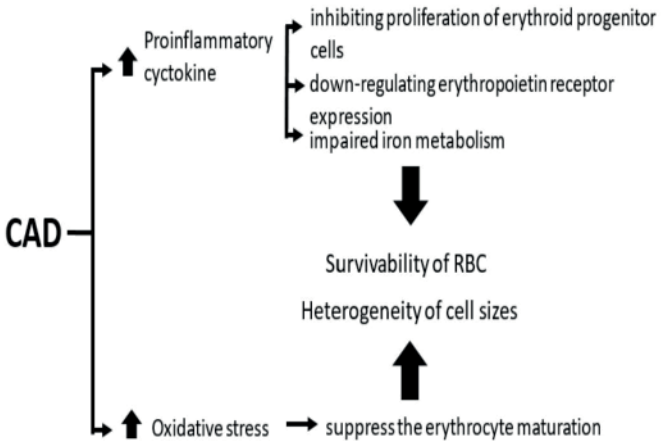
The result of the present study suggest that higher than median RDW value at baseline examination showed independent and significant correlation with multiple vessel disease. The association between RDW and vessel score added prognostic information to estabilshed risk factors.

RDW as part of routine complete blood count analysis is a parameter that measure size variation of circulating red blood cells. Elevated RDW is associated with anisocytosis in peripheral blood smear which can impair blood flow through microcirculation.[8] Higher RDW value can be seen in patients with red blood cell production problems, such as iron deficiency, folate deficiency, and B12 deficiency. It can also be seen in patient with hemolysis and patient who receive blood transfusion.[9]

CAD is usually associated lipid disorder.[3] Lipid disorder increases total cholesterol erythrocyte membrane (CEM) levels which can alter cell deformability and affect the lifespans of circulating erythrocytes.[10, 11] Decreasing lifespans of erythrocyte is responsible for elevated RDW values.

Chronic inflammatory process is one of the pathognomic sign of CAD. Patients with CAD have higher release of pro-inflammatory cytokines.[12] Pro-inflammatory cytokines inhibit proliferation of erythroid progenitor cells, down-regulating erythropoeitin receptor and also responsible for impaired iron metabolism in CAD patients.[13] These process will eventually lead to decrease survivability of RBC. On the other hand, CAD also correlate with higher level of oxidative stress which can suppress erythrocyte maturation and result in heterogeneity of cell sizes[14] (**Picture 1**).

Picture 1. Relationship between inflammatory process in CAD and elevated RDW value.



Conflict of Interest

No potential conflict of interest is relevant to this article.

Conclusion

Therefore, it can be concluded that high RDW values at baseline examination has significant relationship with high vessel score. Furthermore, increase baseline RDW is strong and independent predictor of increase coronary artery lesions which can be used as consideration for patients who may benefit from advanced treatment.

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