COMPARISON OF RED BLOOD CELL DISTRIBUTION WIDTH BETWEEN SIMPLE LESION AND MULTIPLE LESION OF CORONARY ARTERY IN ACUTE CORONARY SYNDROME PATIENTS

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Abstract
Introduction: Acute Coronary Syndrome (ACS) is a disease with the highest mortality. The main mechanism of coronary artery disease is atherosclerosis. Atherosclerosis is a multifactorial process that is influenced by various pathophysiological factors. One of these factors is inflammation. Recently, The red blood cell distribution width (RDW) has been investigated as an inflammatory marker in relation to cardiovascular disease. RDW is an easy, inexpensive and widely available examination in health facilities so that RDW can be used as a marker for assessing the severity of coronary artery lesions in patients with ACS.
Aim: The aim of this study was to assess comparison of RDW values between simple lesion and multiple lesion of coronary artery in ACS patients.
Methods: Cross-sectional study was conducted on 97 patients with ACS who underwent coronary angiography at Haji Adam Malik General Hospital Medan from July 2017 to July 2018. Patients were divided into two groups based on the number of coronary artery lesions, simple lesion group (consisting of 0 or 1 vessel disease) and multiple lesions group (consisting of 2 or 3 vessel diseases). Bivariate analysis with student's t test was conducted to compared of RDW values between simple lesion and multiple lesion of coronary arteries in ACS patients. P values <0.05 were statistically significant.
Result: A total of 97 consecutive patients with ACS, 48 patients (49.5%) with simple lesion and 49 patients (50.5%) with multiple lesion. The mean value of RDW in multiple lesion group was 13.4 ± 0.71%, while in multiple lesion was 12.17 ± 0.37% . There were significant diffrences in RDW values between simple lesion and multiple lesion group in ACS patients (p <0.001).
Conclusion: RDW value in multiple lesion group was significantly higher compared to simple lesion group in ACS patients.

Introduction
The main mechanism of coronary artery disease is atherosclerosis. Atherosclerosisis a multifactorial disease process that is influenced by various pathophysiological factors. One of these factors is inflammation[1,2]. Inflammation plays an important role in the development of atherosclerotic plaques, plaque rupture, and thrombosis, which are the initial factors in occurrence of ACS.

RDW has been reported as a biomarker of worsening atherosclerosis and inflammatory marker associated with early inflammatory biomarkers such as C–reactive protein (CRP), interleukin-6 (IL), tumor necrosis factor-α (TNF).[1,2,3] RDW is a parameter of variability (heterogeneity) in size of circulating red blood cells and is routinely reported as part of an automated full blood count.[4] RDW is an easy, inexpensive and widely available examination in every health facility. Therefore, this study was conducted to assess comparison of RDW values between simple lesion and multiple lesion of coronary artery in ACS patients.

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Methods

Study Samples
This study was conducted using secondary data of patients with a diagnosed of ACS who underwent a coronary angiography at Haji Adam Malik General Hospital Medan from July 2017 to July 2018, with the approval of local ethics committee.

Study Design
This research is an observational analytic study with cross sectional design, using secondary data by looking at medical records of ACS patients who underwent coronary angiography at Haji Adam Malik General Hospital Medan from July 2017 to July 2018.

Angiography results were divided based on vessel score; 0 vessel disease was defined as the diameter of the stenosis in coronary artery reaching less than 50%, 1 vessel disease was defined as the diameter of the stenosis in one main coronary artery reaching more than and equal to 50%, 2 vessel was defined as the diameter of the stenosis in two main coronary arteries reaching more than and equal to 50%, and 3 vessels disease was defined as the diameter of the stenosis in three main coronary arteries reaching more than and equal to 50%. The study sample was divided into two groups; simple lesion group was defined as patient with angiography results showed consisting of 0 or 1 vessel disease, and multiple lesion groupif consisting of 2 or 3 vessel disease. The RDW and other laboratory values were obtained from the collected data at the time of admission to the emergency cardiology department before angiography was conducted. The reference value of the RDW value in our laboratory was 11.5% -14.5%. All demographic data of patients and clinical history of risk factors such as diabetes mellitus, hypertension, dyslipidemia, and smoking were collected from medical records.

Inclusion criteria were patients with age $\geq$ 18 years with diagnosis of ACS who underwent a coronary angiographyat Haji Adam Malik General Hospital Medan and no history of underwent spercutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG).

Exclusion criteria were incomplete medical record data, patients with anemia (i.e with hemoglobin level of < 12gm/dl in males and < 11 gm/dl in females), patients who have previously been diagnosed with ACS, patients who have a history of heart valve disease, congenital heart disease, cardiomyopathy or other heart disease, blood disorders, anemia and recent blood transfusion, chronic liver disease , chronic kidney disease, malignancy, systemic collagen disease, infectious disease, pregnancy, and patients with estrogen replacement therapy, patients with a history of trauma, surgery, and burns.

Statistical Analysis
Continuous variables were tested for normal distribution by the Kolmogorov-Smirnov test. Categorical variables are presented as percentages and compared with Chi-square test or Fisher's test. Continuous variables are presented as means and standard deviation (SD), and compared with student's t test or the Mann-Whitney U test. A p value <0,05 was considered statistically significant. All statistical analyses were perfomed with SPSS version 22.

Results
Total number of sample included in the study were 97. In simple lesion group there were 48 patients (49,5%) and in multiple lesion were 49(50.5%). On group analysis, the mean age of presentation in simple lesion group was 51,71 $\pm$ 7,85 years, whereas in multiple lesion group was 55,80 $\pm$ 7,03 years (p=0,008). Males were predominant than the females (89,7% vs 10,3%). In group multiple lesion, the most common risk factor was dyslipidemia seen in 21 (42,9%) , followed by diabetes in 17 (34,7%), smoking in 15 (30,6%) and hypertension in 12 (24,5%) patients. The differencein mean of hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), leukosit, platelet, ureum, creatinin, glucose, and lipid profile between the two group was statistically insignificant (p>0,05). The most common diagnosis in multiple lesion group was STEMI in 28 57,1%, followed by NSTEMI in 16 32,7%, and UAP in 5 10,2% patients. The baseline

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characteristics of patients in both groups are shown in table 1. The difference in mean RDW values between the two groups was statistically significant (12,17 $\pm$ 0,37% vs 13,40 $\pm$ 0,71%, p< 0,0001) (table 2)

Table 1. Baseline characteristics of patients

Parameter	Simple lesion (n=48)	Multiple lesion (n=49)	p-value
Sex, (n, %)			
Male	42 (48,3)	45 (51,7)	0,524
Female	6 (60,0)	4 (40,0)	
Age (years), (mean±SD)	51,71±7,85	55,80±7,03	0,008
Risk factors, (n, %)			
Diabetes mellitus	14 (45,2)	17 (54,8)	0,559
Hypertension	4 (8,3)	12 (24,5)	0,061
Dyslipidemia	20 (48,8)	21 (51,2)	0,906
Smoking	7 (31,8)	15(68,2)	0,059
Diagnosis (n, %)			
STEMI	30 (51,7)	28 (48,3)	
NSTEMI	4 (20,0)	16 (80,0)	0,003
UAP	14 (73,7)	5 (26,3)	
Laboratory parameters			
Hemoglobin (mg/dL±SD)	14,76±0,89	14,60±1,02	0,410
Hematocrit (%±SD)	43,83±3,01	43,78±3,38	0,929
MCV (fL±SD)	87,56±2,91	87,02±3,03	0,372
MCH (pg±SD)	29,39±1,17	28,95±1,22	0,071
WBC (10^3/μL±SD)	8,99±1,63	9,06±1,42	0,827
Platelet (10^3/mm±SD)	280,52±80,67	268,30±75,56	0,443
Ureum (mg/dL±SD)	30,10±11,92	28,37±10,15	0,441
Creatinine (mg/dL±SD)	0,82±0,27	0,88±0,26	0,291
Glucose (mg/dL±SD)	139,88±65,01	161,02±95,35	0,206
Cholesterol (mg/dL±SD)	173,17±42,69	167,18±39,75	0,477
Triglyceride (mg/dL±SD)	168,60±69,71	146,12±62,27	0,097
HDL (mg/dL±SD)	39,52±11,85	37,76±7,77	0,389
LDL (mg/dL±SD)	111,21±37,62	113,98±35,32	0,709
RDW >14,5%	0 (0)	4 (4,1)	

WBC= white blood cell, MCV= mean corpuscular volume, MCH= mean corpuscular hemoglobin, HDL= high density lipoprotein, LDL= low density lipoprotein, SD= standard deviations, NSTEMI= non-ST elevation myocardial infarction, STEMI= ST elevation myocardial infarction, UAP= unstable angina pectoris, RDW= red blood cell distribution width

Table 2. Mean of RDW values

RDW (%)	Simple lesion group (n=48)	Multiple lesion group (n=49)	P value
Mean	12,17	13,40	0,0001
SD	0,37	0,71	

SD= standard deviations

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Disscusion

The main mechanism of coronary artery disease is atherosclerosis. Atherosclerosis is a chronic inflammatory disease. The formation of RDW is stimulated by condition of hypoxia, inflammation, endothelial dysfunction, and oxidative stress. The pathophysiological mechanism underlying coronary artery disease is atherosclerosis process. Atherosclerotic plaques cause total or sub-total stenosis of the coronary artery resulting in decrease oxygen in blood (hypoxemia), which stimulates the kidneys to secrete erythropoietin to stimulate erythropoiesis in bone marrow resulting theimmature red blood cells in bone marrow to enter thecirculation causingan increase the proportion of red blood cell size in peripheries that is reflected as an increase in RDW.[5] Hypoxemia is also resulted by an increase in inflammatory process and oxidative stress which lead to an increase in RDW through red blood cell destruction which causes shortening of the age of red blood cells and disruption of red blood cell maturation. Shortening of the age of red blood cells cause an increase in RDW. An increasedin RDW cause a decrease in deformability of red blood cells and an increases in blood viscosity, causing an impairs of coronary blood flow and subsequent myocardial ischemia.[6,7] Some physiological conditions (for example, pregnancy, aging or physical exercise) and pathological (for example, ineffective red blood cell production {such as iron deficiency, B12 or folate deficiency}, and hemoglobinopathies), increased red blood cell destruction (such as hemolysis), or after blood transfusions can interfere erythropoiesis process and hence increase the heterogeneity of red blood cell size which results an increase in RDW.[8]

In this study showed a significant difference of mean age in both groups. Age in multiple lesion group was 4 years older than simple lesion group. The mean of age in simple lesion group was 51.71 ± 7.85 years , whereas in multiple lesion group was 55.80 ± 7.03 years. This results was in line with previous studies conducted by Sahin, et al. They found a significant difference in mean of age in high syntax score group and low syntax score group (66 ± 10 years vs 63 ± 13 years, p= 0.009).[9]Nagula et al reported that RDW values was significantly higher in patients with high gensini scores than in patients with moderate to low gensini score (14.68 ± 1.10, 14.55 ± 1.07, 14.53 ± 0.88, p <0,0001).[10] Akin et al reported that RDW values was significantly higher in patients with high syntax score compared to patients with moderate to low syntax score ($15.1\% \pm 1.7\%$ vs. $14.1\% \pm 1.7\%$, p <0.001) and there was a positive correlationbetween high RDW values and severity of CAD assessed by syntax scores in AMI patients.[11] Isik et al reported RDW values was higher in CAD patients compared to patients without CAD ($14.4\% \pm 1.3$ vs $12.5\% \pm 0.9$, p <0.001).[12] Acikgoz et al reported that mean of RDW values in patients with significant arterial stenosis was higher than in normal blood flow assessed by fractional flow reserve (FFR) ($14.19\% \pm 0.73$ vs. $13.69\% \pm 0.77$, p <0.001).[13]

Conclusion

The mean of RDW values in multiple lesion group was higher compared to simple lesion groupin ACS patients.

Suggestion

In this study, there were only four patients with RDW values above normal range (> 14.5%), so further studies with larger samples were needed to obtain a cut-off RDW values in predicting severity of coronary artery lesions at Haji Adam Malik General Hospital Medan.

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