

INDONESIAN JOURNAL OF  
**CLINICAL PATHOLOGY AND  
 MEDICAL LABORATORY**  
 Majalah Patologi Klinik Indonesia dan Laboratorium Medik

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## ANALYSIS OF RED BLOOD CELL DISTRIBUTION WIDTH COEFFICIENT OF VARIATION ON STROKE PATIENT

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### ABSTRACT

Stroke is a functional disorder attributed to acute focal or global brain injury by vascular cause and persists more than 24 hours. Stroke is divided into ischemic and hemorrhagic strokes. Red Blood Cell Distribution Width (RDW) is a measurement of erythrocyte volume variation in blood circulation. Increased RDW reflects the inflammation that plays a role in the development of atherosclerosis in stroke. This study aims to analyze differences in RDW-CV values in patients with stroke. The design was cross-sectional with aretrospective approach, secondary data from medical records of inpatients with stroke from January to December 2016 at the Dr. Wahidin Sudirohusodo Hospital. The study population consisted of 490 patients aged  $\geq 18$  years old. The Kruskal-Wallis, Mann-Whitney, and ANOVA one way tests were used to analyze differences in RDW-CV values in patients with ischemic and hemorrhagic stroke. Mann-Whitney test results showed no significant difference in RDW-CV values between groups of ischemic and hemorrhagic stroke ( $p$  0.96). Kruskal-Wallis and ANOVA oneway tests showed no significant difference in RDW-CV values between four groups of patient outcomes in ischemic and hemorrhagic stroke ( $p$  0.13 and  $p$  0.35 consecutively). There were no significant RDW-CV values between ischemic and hemorrhagic stroke. There was no significant difference between RDW-CV values of four groups of patient outcomes in ischemic and hemorrhagic stroke. RDW-CV values cannot be used to distinguish both ischemic and hemorrhagic stroke, including the prediction of stroke mortality

**Key word:** Stroke, ischemic stroke, hemorrhagic stroke, RDW, RDW-CV

### INTRODUCTION

Stroke by definition from World Health Organization (WHO) is focal brain functional disorder with a syndrome or an acute or global clinical marker which develops fast with the duration of more than 24 hours (except interrupted by surgery or death) without any apparent cause other than brain blood flow disorder. Stroke can be caused by ischemia or brain hemorrhage. Ischemic stroke is caused by cerebral focal occlusion. Hemorrhagic stroke can be in the form of intracerebral bleeding or subarachnoid bleeding.<sup>1,2</sup>

Stroke is the second cause of death after ischemic heart disease (9%) and the primary cause of disability in the world. Medical Department Survey in 2007 found that stroke was the leading cause of death in the age of more than 45 years (15.4%) with stroke prevalence of 0.8% disability because of stroke. In 2002, stroke was the sixth cause for the decrease of Disability Adjusted Life Years (DAL.Ys).<sup>2-4</sup>

Red Blood Cell Distribution Width (RDW) is a

measurement of red blood cell volume variation in the circulation. RDW is reported as Coefficient of Variation (CV) and Standard Deviation (SD). RDW-SD value (stated in fl unit) is a real measurement from histogram distribution width of the red blood cell size and is measured by counting the width on the 20% level above the basic line of the histogram. The RDW-CV value (stated in % unit) is calculated from Standard Deviation (SD) of red blood cell volume and Mean Corpuscular Volume (MCV).<sup>5-10</sup>

Some researchers propose a theory, that decrease of RDW value can reflect inflammation condition related to theadverse clinical result. Inflammation plays an essential role in the development of ischemic stroke and atherosclerosis. Proinflammation cytokines can cause the increase of RDW value by damaging red blood cells and causes reticulocyte excretion to circulation because of the disturbance of iron metabolism and erythropoietin responses.<sup>10-12</sup>

Ani's *et al.* research concluded that the decrease of RDW relates to stroke and high RDW can predict

the mortality of the patient who experienced a stroke.<sup>10</sup> Jia's research *et al.* stated that RDW value was higher on patients with primary ischemic stroke who had carotid arterial atherosclerosis compared with patients who did not suffer from carotid arterial atherosclerosis.<sup>13</sup>

Researches in the relation of RDW and stroke in Indonesia are very limited. Investigations in Makassar havenot been conducted yet. RDW is also a cheap routine examination. The outcome is RDW-CV really has a correlation with stroke and its evaluation, thus this examination can be used as one of the indicators of stroke prognoses which is cheaper and easier to do. The researcher is interested in conducting a research on the relation of RDW and stroke based on the considerations above. This research aimed to analyze differences in RDW-CV value on stroke patient in the Dr.Wahidin Sudirohusodo Educational Public Hospital, Makassar.

The research aims to analyze value differences of RDW-CV between ischemic stroke patients with hemorrhagic stroke and evaluation of its outcome.

## METHODS

The research was conducted by cross-sectional with retrospective approach done by taking inpatient data with stroke during the period of January to December 2016 in Medical Record Installation of the Dr. Wahidin Sudirohusodo Educational Public Hospital, Makassar. The inclusion criteria were stroke patients who had been diagnosed by the clinical manifestation and had laboratory data about RDW-CV examination. The patient data were excluded if the stroke patient was found to have cardiovascular history, anemia (male

adult <13 g/dL), unpregnant adult female (<12 g/dL), kidney failure, and liver failure.

Red blood cell distribution width value is erythrocyte size variation which was reported as part of complete blood count and was measured by using hematology analyzer. Stroke patient outcome was stroke patients condition when they were discharged from the hospital.

The result of the research was analyzed by using comparative test Kruskal-Wallis and Mann-Whitney test abnormal distribution data interval and also ANOVA one way test on normal data distribution. A value which is significant if  $p < 0.05$ .

## RESULT AND DISCUSSION

Four hundred ninety patients were taken as the research subject (170 hemorrhagic stroke patients and 320 ischemic stroke patients) with the characteristics in Table 1. The highest amount of stroke patients were male amounting to 274 patients (55.9%). The most senior age group was 41-60 years which were 226 patients (46.1%).

The research showed that stroke happened more in males than females. The result showed that stroke was experienced more in old patients. Ghani and Mihardja's research mentioned that along with the increase of age the stroke prevalence increased where the age of  $\geq 55$  5.8 times risk compared with the age group of 15 – 44 years. Zank *et al.* found stroke incidence in the USA, England, French, Germany, Italy, and Spain was higher in male than female.<sup>4</sup>

The characteristics of ischemic and hemorrhagic stroke patient can be seen in Table 2. Males dominate both in ischemic and hemorrhagic stroke. They also happened more in old age of 61 – 80 years

**Table 1.** General characteristics of the research sample

Variable		Amount (n = 40)	Percentage (%)
Stroke	Ischemic	320	65.3
	Hemorrhagic	170	34.7
Sex	Male	274	55.9
	Female	216	44.1
Age group	21 – 40 years	28	5.7
	41 – 60 years	226	46.1
	61 – 80 years	211	42.8
	81 – 100 years	26	5.4
	Get well	181	36.9
Output	Well recovered	124	25.3
	Died < 48 hours	81	16.5
	Died > 48 hours	104	21.3

**Table 2.** The characteristics of the ischemic and hemorrhagic stroke patient

	Variable	Amount (n = 40)	Percentage (%)
Sex	Male	274	55.9
	Female	216	44.1
Age group	21 – 40 years	28	5.7
	41 – 60 years	226	46.1
	61 – 80 years	211	42.8
	81 – 100 years	26	5.4
	Mean (2SD)		
Median (min–max)			
Output	Get well	181	36.9
	Well recovered	124	25.3
	Died < 48 hours	81	16.5
	Died > 48 hours	104	21.3

p\* Mann – Whitney Test

**Table 3.** Comparison of RDW-CV value in ischemic and hemorrhagic stroke

Variable	Ischemic stroke (n = 320) Median (min – max)	Hemorrhagic stroke (n = 170) Median (min – max)	p *
RDW - CV (%)	13.0 (10.2 - 23.0) %	13.1 (10.3 – 23.3) %	0.96

p\* Kruskal – Wallis Test

and hemorrhagic stroke mostly occurred in the group of 41 – 60 years. The majority of patient outcome in the ischemic stroke that got well (40.0%) and recovered (32.5%). The hemorrhagic stroke patient outcome was dominated by patients death (57.1%) where in that case of the majority of patients died (57.1%) > 48 hours after hospitalized.

This research showed that patients who were hospitalized in Wahidin Sudirohusodo, Makassar with ischemic stroke diagnosis (65.3%) were greater than hemorrhagic (34.7%). The result is in line with O'Donnel's research, *et al.* who conducted research and found that the percentage of ischemic stroke incident was higher (78%) than hemorrhagic stroke.<sup>14</sup>

The findings showed that outcome in ischemic stroke majorly got well (40.0%) and recovered (32.5%) while hemorrhagic stroke was dominated by patients death (57.1%). Setyopranoto mentioned that the mortality of stroke patients settled the third rank after coronary heart and cancer disease where most of the death cause was due to ischemic stroke (51.58%). The result was not in accordance with Setyopranoto statement, where the most mortality level of hemorrhagic stroke was higher than ischemic stroke.<sup>15</sup>

An RDW-CV value was compared between the ischemic stroke patient group and hemorrhagic

stroke. The average RDW-CV value in ischemic stroke patient is 13% and in hemorrhagic stroke was 13.1%. Data interval was found abnormal after being analyzed by normality test Kolmogorov-Smirnov so comparative test Mann-Whitney was used. The result of the RDW-CV analysis in the stroke patients can be seen in Table 3. Comparative test Mann-Whitney showed there is no meaningful difference in RDW-CV value between the ischemic stroke patient group and hemorrhagic stroke with p-value 0.96.

The RDW-CV value was also compared according to the result of ischemic stroke patient outcome. Data interval was found abnormal after being analyzed by normality test Kolmogorov-Smirnov so that Kruskal-Wallis comparative test is used. The result of RDW-CV analysis compared with ischemic stroke patient outcome can be seen in Table 3. Kruskal-Wallis test showed there was no meaningful difference in RDW-CV based on the result of ischemic stroke patient outcome with the p-value 0.13.

The RDW-CV value was also compared under the result of hemorrhagic after being analyzed by Kolmogorov-Smirnov normality test so that ANOVA one way test was used. The result of RDW-CV analysis compared with hemorrhagic stroke patient

**Table 4.** Comparison of RDW-CV value according to ischemic stroke patient outcome

Variable	Get well (n = 128) Median (min – max)	Die < 48 hours (n = 35) Median (min – max)	Die > 48 hours (n = 53) Median (min – max)	p*
RDW (%)	13.8 (10.8 – 23.0) %	13.2 (11.2 – 19.0) %	13.2 (10.2 – 20.8) %	0.13

p\* ANOVA one way test

**Table 5.** Comparison of RDW-CV value according to hemorrhagic stroke patient outcome

Variable	Get well (n = 53) Median (Min - max)	Recovered (n = 20) Median (Min - max)	Died < 48 hours (n = 35) Median (Min - max)	Died > 48 hours (n = 20) Median (Min - max)	p*
RDW-CV (%)	13.0 (10.4 - 17.2 %)	13.1 (10.3 - 17.9) %	13.1 (10.4 - 17.2) %	33.1 (10.4 - 17.2) %	0.35

outcome can be seen in Table 5. ANOVA oneway test showed that there was no meaningful difference in RDW-CV value based on the result of hemorrhagic stroke patient outcome with p-value 0.35.

The research result showed that there was no meaningful difference ( $p = 0.96$ ) between RDW-CV value with ischemic stroke group and hemorrhagic stroke. The research result also showed that there was no significant difference ( $p = 0.13$  and  $p = 0.35$ ) between RDW-CV value with the ischemic stroke patient outcome and hemorrhagic stroke. The research result was not following Anik's *et al.* research in 2009 which concluded that the increase of RDW was related to stroke incident and higher RDW can independently predict the mortality because of cardiovascular disorder in patients who experienced a stroke.<sup>10</sup> Vijayashee *et al.* found that RDW was higher than 13% was related to the increase of stroke incident risk but RDW value did not show the meaningful relationship with the degree of stroke acuteness.<sup>16</sup> Jia *et al.* mentioned that RDW value was higher in patients with carotid arterial atherosclerosis compared with non-carotid arterial atherosclerosis where this research patients with primary ischemic stroke.<sup>13</sup>

Atherosclerosis incidence is a chronic inflammation process which is persistent and as one of the stroke causes. Chronic inflammation triggered the secretion of inflammation mediators such as TNF- $\alpha$ , IL-1, and IL-6 which were assumed to change hematopoiesis physiology especially the erythrocyte morphological changes which affect the decrease of RDW. Inflammation mediator IL-6 and TNF- $\alpha$  hindered erythropoietin gene transcription GATA-2 and nuclear factor-h15, so erythrocyte maturation

was disturbed and caused immature erythropoietin in the kidney entering the blood flow. The cytokine also disrupted the proliferation of erythroid progenitor cell in the bone marrow is suppressed.<sup>10,17-20</sup>

The weakness of the research which could cause disagreement with other studies was that this research did not compare RDW value of stroke patients with RDW value of the normal control. Another cause of dispute was that this research did not consider factors such as the duration of stroke attack before taking RDW data, medical record of the previous stroke, and other diseases in which chronic inflammation happened besides diseases mentioned in exclusion criteria. Another research limitation was that the data taken was the medical data record which only saw RDW-CV value without considering other infections or inflammations in patients and it did not relate to the other inflammation markers so that it was difficult to avoid bias.

## CONCLUSION AND SUGGESTION

In this research, the result showed that there was no difference in RDW-CV value between ischemic and hemorrhagic stroke group. RDW-CV value of ischemic and hemorrhagic stroke patients with the outcome of recovery got well, died <48 hours and also died >48 hours did not have a significant difference. The RDW-CV value could not be used to differentiate the highest type of stroke or to predict stroke patient mortality.

Based on the research results it was suggested that it is necessary to conduct further research by

comparing an RDW-CV value with other inflammation markers such as Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP), IL-6, TNF- $\alpha$ , in stroke patients to see whether there was a relationship between inflammation and stroke.

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