

## Analysis of RDW and PDW Levels as Predictors of Severity in Acute Coronary Syndrome Patients

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### ABSTRACT

Acute coronary syndrome (ACS) is a major cause of morbidity and mortality in CHD patients in the world and causes around a third of total deaths in the age group >35 years. The mortality rate of patients hospitalized due to ACS in Indonesia reaches 32.3%. This figure is one of the highest in the world. Epidemiological studies show an increasing prevalence of acute coronary syndrome (ACS) worldwide. Objective of the research to analyse the RDW and PDW values which can be used as predictors of severity in patients with acute coronary syndrome. The type of research used is a descriptive analytic design with a cross-sectional approach. Analysis of RDW and PDW Levels as predictors of severity in Pure Acute Coronary Syndrome Patients (without comorbidities) There were 42% male and 58% female, average age  $52.50 \pm 12.62$  years, RDW level correlated significantly as a predictor of severity in Acute Coronary Syndrome Patients without comorbidities, but PDW levels were not significantly correlated as predictors of severity in acute coronary syndrome patients without comorbid analysis of RDW and PDW levels in comorbid acute coronary syndrome patients. RDW and PDW are significantly correlated as predictors of severity in patients with acute coronary syndrome, comorbidities in acute coronary syndrome most of the comorbidities are diabetes mellitus, kidney disease, hypertension and sepsis. So, the levels of RDW and PDW can be a predictor of the severity of comorbid acute coronary syndrome.

### 1. Introduction

The Cardiovascular disease is still a global health problem, both in developed and developing countries. Data from the Global Burden of Cardiovascular Disease (2020) shows that there were 271 million cardiovascular disease events in 1990 and this has almost doubled to 523 million events in 2019<sup>1</sup>. Coronary heart disease, especially coronary artery disease (CAD), is one of the cardiovascular diseases that causes the highest death rate, namely more than 7.4 million deaths. The American Heart Association identified that there are 17.3 million deaths each year caused by heart disease and this death rate is expected to continue to

increase until 2030. In the United States, cardiovascular disease is the leading cause of death, namely 836,456 deaths and 43.8% of them are caused by coronary artery disease (CAD), the majority of people with acute coronary syndrome<sup>2</sup>

Acute coronary syndrome (ACS) is the main cause of morbidity and death in coronary heart disease patients in the world and causes approximately one third of total deaths in the age group >35 years<sup>3</sup>. 4.5. The death rate for patients hospitalized due to acute coronary syndrome (ACS) in Indonesia reached 32.3%. This figure is one of the highest in the world<sup>4</sup>. Epidemiological studies show an increasing prevalence of

acute coronary syndrome (ACS) worldwide. Data from the World Health Organization (WHO) states that there has been an increase in deaths due to ACS reaching 42%. The morbidity and mortality rates for ACS are mainly influenced by the progress of health facilities and services in each country<sup>2</sup>.

Epidemiological studies in Indonesia regarding ACS are still very limited. However, based on Basic Health Research data<sup>5</sup>, the prevalence of coronary heart disease as the main etiology of acute coronary syndrome (ACS) in Indonesia is 1.5%, with the highest prevalence ranking in North Kalimantan Province, namely 2.2%, Special Region Yogyakarta is 2% and Gorontalo is 2%<sup>5</sup>.

Various diagnostic and therapeutic methods have developed in recent years, but globally cardiovascular disease remains the leading cause of death. Cardiac marker examination to see signs of myocardial tissue necrosis requires quite expensive reagents and adequate laboratory equipment. Therefore, routine laboratory tests are needed so that they can predict worsening. There is a need for risk assessment and stratification as well as prognosis evaluation, so that ideal diagnostic markers are needed, have high sensitivity and specificity at a low price, can be accessed quickly, are non-invasive and can be examined in a laboratory with simple facilities.

Several simple markers of standard whole blood components have been studied, namely red cell distribution width (RDW) and Platelet Distribution Width (PDW). Red cell distribution width (RDW), reflects the variability in erythrocyte size. Disruption of erythropoiesis can result in red blood cell heterogeneity which is believed to coincide with the occurrence of several individual pathological changes. Several previous studies have found a strong correlation between the RDW value and the degree of mortality and progression of cardiovascular disease, even stronger than traditional risk factors. The RDW value can be a predictive indicator of cardiovascular disease morbidity and mortality<sup>6</sup>.

Platelets play an important role in the pathogenesis of acute coronary syndrome. Some platelet indices measured during platelet activation are Platelet Distribution Width (PDW) and Mean Platelet Volume (MPV). Platelet Distribution Width (PDW) is a component of a complete blood test that is easy to do and cheap<sup>7</sup>. PDW is a direct measurement that reflects variability in platelet size, indicating the relative width of platelet distribution in an index of platelet heterogeneity volume. A high PDW value indicates a large increase in platelet production. Several previous studies have shown that PDW and MPV increase during platelet activation, but PDW is a more specific marker of MPV<sup>8</sup>.

Based on this background, researchers want to look at routine haematology parameters that can be used as prognostic markers for worsening in acute coronary syndrome patients so that they can be used by clinicians in treating heart patients.

## 2. Methods

The type of research used is a descriptive analytical design with a cross-sectional approach. The subjects of this research were patients with acute coronary syndrome who were hospitalized at RSUP dr. Chasan Boesoirie Ternate in the period January 2021 to June 2023. The sampling technique was carried out by purposive sampling or the sample was deliberately selected by the researcher based on the results of an EKG examination which diagnosed acute coronary syndrome. The total population

was 120 patients with acute coronary syndrome and there were 74 patients who had complete data.

The severity of acute coronary syndrome is based on the length of patient treatment until recovery<sup>9</sup>; treatment for 1 - 3 days and recovery in the mild category, treatment over 3 days and recovery in the severe category (in this study the average was 7 days), patients during the treatment period ultimately died in the death category. This research is analytical research with numerical and categorical variables and the results analysed using the Statistical Product for Social Science (SPSS) version 16.0 program will be presented in the form of narratives, tables and graphs.

The analysis carried out was a univariate analysis on each research variable. Numerical variables will be presented in the mean with standard deviation for normal data distribution and correlating the RDW and PDW variables with the degree of severity with a value  $< 0.05$  meaning significant correlation and testing the strength of the correlation (R) with a value of: 0.00 - 0.25: very weak correlation. 0.25 - 0.50: moderate correlation. 0.50 - 0.75: strong correlation. 0.75 - 0.99: very strong correlation<sup>10</sup>. Praveen Nagula's 2017 research report reported that an RDW value  $> 14.3\%$  diagnoses acute coronary syndrome which describes the degree of clinical severity and a PDW level  $> 17$  fl is associated with the severity of acute coronary syndrome<sup>11</sup>.

The results of the analysis are described in the form of a narrative based on a theoretical review and comparison of several research results by other researchers.

## 3. Results

The characteristics of the 74 acute coronary syndrome patients who were the object of this study are described in the following table: **(Table 1)**

**Table 1:** Characteristics of Acute Coronary Syndrome Patients.

Characteristics	Amount (N)	Percentage (%)
Gender	74	100
Male	44	60
Female	30	40
Age (Mean)	58.07± 11.032	
Diagnosis SKA	20	26
SKA+comorbidities	54	74
Degree of Severity		
Light	36	48
Heavy	33	45
Death	5	7

The table above illustrates that of the 74 patients, 60% of them were men and 40% women, with an average age of approximately 58 years, while there were 20 patients with pure acute coronary syndrome (no comorbidities) (26%), with comorbidities (comorbidities) in 54 patients (74%). Based on the severity of the patients, there were 36 patients in the mild category (48%), 33 patients in the severe category (45%) and 5 patients (7%) who died.

Analysis of RDW and PDW Values as Predictors of Severity in Acute Coronary Syndrome Patients. The diagnosis of acute coronary syndrome is in patients with acute coronary syndrome which consists of pure acute coronary syndrome and acute coronary syndrome with comorbidities. The results of the SPSS 16 analysis to determine the existence of a correlation. The RDW and PDW values as predictors of the severity of acute coronary syndrome are described in the following table **(Table 2)**.

**Table 2:** Characteristics of Acute Coronary Syndrome.

Characteristics	N (%)	Sig (1-tailed)	R
Gender			
Male	44(60)		
Female	30(40)		
Age ( Mean±SD)	58.07± 11.032		
Value RDW (Mean±SD)	13.3709±3.00222	0.000	0.587
value PDW (Mean±SD)	15.5846±2.87550	0.000	0.383
Degree of severity			
Light	36 (48)		
Heavy	33 (45)		
Death	5 (7)		

The table above illustrates that there were 74 acute coronary syndrome patients consisting of 44 male patients (60%) and 30 female patients (40%) with an average age of 58.50 ± 11.32 years. The degree of severity in the mild category was 36 patients (48%) with a treatment period of 1 to 3 days and were declared cured, while those classified as severe were 33 patients (45%) with an average treatment period of 6 days and 5 patients (7%) died. The average RDW value is 13.3709 ± 3.00222 with a correlation to the degree of severity of 0.000 or there is a significant correlation, so that RDW can be a predictor of severity in cases of Acute Coronary Syndrome with a correlation strength value of 0.587, including strong correlation strength. The average PDW value is 15.51 ± 3,000 with a correlation to the degree of severity of 0.000 or there is a significant correlation so that PDW can be a predictor of severity in cases of Acute Coronary Syndrome with a relationship strength value of 0.383, including moderate correlation strength. Analysis of RDW and PDW Values as Predictors of Severity in Pure Acute Coronary Syndrome Patients.

The diagnosis of pure acute coronary syndrome is a patient who has acute coronary syndrome only, without any other comorbidities. The results of the SPSS 16 analysis to determine the existence of a correlation. The RDW and PDW values as predictors of the severity of acute coronary syndrome are described in the following table (Table 3).

**Table 3:** Characteristics of Pure Acute Coronary Syndrome.

Characteristics	N (%)	Sig (1-tailed)	R
Gender	20		
Male	8 (42)		
Female	12 (58)		
Age (Mean±SD )	58.50±12.62		
Value RDW (Mean±SD)	12.722±1.31	0.023	0.451
value PDW (Mean±SD)	15.58±3.11	0.202	0.197
Degree of severity			
Light	18 (95)		
Heavy	2 (5)		
Death	2 (5)		

The table above illustrates that there were 20 patients with pure acute coronary syndrome consisting of 8 male patients or 42% and 12 female patients or 58% with an average age of 58.50 ± 12.62 years with mild severity in 18 patients (95 %) who underwent treatment for 1 to 3 days and were declared cured, while those classified as severe were 2 patients (5%) who underwent treatment for 6 days. The average RDW value is 12,722 ± 1.31, with a correlation value to the degree of severity of 0.023 or there is a significant correlation, so that RDW can be a predictor of severity in cases of Pure Acute Coronary

Syndrome, with a correlation strength value of 0.451, including moderate relationship strength. The average PDW value is 15.58 ± 3.11, while the correlation value with the degree of severity is 0.202 or there is no significant correlation, so PDW cannot be a predictor of severity in cases of Pure Acute Coronary Syndrome.

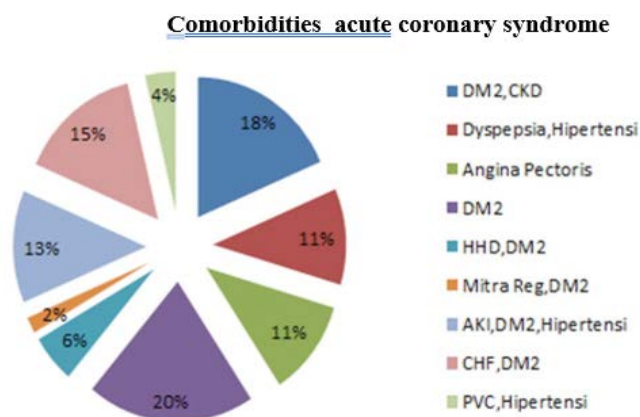
Analysis of RDW and PDW Values as Predictors of Severity in Patients with Comorbid Acute Coronary Syndrome (the presence of comorbidities). The diagnosis of comorbid acute coronary syndrome is a patient who suffers from acute coronary syndrome and the presence of other comorbidities, most of which are comorbid diseases type 2 diabetes, hypertension and kidney disease. The results of the SPSS 16 analysis to determine the existence of a correlation. The RDW and PDW values as predictors of the severity of acute coronary syndrome are described in the following table (Table 4).

**Table 4:** Characteristics of comorbid acute coronary syndrome.

Characteristics	N	Sig (1-tailed) R
Gender	54	
Male	36	
Female	18	
Age (Mean±SD )	57.91±10.5	
Value RDW (Mean±SD)	13.55±3.44	0.000 0.615
Value PDW (Mean±SD)	15.5±2.88	0.004 0.335
Degree of severity		
Light	18	
Heavy	31	
Death	5	

The table above illustrates that there were 54 pure acute coronary syndrome patients consisting of 36 men (66%) and 18 women (34%) with an average age of 57.91 ± 10.5 years with a mild severity of 18 patients who had undergone were hospitalized for 1-3 days and were declared cured, while those classified as serious were 32 patients who underwent hospitalization for 4-32 days and were declared cured, while 5 patients who died were hospitalized for 1-5 days. The average RDW value is 13.55 ± 3.44, with a correlation value to the degree of severity of 0.000 or has a significant correlation with a correlation strength of 0.615 in the very strong category. The average PDW value is 15.5 ± 2.88, while the correlation value for the degree of severity is 0.004 or has a significant correlation with a correlation strength of 0.335 in the medium category.

The comorbidities in people with acute coronary syndrome in the study mostly had cardiovascular disease, diabetes mellitus, chronic kidney disease, dyspepsia as shown in the curve below: (Figure 1)



**Figure1:** Data on comorbidities of Acute Coronary Syndrome.



The picture above describes several comorbidities in patients diagnosed with acute coronary syndrome, including type 2 diabetes mellitus and CKD (chronic kidney disease) at 18% and dyspepsia. Hypertension was 11% and angina pectoris was 11%. Type 2 diabetes mellitus alone is 20%, HHD and type 2 diabetes mellitus is 8%, partner regurgitation and type 2 diabetes mellitus is 2%, kidney failure, type 2 diabetes mellitus and hypertension is 13%, sufferers of CHF and type 2 diabetes mellitus are 15%, PVC and hypertension by 4%. Some of the dominant comorbidities in acute coronary syndrome patients include type 2 diabetes mellitus at 72%, while cardiovascular disease is 51% and kidney failure is 13%. Data on acute coronary syndrome with comorbidities who died are described in the following table: (Table 5)

**Table 5:** Data on comorbid ACS patients who died.

No	Gender	Age	RDW	PDW	SKA comorbide
1	L	69	14.9	17.8	AHF, CKD, DM2
2	L	65	20.7	18.2	ADHF, DM2
3	L	50	16.74	18.4	CHF, AKI, SUPRAVENTRIKULAR TATHICARDI
4	P	67	14.9	18.1	ADHF., DM2, Hipertension
5	P	64	13.07	18.4	CKD, SEPSIS,

Data on 5 patients with acute coronary syndrome who died after being hospitalized, consisting of 3 male patients and 2 female patients, most of them were over 60 years old and only one patient was 42 years old. The RDW values for the 4 patients were above normal. and only 1 patient was in the normal category (RDW normal value <14.3%). The PDW value for the 5 patients had a high PDW (normal PDW value <17 fl)

#### 4. Discussion

The results of this study prove that the RDW value can be a predictor of the severity of acute coronary syndrome patients with relatively strong significance. As the results of <sup>12</sup> research show, the RDW value can be a predictor of severity in acute coronary syndrome patients. In contrast to the research of <sup>13</sup>, the sensitivity and specificity of the RDW and PDW values were too low as biomarkers in cases of acute coronary syndrome in short periods, but in long periods of examination they could be used as supporting biomarkers for the severity and morbidity of acute coronary syndrome.

The PDW value in the results of this study can be a predictor of the severity of acute coronary syndrome patients with moderate correlation strength. The above results are in line with research by Bekler et al which showed that an increase in PDW levels >17 fl was associated with the severity of coronary heart disease with acute coronary syndrome. In the same study, increased PDW was found in patients with diabetes mellitus and myocardial infarction was positively associated with a high Gensini score. In different studies, PDW was greater in patients with ACS than non-ACS<sup>14</sup>. The results of the analysis of the RDW value as a predictor of severity in pure acute coronary syndrome patients show a correlation or the RDW value can be used as a predictor of the severity of pure acute coronary syndrome with moderate correlation strength. However, the PDW value cannot be a pure predictor of the severity of acute coronary syndrome because the strength of the correlation is very weak. In acute coronary syndrome there is not only an increase in the RDW or PDW value but there is vasoconstriction of the heart's blood vessels

which narrow as a result of stress or depression, as research reports by<sup>15</sup> show that stressful conditions will trigger several reactions, such as increased blood pressure, narrowed blood vessels. which results in breathing more quickly and feeling short of breath, these are common symptoms of acute coronary syndrome. Research by<sup>16</sup>. Depressed patients with acute coronary syndrome have poorer outcomes compared to patients without depressive symptoms. Vasoconstrictive response to anxiety felt during anticipation of pain in acute coronary syndrome, as well as research reports by<sup>17</sup> that acute stress has also been associated with platelet hyperactivity, increased blood viscosity and haemoconcentration, potentially increasing the risk of thrombosis and other cardiovascular complications mediated through platelet hyperactivity and increased blood viscosity resulting in acute coronary syndrome.

The pathophysiological mechanisms of the relationship between RDW and PDW in cardiovascular disease are still unclear. Does an increase in RDW or PDW have a direct influence on cardiovascular disease, especially acute coronary syndrome, is it just a marker or does it reflect other disorders that occur in the body<sup>18</sup>.

Another study related to acute coronary syndrome by<sup>19</sup>, reported that factors that can increase the risk of coronary heart disease and acute coronary syndrome include smoking, lack of physical activity, unhealthy eating patterns and alcohol abuse. Cigarette consumption can trigger the formation of atherosclerotic plaque (an increase in the RDW value), stimulate sympathetic nerve activity and increase the formation of Reactive Oxygen Species which makes it possible to suffer from acute coronary syndrome. therefore, acute coronary syndrome patients with comorbidities caused by smoking habits, lack of exercise, unhealthy eating patterns and alcohol consumption will increase the RDW value.

Acute coronary syndrome patients with accompanying or comorbid diseases, in this study it was found that the majority of acute coronary syndrome patients had diabetes mellitus. This is as research by<sup>20</sup> states that diabetes worsens the development of atherosclerosis and is associated with an increased risk of developing acute coronary syndrome. Likewise, the results of <sup>21</sup> research found that 72.6% of ACS sufferers experienced hyperglycaemia. Hyperglycaemia occurs in patients who are male and aged more than 55 years. Symptoms of specific chest pain were complained more frequently in hyperglycaemic sufferers (66.7%) than normoglycemic sufferers (47.1%). However, different research by<sup>22</sup> from the results of the study stated that there was no relationship between CHF, ACS and DM in SKA patients treated at Abdoel Moeloek Hospital. Meanwhile, acute coronary syndrome patients with concomitant kidney failure are related to acute coronary syndrome. From the results of research by<sup>23</sup>, acute coronary syndrome patients treated at Kandaaw General Hospital mostly had kidney failure, hypertension and type 2 diabetes mellitus. Bekler, et al. research shows that that increasing PDW levels (>17%) is associated with the severity of coronary heart disease with acute coronary syndrome, especially for acute coronary syndrome patients with comorbidities.

#### 5. Conclusion

The Most of the patients with acute coronary syndrome are 60% men and 40% women, with an average age of 58 ± 11.03 years. The RDW and PDW values are significantly correlated as predictors of severity.

For coronary syndrome patients without comorbidities, there are 42% men and 58% women with an average age of  $58.50 \pm 12.62$  years. Only the RDW value is significantly correlated as a predictor of severity in acute coronary syndrome patients without comorbidities, while the PDW value is not correlated. significant as a predictor of severity in acute coronary syndrome patients without comorbidities.

In patients with comorbid acute coronary syndrome, there are 66% men and 34% women, average age  $57.91 \pm 10.5$  years, RDW and PDW values are significantly correlated as predictors of severity in patients with comorbid acute coronary syndrome.

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### Conflicts of interests

The authors declares that there is no conflict of interest.

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