Research Article

Effect of Mean Platelet Volume on Outcome of Stroke Infark in Elderly Patient

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ABSTRACT

Background: Hyperreactivity and activation of platelet play a role in the occurrence and severity of ischemic stroke in geriatric patients. Mean Platelet Volume (MPV) describes levels of stimulation as well as platelet production rates that may affect the incidence of ischemic stroke and its clinical outcome. **Objective:** To determine the effect of MPV on the outcome of stroke infarction in geriatric patients. **Methods:** This was a cohort study. MPV measured at hospital admission. Statistical analysis carried out by Receiver of Curve (ROC) test to determine the MPV cut off point and Chi-square to determine the relationship between MPV and infarction of stroke patient using SPSS v.22. **Results:** There were 52 stroke patients with mean age 68.25+6.06 years. Clinical outcomes deteriorated in 38 (73.08%) patients. The AUC value of MPV was 73.3% (p=0.011) with MPV cut off point 10.85fl. Deterioration occurred in 10 (43.38%) patient with MPV >10.85fl. The Chi-square test result was (p<0.001) showing a difference between the groups (RR 3.125 CI 95% 1.134-8.761). **Conclusion:** Ischemic stroke patients with MPV levels >10.85fl at hospital admission had 3 times chance of deterioration. MPV can be used as prognostic factor for clinical outcome of acute ischemic stroke in geriatric patients.

Keywords: geriatric, ischemic stroke, mean platelet volume

1. Introduction

Stroke is the second leading cause of mortality in the world and the third cause of morbidity in Global diseases [1]. Report from the World Health Organization (WHO) shows that every year there are 15 million people worldwide suffering from strokes. According to the American Heart Association (AHA), there are an estimated 3 million stroke patients per year in the United States with 500,000 new cases [2]. In Indonesia, the prevalence of strokes reached 8.3 per 1,000 inhabitants. The region which had the highest prevalence was Nangroe Aceh Darussalam (16.6 per 1,000 population) and the lowest was Papua (3.8 per 1,000 population). Stroke along with hypertension, ischemic heart disease and another heart diseases, are also the main non-communicable diseases that cause death in Indonesia [3].

The incidence of stroke increases with age, with 69% of people are aged over 65 years and 34.4% are older than 75 years [1]. Age-based mortality is 15.9% for people under 65 years and 23.5% for ages above 65 years.[4] Of all stroke patients in Indonesia, ischemic stroke is the most common type (52.9%); followed by intracerebral hemorrhage, embolism and subarachnoid hemorrhage with an incidence rate of 38.5%; 7.2% and 1.4% [5].

Ischemic stroke is closely related to platelet function because platelet adhesion and aggregation processes occur mostly in hyperactive platelets. Thrombosis is a major complication of the atherosclerotic process which involves the activation and aggregation of platelets that develop from atheromic plaque ulceration.

Atherothrombosis triggers local occlusion and embolism in the distal region, with clinical manifestations that can be seen in ischemic stroke [6].

Hyperreactivity and platelet activation contribute to the incidence of ischemic stroke which is an inflammatory response. Platelet size has been shown to describe platelet activity. Metabolically and enzymatic large platelets are more active than small platelets and produce more thromboxane A2. Mean Platelet Volume (MPV) describes stimulation levels and platelet production rates. Platelet activation can be indirectly measured by MPV [7].

Several studies have shown that MPV correlates with platelet function and platelet activation of this condition can be assessed through synthesistromboxane, beta-thrombomodulin release, expression of procoagulant function or molecular adhesion8. Muscari et al. in [9], got their study that MPV is increased in geriatric patients and is a risk factor for ischemic stroke events. Previous studies have explained the association of MPV with heart disease, especially the coronary heart, it has been known that platelet activation and aggregation play a role in thrombus formation [10].

Increased inflammatory response in stroke patients with hyperactivity and excessive platelet activation will cause greater thrombos formation so that ischemia in the brain will be heavier. Therefore, an increase in MPV levels in geriatrics as an illustration of platelet hyperactivity can explain the pathophysiology of occlusion in cerebral blood vessels so that MPV can be used as a reference for weighting stroke conditions [11].

2.   Methods

This study is a cohort study to discover the clinical prognostic outcome of ischemic stroke in geriatric patients with the age of more than 60 years old through NIHSS (National Institutes of Health Stroke Scale) examination when first admitted to the hospital whose progresses were evaluated until patients were released from the hospital with monitoring MPV level when patients were first admitted to General Hospital of Dr. Sardjito. The research subjects were hospitalized geriatric patients chosen from Stroke Unit, Neurology Ward, Cardiology Ward in General Hospital of Dr. Sardjito Yogyakarta who were diagnosed with acute ischemic stroke based on history findings, clinical examinations dan head CT scan examination that fulfill the inclusion criteria which are onset less than or equals to 72 hours dan are willing to participate in this study. The exclusion criteria in this study are patients with systemic infection and/or sepsis, previous stroke history and history of chronic diseases, autoimmune diseases or malignancy. All patients with acute ischemic stroke were chosen with consecutive sampling technique. Subjects that met the inclusion and exclusion criteria are included in this study. Every subject or closest family was given explanation about the research flow and was asked for their permission to participate and to sign the informed consent form. History findings, physical and laboratorium examinations to determine the MPV level were then performed to assess worsening neurological deficit using NIHSS when patients were admitted to Stroke Unit, Neurology Ward in General Hospital of Dr. Sardjito Yogyakarta. Subjects were then monitored and NIHSS score assessment were repeated on onset on the 7th day. Consequently, all data were collected in a form and then were analyzed for statistical analysis.

Statistical analysis that was used to determine MPV cut off point as a factor that affects clinical outcome of stroke patients was Receiver of Curve (ROC) test with establishing Area Under Curve (AUC) (good if AUC >50%). If MPV cut off point is known, chi square test is used with Confidence Interval (CI) 95%. Data were processed with the 22nd version of SPSS software.

3.   Results

This research was conducted in August-December 2016 at RSUP Dr. Sardjito Yogyakarta Strokes Unit. The subjects of this study were 52 patients who met the inclusion and exclusion criteria. The sampling technique uses consecutive sampling until the number of samples is reached according to the specified sample size. This research analysis includes descriptive analysis and statistical analysis. Descriptive analysis included the data on the characteristics of all subjects and statistical analysis included the bivariate analysis and multivariate analysis.

Basic Characteristics of Subjects

Based on the results of the study in Table 4, the mean stroke patients were 68.25 + 6.06 years with the youngest age 61 years and the oldest 82 years. The Gender of stroke patients is 23 (44.23%) men and 29 (55.77%) women, with the most recent education being primary school (48.08%).

Table 1. Basic Characteristics of Subjects

Variabel	Mean±SD	Min-Maks	Total	percentage (%)
Age (Year)	68,25+6,06	61-82		
Gender				
Man			23	44,23
Woman			29	55,77
Education				
Primary School			25	48,08
Junior High School			14	26,92
Senior High School			12	23,08
Bachelor			1	1,92
Smoker				
Nonsmoker			30	57,69
Exsmoker			5	9,62
Smoker			17	32,69
Diabetes mellitus			8	15,38
Hypertension			38	73,08
Dyslipidemia			14	26,92
NIHSS 1	5,73+4,56	0-23		
NIHSS 2	6,6+5,75	0-25		
Clinical outcome				
Non Worsening			14	26,92
Worsening			38	73,08
Lesion area				
≥ 2 cm			22	42,31
< 2 cm			30	57,69
Infarct Location				
Cortical			17	32,69
Non Cortical			35	67,31
Mean platelet volume (fl)	10,04+2,04	5,5-12,8		

In result, it was showed that smoker subject was 32.69%, exsmoker was 9.62%. Subject with DM was 15.38%, hypertension was 73.08% and dyslipidemia 73.06%. Mean of NHSS in the first coming was 5.73+4.56 with minimal point 0 and maximal point 23 and mean of evaluation NIHSS increase till 6.6 + 5.75 with minimal point 0 and maximal point 25. Clinical outcome improved in 14 patients (14.93) and worsen in 38 patients (73.08%). Infarct lesion > 2cm was 42.31% with cortical lesion 32.69% and non cortical lesion67.31%. Mean of MPV 10.04 + 2.04 fl (5.5-12.8) fl.

Determination of the MPV cutting point

To find out how much MPV levels are a benchmark for determining high or low as a factor that affects the clinical outcome of ischemic stroke. Next is Figure 1, the curve of receiver of curve.
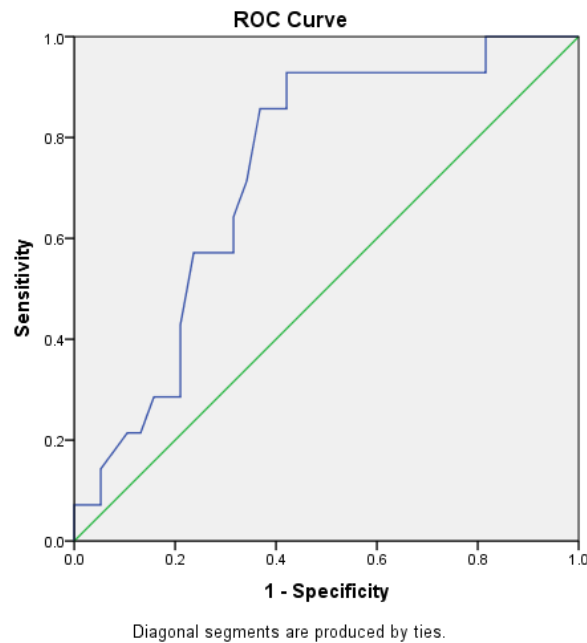
Figure 1. Receiver of Curve

In Figure 1, the MPV ROC curve shows that MPV has a good diagnostic value because the curve is far from the line of 50%. The AUC value obtained from the ROC method is 73.3% p value 0.011. Statistically the AUC value is 73.3% classified as moderate. From the curve, it can be concluded that MPV can be used to determine the worsening of ischemic stroke precisely and significantly with a confidence level of 73.3%. To determine value of MPV using cut point of sensitivity and specificity curve. From the picture, cut point of sensitivity and specificity at the number 2 is 10.85 fl.
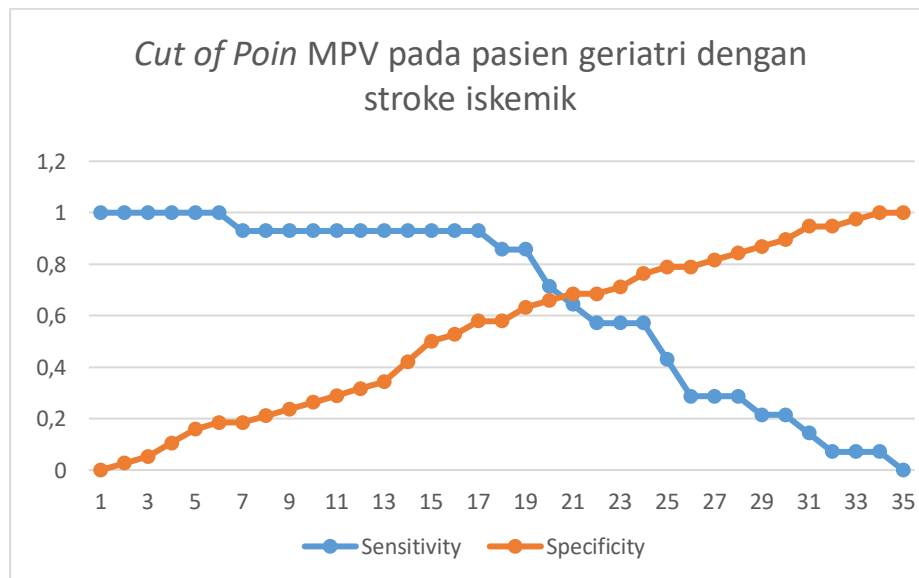
Figure 2. Cut of Point MPV for outcome ischemic stroke patient

Based on figure 2, the cut-off point MPV is 10.85 fl. To find out the relationship between MPV values and clinical outcome of stroke patients, chi-square test was performed. The following table 2 shows the result of the chi-square test.

The Corelation MPV with the clinical outcome ischemic stroke
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Table 2. Cross tabulation between MPV and clinical outcome stroke ischemic in geriatric patients

		Clinical outcome				p-value	RR (IK 95% min-max)
		Worsen		Improve			
		N	%	N	%		
MPV	≥10,85	10	43,48	13	56,52	0,017	3,125 (1,134-8,761)
	<10,85	4	13,79	25	86,21		
	amount	14	26,92	38	73,08		

Based on table 2 show that in the first coming about 10 stroke patients (43.48%) with MPV >10.85 fl have worsening and about 4 patients (13.79%) with MPV <10.85 fl have worsening. Result of Chi Square Test was p 0/017 (RR 3.125 IK 95% 1.134-8.761). It was concluded that in the first coming stroke patients with MPV >10.85 fl have risk to be worsening three times more than stroke patients with MPV <10.85 fl in the first coming.

4. Discussion

In this study we found an association between MPV and outcome of ischemic stroke in geriatric patients. Ischemic stroke patients with MPV levels> 10.45 fl at hospital admission will experience a deterioration of 6 times compared to patients with MPV levels <10.45 fl. Ghahremanfard et al. in [12] study, obtaining MPV results was associated with a degree of ischemic stroke weighting. in line with Verdoia et al. in [13] study, it was found that an increase in MPV was associated with an increased incidence of myocardial infarction and death in patients over 60 years of age. saliva with Ciancarelli et al. in [14], getting MPV results can be used as an inflammatory mediator of ischemic stroke events and is associated with the clinical outcome of ischemic stroke patients. different results from Ntaios et al. in [15] study, MPV is not related to the degree of stroke severity and functional outcome.

Ischemic pathogenesis is initiated by the formation of thrombus in the walls of both blood vessels and the heart. The formation of thrombus in the blood vessels begins with damage in the blood vessels. Damage to blood vessel walls is caused by shear stress and plaque ulceration. the next process is the occurrence of primary hemostasis which ends with the formation of thrombus. Thrombus can cause lumen occlusion of blood vessels where it is formed or experience fragmentation and eventually block in the distal part of the blood vessels. Thrombus can also form inside the heart. Any slowing of blood flow in the heart can cause any thrombus to form. The thrombus formed mostly flows into the brain [16].

The thrombus consists of platelets, erythrocytes, and a small portion of leukocytes trapped in the fibrin [17]. Thrombocytes will aggregate and stimulate release more Thromboxane A2 further stimulate the aggregation of other thrombocyte. It was suspected that increase of mean platelet volume has morethrombotic potency than platelet with small volume. Bigger platelets have more density and aggregate with collagen faster than other platelet. These platelets also have more thromboxane A2 and more expression with glikoproteinIb and IIb/IIIa. This condition will simplify formation of thrombus in patients with increasing of mean platelet volume [17,18].

Formation of thrombus in blood vessel and heart will increase the risk of occlusion in brain blood vessels and cause damage of brain.[18] Mean platelet volume is a marker of platelet function and is associated with thrombocyte activity indications which include aggregation and release of thromboxane A2, platelet factor 4 and thromboglobulin. Platelet size is determined at the time of increased platelet formation and destruction. Large platelets have more dense granules and are stronger than small ones and are more trombogenic.

Platelets are known to have a role in the pathogenesis of atherosclerotic complications and thrombus formation. Greisenegger et al. Argued that there was an increase in MPV in patients with acute myocardial infarction and acute cerebral ischemia. This increase in MPV is associated with a poor prognosis in acute ischemic stroke. Conclusions from this study recommend markers of reflecting platelet function and activity including MPV, release of thromboxane A2, platelet factor 4, thrombomodulin and platelet aggregation. a study by Ghorbani et al aimed to determine whether there was a relationship between MPV and the severity of acute ischemic stroke and to determine the effectiveness of MPV in distinguishing severe and mild

ischemic stroke. in the study it was concluded that MPV is associated with the severity of acute ischemic stroke and has high effectiveness to differentiate severe and mild ischemic stroke.[23]

5. Conclusion
The mean platelet volume can be a prognostic factor in the clinical outcome of acute ischemic stroke in geriatric patients.

6. Data Availability Statement
The datasets generated and analyzed during the current study are not publicly available due to privacy and ethical considerations but are available from the corresponding author upon reasonable request.

7. Ethical Statement
Sumatera Medical Journal (SUMEJ) is a peer-reviewed electronic international journal. This statement below clarifies ethical behavior of all parties involved in the act of publishing an article in Sumatera Medical Journal (SUMEJ), including the authors, the chief editor, the Editorial Board, the peer-reviewer and the publisher (TALENTA Publisher Universitas Sumatera Utara). This statement is based on COPE's Best Practice Guidelines for Journal Editors

8. Author Contributions
All authors contributed to the design and implementation of the research, data analysis, and finalizing the manuscript.

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10. Conflict of Interest
Authors declares no conflict of interest.

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