Plateletcrit as Risk Factor of Major Adverse Cardiac Event in Elderly Patient with Acute Coronary Syndrome

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ABSTRACT

Background. The morbidity and mortality of patients with acute coronary syndrome (ACS) are very high so it is important to do risk factor stratification. Several studies found that plateletcrit plays an important role in predicting mortality in STEMI patients and that it had a significant correlation as a predictor of a coronary slow flow phenomenon correlated with a worse cardiovascular outcome. The aging process is associated with altered platelet activity and a higher rate of vascular disease. The effect of aging on thrombotic function is not fully understood yet, so further research is needed. It is hypothesized that high plateletcrit increases the risk of major cardiovascular events (MACE) in elderly acute coronary syndrome (ACS) patients treated in intensive cardiac care unit (ICCU).
Objective. To determine the role of plateletcrit as a risk factor for major cardiovascular events in elderly acute coronary syndrome patients.
Method. We collected samples of elderly patients who experienced ACS in the period January 2016 - December 2019, recorded plateletcrit data and whether there were MACE incidents or not. The data were processed in SPSS to find a cut off of plateletcrit values which are a risk factor for the occurrence of MACE in elderly patients at Dr. Sardjito Hospital.
Result. A total of 174 study subjects consisted of 58 MACE and 116 non-MACE groups, the results showed that platelecrit ≥0.35 increased the risk of MACE with a *p* value of 0.046 and OR 5.49.
Conclusion. Plateletcrit is statistically significant to the incidence of MACE in elderly coronary syndrome patients who are treated in intensive cardiac are units.

Keywords. Plateletcrit, major adverse cardiovascular events, elderly

ABSTRAK

***Latar belakang**. Morbiditas dan mortalitas pasien sindroma koroner akut (SKA) sangat tinggi sehingga penting untuk dilakukan stratifikasi faktor risiko. Beberapa penelitian menunjukkan plateletcrit berperan penting untuk memprediksi mortalitas pada pasien STEMI dan memiliki korelasi signifikan sebagai prediktor* coronary slow flow phenomenon *serta berkorelasi dengan luaran kardiovaskular yang lebih buruk. Proses penuaan dikaitkan dengan perubahan aktivitas trombosit dan tingkat penyakit vaskular yang lebih tinggi. Pengaruh penuaan terhadap fungsi trombosis belum sepenuhnya jelas sehingga diperlukan penelitian lebih lanjut. Hipotesis pada penelitian ini adalah* plateletcrit *yang tinggi meningkatkan risiko terjadinya kejadian kardiovaskular mayor (KKM) pada pasien sindroma koroner akut usia lanjut selama perawatan di ruang intensif jantung.*
***Tujuan**. Mengetahui peran* plateletcrit *sebagai faktor risiko terjadinya kejadian kardiovaskular mayor pada pasien sindroma koroner akut usia lanjut.*

Metode. *Kami melakukan pengumpulan sampel pasien usia lanjut yang mengalami SKA pada periode Januari 2016 – Desember 2019, mencatat data* plateletcrit *serta ada tidaknya kejadian KKM. Data akan diolah dalam SPSS untuk mencari batasan nilai* plateletcrit *yang menjadi faktor risiko terjadinya KKM pada pasien usia lanjut di RSUP Dr. Sardjito.*

Hasil Penelitian. *Sebanyak 174 subjek penelitian terdiri dari 58 grup KKM dan 116 non KKM, didapatkan hasil platelecrit ≥0.35 meningkatkan risiko KKM dengan nilai* p=*0.046 dan OR 5.49.*

Kesimpulan. *Plateletkrit bermakna secara statistik terhadap kejadian KKM pada pasien sindroma koroner usia lanjut yang di rawat di ruang intensif jantung.*

Kata kunci. *Plateletkrit, kejadian kardiovaskular mayor, lanjut usia*

INTRODUCTION

Cardiovascular disease is the leading cause of death in the world, in 2004 cardiovascular disease was the cause of 17 million deaths, accounting for 30% of all causes of death. Acute coronary syndrome (ACS) which includes acute myocardial infarction with ST segment elevation (STEMI) or without ST segment elevation (NSTEMI) and unstable angina pectoris (UAP), associated with rupture of atherosclerotic plaques and partial or complete thrombotic processes of the arteries the coroner involved. Due to its significant morbidity and mortality rates, it is necessary to carry out risk stratification in ACS patients to determine optimal management, through various clinical and laboratory markers that have been developed.[1]

The occurrence of major cardiovascular events consisting of cardiovascular and non-cardiovascular deaths, recurrent myocardial infarction, stroke and recurrent percutaneous coronary intervention revascularization in hospital ranges from 8-10% in patients with acute coronary syndrome (ACS), whereas according to data from the Intensive Cardiac Care Unit (ICCU) dr. Cipto Mangunkusomo (RSCM) found that the mortality rate of ACS patients during hospitalization in 2010 was 12.1%.[2]

Platelets play a role in inflammation, thrombocytosis and cardiovascular pathophysiology. Thrombocytosis and inflammation play an important role in the initiation and progression of myocardial infarction. Increased thrombosis describes the release of inflammatory mediators that result in inflammatory responses and prothrombotic status. Plateletcrit are similar to hematocrit for erythrocytes, whereas plateletcrit represents the number of platelets in units of blood volume, increased plateletcrit correlates with worse cardiovascular outcomes in coronary heart disease.[3,4]

The aging process is associated with increased platelet activity and higher rates of vascular and thrombotic disease. Platelets in elderly and young humans differ greatly in number, activity and structure. The effect of age on thrombotic function is not completely clear, so further studies are needed to fully explain the relationship between molecular changes in platelets and pathophysiological changes in the vascular system during aging. This study investigated the role of plateletcrit in ACS, especially in elderly patients and to find out whether there was a correlation between plateletcrit value and the occurrence of MACE in the care of elderly patients with ACS who were treated in the cardiac intensive room Dr. Sardjito Hospital.

METHOD

The design of this study used a case control using secondary data of patients treated at the Intensive Cardiac Care Unit (ICCU) Dr. Sardjito Hospital in the period January 2016 - December 2019. Extraction of secondary data from medical records was carried out from August to September 2020.

The study inclusion criteria were patients diagnosed with acute coronary syndrome (ACS) aged ≥ 60 years who received ICCU treatment at Dr. Sarjito Hospital in the period of January 2016 - December 2019. The study exclusion criteria were patients with infectious diseases (written status such as sepsis, pneumonia, urinary tract infections or other infections receiving appropriate treatment or antibiotics), patients with autoimmune diseases, malignancy, use of long-term steroids and patients who go home on their own request.

The independent variable of this study was the plateletcrit. The study-dependent variable was the incidence of MACE which consisted of cardiac death, reinfarction, arrhythmias, hemodynamic disturbances (cardiogenic shock), revascularization, and stroke. Confounding variables were gender, PCI action, diabetes, hypertension, dyslipidemia, smoking, body mass index, TIMI, Grace, hemoglobin, leukocytes, BUN, creatinine, cardiac enzymes: CK / CPK, CKMB, and hs-Troponin I.

The stages of data analysis from the results of this study were to look at the Under Curve Receiver Operating Characteristic Curve (AUC) area to obtain the value of the plateletcrit cutoff point as the risk of MACE in treatment, then determine the Odds Ratio with univariate logistic regression analysis, then the p value (significance) was obtained. Variables with *p* value <0.25 in univariate analysis will be followed by multivariate analysis to get *p*

value (significance), adjusted Odds Ratio with CI 95%.

RESULTS AND DISCUSSION

Basic characteristics data are presented in Table I. The mean age in the group experiencing MACE was 70 years, and the mean age for the non-MACE group was 69 years. There were 58 people for the MACE group and 116 people in the non-MACE group with the percentage of male gender 70.7% and female 29.3% for each group. There were no significant differences in the two groups for variables of age, sex, hypertension, smoking history, dyslipidemia, body mass index, number of vessel disease, Hb, hematocrit, platelet and plateletcrit (PCT) (p> 0.05). Whereas DM, PCI, pulse, systolic blood pressure, diastolic blood pressure, Killip, GRACE, platelet distribution width (PDW), PLCR, neutrophils, lymphocytes, lymphocyte ratio of neutrophils (NLR), BUN, creatinine, GDS, CK / CPK, CKMB and hs-Troponin I showed significant differences between the two groups (p <0.05).

In the results of cardiac catheterization in this study, it was found that the majority of blood vessels involved in the incidence of coronary syndrome in elderly were three-vessel disease. This is in accordance with previous studies where in angiographically elderly patients, left main stenosis and three-vessel disease were more common.[5]

Table 1. Basic Characteristics Data

		MACE				*P*
		Yes (n=58)		No (n=116)		
Age		70 (60 – 82)		69 (60 – 88)		0.646
Age group	60-74	42	72.4%	84	72.4%	1.000
	75-90	16	27.6%	32	27.6%	
Sex	Male	41	70.7%	82	70.7%	1.000
	Female	17	29.3%	34	29.3%	
MACE	Cardiac arrest	25	43.1%			
incident	Arrythmia	4	6.9%			
	Stroke	3	5.2%			
	Cardiogenic shock	24	41.4%			
	Re-infarct	2	3.4%			
Death	Yes	58	100.0%			
	No	0	0.0%			
PCI	Yes	22	37.9%	68	58.6%	0.010*
	No	36	62.1%	48	41.4%	
DM	Yes	26	44.8%	27	23.3%	0.004*
	No	32	55.2%	89	76.7%	
HT	Yes	40	69.0%	79	68.1%	0.908
	No	18	31.0%	37	31.9%	
Smoking status	Yes	35	60.3%	53	46.9%	0.096
	No	23	39.7%	60	53.1%	
Dyslipidemia	Yes	15	26.3%	33	28.7%	0.743
	No	42	73.7%	82	71.3%	

Heart rate		89,5 (35 – 150)		73 (30 – 160)		0.000*
SBP		117 (70 – 190)		130 (80 – 240)		0.001*
DBP		70 (40 – 100)		78 (40 – 120)		0.000*
KILLIP	1	27	51.9%	85	87.6%	0.000*
	2	9	17.3%	10	10.3%	
	3	5	9.6%	1	1.0%	
	4	11	21.2%	1	1.0%	
GRACE		147 (86 – 281)		12,75 (7,10 – 17,30)		0.000*
Body Mass Index		23,83 (17,58 – 31,25)		37,70 (23,10 – 52,20)		0.323
Number of affected blood vessels (vessel disease)	1	9	21.4%	21	23.9%	
	2	10	23.8%	33	37.5%	
	3	22	52.4%	34	38.6%	
Hb		12.10 (5,5 – 18,1)		12.70 (7,1 – 17,3)		0.279
Hmt		35.80 (17,5 – 54,7)		37.70 (23,1 – 52,2)		0.190
Platelet		238.00 (87 – 525)		243.00 (131 – 2122)		0.627
PDW		12.05 (8,3 – 17,6)		10.9 (7,5 – 19,8)		0.036*
P-LCR		28.90 (12,7 – 48)		25.5 (9,7 – 49,3)		0.035*
PCT		.20 (0,1 – 0,6)		.30 (0,1 – 0,5)		0.891
Netrofil %		80.70 (39,4 – 93,7)		69.7 (32,8 – 90,6)		0.000*
Limfosit %		11.65 (2,4 – 53)		19.1 (5,3 – 51.6)		0.000*
NLR		6.85 (0,75 – 38,9)		3.71 (0,7 – 16,7)		0.000*
BUN		28.95 (1,61 – 151)		15.00 (6,7 – 61)		0.000*
Creatinin		1.83 (0,68 – 370)		1.19 (0,5 – 12)		0.000*
RBG		177.00 (26 – 1991)		130.00 (13 – 434)		0.000*
CK/CPK		262.00 (33 – 5088)		140.00 (13 – 4438)		0.013*
CKMB		53.50 (3,4 – 940)		3 (4,1 – 838)		0.006*
Hs Troponin I		15742 (12,9 – 40000)		71.70 (1,5 – 40000)		0.000*

Description: MACE: major cardiovascular event; PCI: percutaneous coronary intervention; DM: diabetes mellitus; HT: hypertension; SBP: systolic blood pressure; DBP: diastolic blood pressure; KILLIP: Killip score; GRACE: The Global Registry of Acute Coronary Events; PDW: Platelet Distribution Width; P-LCR: Platelet Large Cell Ratio; PCT: plateletcrit; NLR: neutrophil lymphocyte ratio; RBG: random blood glucose; CK / CPK: Creatine Kinase / Creatine Phosphokinase; CKMB: Creatine Kinase-MB

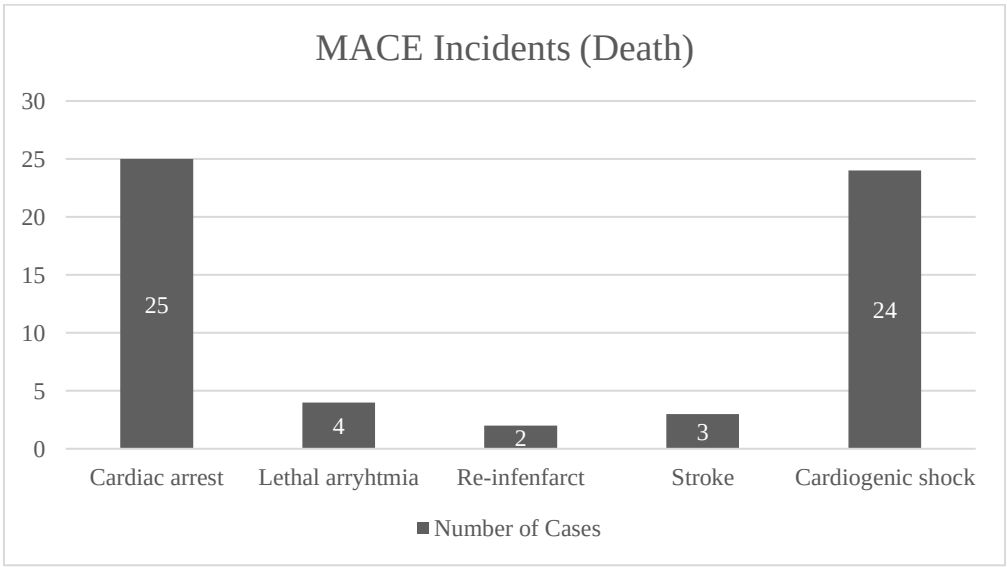

Figure 1. Major Cardiovascular Events in the Study

The results showed 58 cases of fatal MACE events who died, consisting of 25 people who died with information about cardiac arrest, 24 people died with cardiogenic shock, 4 people with lethal arrhythmias, 2 people with re-infarction, and 3 people with stroke events.

The ROC curve analysis showed the plateletcrit cut-off rate was 0.35 with a specificity of 95.7% and a sensitivity of 17.2%.

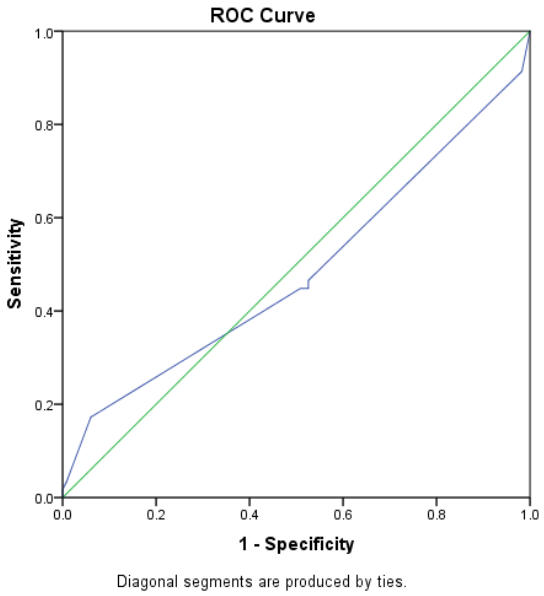

Figure 2. Graphic Receiver Operating Curve (ROC)

Table 2. Plateletcrit Relationship to MACE Based on the ROC Curve

AUC	P	CI 95%	Cut off	Sn	Sp	PPV	NPV	LR+	LR-
0.494	0.900	0.397 – 0.592	0.35	17.2%	95.7%	66.7%	69.8%	4.00	0.86

In the bivariate analysis, the results showed that patients with a plateletcrit count ≥0.35 had a MACE as much as 66.7% and those who did not experience a MACE were 33.3%. Statistically significant results were obtained for the plateletcrit cut-off value ≥ 0.35 with p = 0.008 (p <0.05) and OR = 4.63.

Table 3. Plateletcrit Relationship to MACE of Elderly ACS Patients

		MACE				*p*	OR	CI 95%
		Yes		No				
		N	%	N	%			
PCT	≥ 0.35	10	66.7%	5	33.3%	0.008	4.63	1.50 – 14.26
	< 0.35	48	30.2%	111	69.8%			

PCT: plateletcrit; MACE: major cardiovascular event; OR: Odds ratio; CI: confidence interval

From univariate analysis obtained plateletcrit, PCI, DM, pulse, blood pressure, KILLIP class, GRACE, platelet distribution width (PDW), neutrophils, lymphocytes, lymphocyte neutrophil ratio (NLR), BUN, creatinine, GDS, CK / CPK, CKMB and hs-troponin I was statistically significant to the incidence of MACE with a *p* value <0.05.

Platelecrit ≥ 0.35 will increase the incidence of MACE by 5.49 times with a value of $p = 0.046$. The presence of DM comorbid increases the risk of MACE incidence by 6.4 times with a value of $p = 0.001$. A smoking history increased the risk of MACE incidence by 3.09 times with a value of $p = 0.02$. PCI action reduces the risk of MACE occurrence by 0.17 times with a value of $p = 0.000$.

This study showed that there were differences both clinically and statistically in the plateletcrit number in the group that experienced MACE and did not experience MACE. It is known from the results of this study that the cut-off plateletcrit with MACE is ≥0.35 and the OR value is 4.63 and it is statistically significant where the value of $p = 0.008$ is obtained. The results of this study are consistent with previous studies where plateletcrit should be correlated with worse cardiovascular outcomes in coronary heart disease.[3,4]

Table 4. Univariate Analysis of Confounding Variables Against MACE

		Univariat		
		P	OR	CI 95%
PCT	≥ 0.35	0.008	4.63	1.50 – 14.26
	< 0.35			
PCI	Yes	0.011	0.43	0.23 – 0.82
	No			
DM	Yes	0.004	2.68	1.37 – 5.25
	No			
Smoking Status	Yes	0.097	1.72	0.91 – 3.28
	No			
Heart rate		0.000	1.03	1.02 – 1.05
SBP		0.001	0.97	0.97 – 0.99
DBO		0.000	0.95	0.93 – 0.97
KILLIP	1.00			
	2.00	0.041	2.83	1.04 – 7.69

	3.00	0.014	15.74	1.76 – 140.68
	4.00	0.001	34.63	4.27 – 280.65
GRACE		0.000	1.02	1.01 – 1.03
BMI		0.657	1.02	0.94 – 1.11
Number of affected blood vessels (vessel disease)		0.454	1.19	0.75 – 1.89
Hmt		0.118	0.96	0.90 – 1.01
PDW		0.044	1.17	1.01 – 1.38
P-LCR		0.050	1.05	1.00 – 1.09
Netrofil %		0.001	1.05	1.02 – 1.08
Limfosit %		0.003	0.94	0.91 – 0.98
NLR		0.000	1.15	1.07 – 1.25
BUN		0.000	1.05	1.03 – 1.07
Creatinin		0.007	1.58	1.13 – 2.19
RBG		0.000	1.01	1.01 – 1.01
CK/CPK		0.001	1.00	1.00 – 1.00
CKMB		0.023	1.01	1.00 – 1.01
hsTroponin I		0.000	1.00	1.00 – 1.00

Description: MACE: major cardiovascular event; PCI: percutaneous coronary intervention; DM: diabetes mellitus; HT: hypertension; SBP: systolic blood pressure; DBP: diastolic blood pressure; KILLIP: Killip score; GRACE: The Global Registry of Acute Coronary Events; PDW: Platelet Distribution Width; P-LCR: Platelet Large Cell Ratio; PCT: plateletcrit; NLR: neutrophil lymphocyte ratio; RBG: random blood glucose; CK / CPK: Creatine Kinase / Creatine Phosphokinase; CKMB: Creatine Kinase-MB

Table 5. Multivariate Analysis of Confounding Variables on MACE Incidence

		Multivariat		
		p	OR	CI 95%
PCT	≥ 0.35 < 0.35	0.046	5.49	1.03 – 29.26
PCI	Yes No	0.000	0.17	0.06 – 0.44
DM	Yes No	0.001	6.40	2.24 – 18.26
Smoking status	Yes No	0.020	3.09	1.19 – 8.02
Heart rate		0.001	1.04	1.01 – 1.06
NLR		0.043	1.14	1.01 – 1.28
BUN		0.022	1.04	1.01 – 1.07

PCT: plateletcrit; PCI: percutaneous coronary intervension; DM: diabetes melitus; NLR: neutrophil lymphocyte ratio

Diabetes is a variable that has a significant effect on MACE, from this study the value of $p = 0.001$, and the OR value of 6.4 where when a person has a history of diabetes, the risk of developing MACE increases by 6.4 times. The hyperglycemia state causes cell injury caused by a higher inflammatory response, increased levels of the intercellular adhesion molecule (ICAM-1), increased production of superoxide radicals and other reactive oxygen species (ROS) by oxidative stress which in the long run increases the risk of MACE in ACS patients.[6,7]

Pulse affects the incidence of MACE where in this study the value of $p = 0.001$ with an OR value of 1.04 means that if the pulse increases, the incidence of MACE increases 1.04 times. Heart rate affects myocardial oxygen demand and coronary

perfusion also causes progression of plaque rupture. Increased heart rate will increase hemodynamic and vascular mechanical stress, increased heart rate also has an impact on pro-atherogenicity, endothelial dysfunction, shear stress, oxidative stress, inflammation, increased aortic distensibility and vascular stiffness which increases the risk of MACE in ACS patients.[8]

The ratio of lymphocyte neutrophils is also a significant variable for MACE with a value of $p = 0.043$ and an OR value of 1.14 which means that each increase in NLR increases the risk of MACE by 1.14 times. The NLR data is obtained from the ratio between neutrophils and lymphocytes, so that it becomes a practical and simple and cost-effective parameter which may be useful in the future as a risk strategy for patients with acute coronary syndrome.

The value of BUN has a significant effect where each increase of 1 point increases the risk of 1.04 times the incidence of MACE with a value of $p = 0.02$ Creatinine concentration is associated with oxidative stress, endothelial dysfunction, progressive atherosclerosis, and hypercoagulation which increases cardiovascular risk. Creatinine values describe the pathophysiological mechanisms in the form of low cardiac output, decreased blood flow to the kidneys, excess volume and impaired left ventricular diastolic function which will increase the risk of developing MACE in ACS patients.[9,10]

CONCLUSION

Plateletcrit plays a role as a risk factor for the occurrence of MACE clinically and also statistically with $p = 0.046$ and OR 5.49. The cut off plateletcrit in this study was 0.35. Other variables that increase the risk of MACE are DM, smoking history, pulse, neutrophil lymphocyte ratio and BUN with p value < 0.05. PCI action reduces the risk of MACE occurrence with a value of $p = 0.000$ and OR 0.17.

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