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Modified Shock Index as a Simple and Strong Predictor of In-Hospital Mace among Patients with St-Segment Elevation Myocardial Infarction

T Fauzan Atsari*[1], Harris Hasan[1], Zainal Safri[1], Zulfikri Mukhtar[1], Refli Hasan[1], Cut A. Andra[1]

[1]Department of Cardiology and Vascular Medicine, University of Sumatera Utara, Adam Malik Hospital, Medan, Indonesia

Abstract : Background: Current risk scores of ST-segment elevation myocardial infarction (STEMI) need sophisticated algorithm and were limited for bedside use. Prompt identification of higher risk patients presenting with STEMI will allow a more aggresive strategy and approach. The aim of this study was to evaluate the modified shock index as a predictor ofin-hospital major adverse cardiovascular events (MACE) in patients with STEMI.

Method : This cohort ambispective study included 74 consecutive patients with STEMI from February 2018 until September 2018 admitted to Adam Malik General Hospital. The blood pressure (BP) and heart rate (HR) measured at emergency department were used to calculate MSI (HR/mean artery pressure). Patients were divided into groups with MSI <1.3 and ≥1.3,respectively, based on the receiver operating characteristic curve analysis from previous studies. MSI and clinical variables were compared between groups of patients with in-hospital MACE with a group of patients who did not experience in-hospital MACE which are mortality, acute heart failure, cardiogenic shock, and malignant arrhythmias.

Result : Of the 74 STEMI patients in this study, 28 (37.8%) patients experienced MACE, and there were 19 (79.2%) of them who had MSI values≥ 1.3. A significant relationship was found between the modified shock index value and the incidence of acute heart failure (OR 14,857, 95% CI 4.25-51.89, p <0.001). Multivariate analysis shows that MSI ≥ 1.3 is an independent factor to predict the occurrence of MACE in this study [OR 8.34 (5.15-34.66), p=0.001].

Conclusion : The modified shock index is a simple and easy to acquire and can be an independent factor for predicting major cardiovascular events during treatment in patients with acute myocardial infarction with ST segment elevation. The simplicity of this proposed index makes its use accessible in large-scale clinical practices for risk stratification during first contact with patients.

Keyword : Modified Shock Index; MACE; STEMI; Myocardial Infarct.

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Introduction

ST Elevation Myocardial Infarction (STEMI) is one of theacute coronary syndromes (ACS) spectrum which still a major health problem in industrialized and developing countries with incidence rates ranging from 27% to 47%. In Indonesia, based on the Jakarta Acute Coronary Syndrome (JAC) registry analysis which carried out in the National Cardiovascular Center Harapan Kita (NCCHK) emergency department showed that there were 654 STEMI patients among the 2103 acute coronary syndrome patients, and most of those patients (59%) did not receive acute reperfusion therapy and 52% of the patients were inter-hospital referrals. Mortality rates during the hospitalization period of STEMI patients who did not receive reperfusion therapy were higher than those of patients who received both fibrinolytic and primary PCI. (13.3% vs. 6.2% vs. 5.3%).[1]

Risk stratification for patients with STEMI is very important to identify those patients who deserve advanced measures. At present, several systems of risk stratification such as Thrombolysis in Myocardial Infarction (TIMI), Global Register Acute Coronary Events (GRACE), and CADILLAC risk score are used, but the sophisticated calculation usually makes them inconvenient to operate at bedside in daily clinical practice.[2]The concept of shock index (SI), defined as the ratio of heart rate and systolic blood pressure, first introduced by Allgower et al, in 1967 as a simple and effective means for gauging the degree of hypovolemia in hemorrhagic and infectious shock states.[3]Itspredicting value for the outcome also has been fully demonstrated in thepatients with trauma.[9-12]Shock index can also be applied to patients with sepsis, pulmonary embolism, and stroke.[15,16] Huang et al suggested that admissionSI of 0.7 or greater is a useful predictor for short-term outcomes inthe patients with STEMI.[4] Other studies also indicated that an SI of 0.8 ofgreater is a novel predictor for in-hospital and long-term mortality in thepatients with STEMI.[5,6] These results provided a simple index forrisk stratification in the patients with STEMI.

A new index, modified shock index (MSI), is created asthe ratio of HR and mean artery pressure (MAP) because DBP isan undeniable parameter when determining clinical severity. It is noticed that SI uses only systolic blood pressure, but diastolic blood pressure (DBP) is also of undeniable importance when determining patient’s clinical severity.[7]Somestudies have found that MSI is a better predictor than SI for the outcomein adult patients with trauma.[13,14]Furthermore, the aim of this study is to assess whether MSI could be a predictor of MACE in the patients with STEMI.

Method

Population and Design

This prospective study included 74 consecutive patients with acute STEMI admitted to the emergency department (ED) in Adam Malik General Hospital in Medan, Indonesiafrom February 2018 until September 2018. The inclusion criteria are patients arrivingin the ED within 48 hours after symptom onset, and then diagnosed withacute STEMI.ST-segment elevation myocardial infarction was defined asfollows: chest pain or equivalent symptoms in combination withdynamic electrocardiographic changes consistent with STEMI (in thepresence of ST elevation at least two contiguous leads$\geq$ 2.5 mm in men < 40 years, $\geq$ 2mmin men $\geq$ 40 years, or $\geq$ 1.5 mm in women in leads V2-V3 and/or $\geq$ 1 mm in the other lead and increased serum biochemical markers of cardiac necrosis,including creatine kinase–MB and troponin I. The exclusion criteria arepatients with second and third degree av block, atrial fibrillation, cardiogenic shock at admission, pacemaker rhythm, and patients with severe comorbid such as sepsis, non-cardiogenic shock, stroke, burn, acute or chronic renal failure who need dialysis. Patients who met the inclusion and exclusion criteria were then provided with written informed consent and recruited as subjects.

All patients received standard medication therapy according to theguidelines for the management ofSTEMI, including antiplatelet and anticoagulation, statins, angiotensinconvertingenzyme inhibitor or angiotensin receptor antagonists, nitrates,β-blockers, calcium channel blockers. The use of vasoactivedrugs including dopamine,dobutamine, adrenaline, noradrenaline, was recorded.

The BP and HR measured (stand mercurial sphygmomanometer, Jinsan medical co ltd, Taiwan) atED were used to calculate MSI. Blood pressure and HR weremeasuredtwice with 1-minute interval, and their average was used as final value.Modified shock index is the ratio of HR to mean blood pressure(MAP). Here, $MAP = [(DBP \times 2) + SBP]/3$.The cutoff value of MSI was referred as 1.3 in the study by Gloria Abreu.[8] In this study, major adverse cardiac events (MACE) include all-causemortality, heart failure, life threatening arrhytmias, and cardiogenic shock during hospital treatment.

Statistical Analysis

All statistical analyseswere carried out using the SPSS statistical software,version 19.0.The data were presented withmean ± SD or median and interquartile range for continuous variables. Categorical variables presented as percentage. The normality test for continuous variables in all study subjects using one sample Kolmogorov Smirnov (n> 50). In continuousvariables compared with two free samples T test (Two Samples Independent Student's t-test) on normal distributed data or Mann Whitney U Test test if the data is not normally distributed.In categorical variables, an analytical test is performed using chi squared or fisher tests. For variables that were found to be significant in the bivariate analysis test, were entered into the multivariate test with logistic regression test and p value < 0,05 was considered as statistically significant.

Result

In this study, we enrolled 74 patients who have met the inclusion and exclusion criteria as subjects.The subjects were then divided into two groups based on the value of modified shock index.The first group is patients with highmodified shock index value (≥ 1.3), while the second group is the subject with lowmodified shock index value (< 1.3).There were 54 people (72.9%) had high modified shock index value and 20 people (27.1%) had low modified shock index value.

The results of this study indicate that there are some statistically significant differences between groups with low modified shock index and groups with high modified shock index values, which are systolic blood pressure, diastolic blood pressure, mean blood pressure, heart rate, infarct location, TIMI score, ejection fraction, and the initial blood glucose value. In terms of systolic and diastolic blood pressure, it was seen that group withlow modified shock index had a higher systolic and diastolic blood pressure with 124 mmHg and 80 mmHg versus 103 mmHg and 64 mmHg (p <0.001) (Table 1).

Table1.Baseline Characteristic of Subject Study

Variables	**Modified Shock Index**		**p value**
	<1.3 (Low) (n=54)	**≥1.3 (High) (n=20)**	
Age (years±SD)	55.31 ± 9.71	58.35 ± 10.34	0.245
Sex (n,%) Male Female	 41 (75.9) 13 (24.1)	 16 (80) 4 (20)	1
Family history (n,%)	1 (1.9)	0 (0)	1
BMI (kg/m^2±SD)	25.11 ± 3.15	25.38 ± 3.98	0.758
Risk Factor (n,%) Hypertension Diabetes Mellitus Dyslipidemia Smoking	 33 (61.1) 13 (24.1) 14 (25.9) 38 (70.4)	 9 (45) 15 (75) 5 (35) 13 (65)	 0.214 <0.001 0.935 0.658
Blood Pressure, (mm Hg±SD) Systolic Diastolic	 124.81 ± 21.34 80.18 ± 12.05	 103 ± 7.32 64 ± 5.02	 <0.001 <0.001
MAP, mmHg	95.06 ± 14.24	76.99 ± 4.03	<0.001
Heart Rate (beat/min)	74.5 ± 13.8	110.95 ± 10.2	<0.001
Chest Pain Onset(n,%), hour ≤ 12 > 12	 25 (46.3) 29 (53.7)	 6 (30) 14 (70)	0.207

Infarct Location (n,%) Anterior Inferior	 27 (50) 27 (50)	 18 (90) 2 (10)	0.012
TIMI Risk (n,%) ≤ 4 > 4	 39 (72.2) 15 (27.8)	 4 (20) 16 (80)	<0.001
Ejection Fraction (%±SD)	44.91 ± 8.09	37.35 ± 6.53	0.002
Hb (g/dL±SD)	13.86 ± 2.12	13.39 ± 1.69	0.476
Leukocytes (/mm±SD^3)	13,993.33 ± 3,714.60	13,011.5 ± 2,768.53	0.286
Ureum (mg/dL±SD)	28.7 ± 10.73	32.7 ± 20.35	0.908
Creatinine (mg/dL±SD)	1.04 ± 0.37	1.14 ± 0.60	0.976
Initial Blood Glucose (mg/dL±SD)	145.43 ± 69.03	215.40 ± 94.39	<0.001

Based on the treatment given, there were no statistically significant differences between low modified shock index group and high modified shock index group values on some treatments, which are reperfusion strategies, anticoagulant administration, antiplatelet administration, and administration of other drugs such as beta blockers, ACE inhibitors, nitrates,statins, and amiodarone administrations. However, when compared between the two groups, groups with high modified shock indexreceived more diuretic therapy, 17 people (85%) compared to 16 people (29.6%) (p <0.001) in the group with lowmodified shock index, and inotropic administration was 7 people (35%) compared to 3 people (5.6%) with a p value of 0.003 (Table 2).

Table 2.Treatment characteristics of the study population

Variable	**Modified Shock Index**		**p value**
	<1.3 (Low)	**≥1.3 (High)**	
Reperfusion Strategies (n,%) Primary PCI Fibrinolytic Elective PCI Without Reperfusion	 32 (59.3) 5 (9.3) 8 (14.8) 9 (16.7	 12 (60) 2 (10) 2 (10) 4 (20)	0.95
Anticoagulant (n,%) Enoxaparin Fondaparinux UFH	 39 (72.2) 14 (25.9) 1 (1.9)	 13 (65) 5 (25) 1 (5)	0.341
Antiplatelet (n,%) Aspirin Clopidogrel	 54 (100) 54 (100)	 20 (100) 20 (100)	 0.23 0.23
Other: (n,%) Beta blocker ACE Inhibitor Nitrate Statin Diuretic Inotropic Amiodarone	 23 (61.1) 40 (74.1) 48 (88.9) 54 (100) 16 (29.6) 3 (5.6) 1 (1.8)	 16 (80) 16 (80) 17 (85) 20 (100) 17 (85) 7 (35) 2 (10)	 0.127 0.764 0.696 0.523 <0.001 0.003 0.154

The modified shock index has a relationship with the occurrence of heart failure. Groups with high modified shock index values appear to have a higher risk of heart failure. In groups with high modified shock index, there were 13 people (68.4%) who had heart failure, while from all patients who did not have heart failure only 7 people (12.7%) had a high modified shock index and this was statistically significant (OR 14,857; 95% CI 4,253-51,899; p <0.001) (Table 4). Based on these results showed that in patients with a high modified shock index had a risk of 14.8 times experiencing heart failure compared with patients with a low modified shock index during treatment. In this study high modified shock index value has no relationship with the incidence of death, cardiogenic shock, and malignant arryhtmias (Table 3).

Table 3.Bivariate Analysis of Modified Shock Index and MACE

MACE	Modified Shock Index		p value
	<1.3 (Low)	**≥1.3 (High)**	
Death (n,%)			0.07
Yes	0 (0)	2 (10)	
No	54 (100)	18 (90)	
Heart Failure (n,%)			<0.001
Yes	6 (11.1)	13 (65)	
No	48 (88.9)	7 (35)	
Cardiogenic Shock (n,%)			0.334
Yes	3 (5.6)	3 (15)	
No	51 (94.4)	17 (85)	
Malignant Arrythmia (n,%)			0.176
Yes	1 (1.9)	2 (10)	
No	53 (98.1)	18 (90)	

Table 4.Bivariate Analysis of Modified Shock Index and Heart Failure

	Heart Failure			CI 95%	
	Yes	**No**	**OR**	**min**	**maks**
Modified Shock Index			14.857	4.253	51.899
High	13 (68.4)	7 (12.7)			
Low	6 (31.6)	48 (87.3)			

After adjusting admission variables by univariate analysis, we performed multivariate analysis to find out which independent variable is the most dominant and affect the occurrence of in-hospital MACE in STEMI patient and revealed modified shock index is evidently the most dominant predictor for in-hospital MACEs after myocardial infarction (Table 5).

Table 5.Multivariate Analysis of Factors Affecting MACE

Parameter	P value	OR	Lower	Upper
TIMI Score	0.002	3.93	1.35	28.37
Modified Shock Index	0.001	8.34	5.15	34.66

Pearson correlation analysis between modified shock index and TIMI score found a significant positive correlation with p <0.001 and coefficient R = 0.536 indicating moderate strength (Table 6).

Table 6. Correlation Between Modified Shock Index and TIMI Score

		TIMI Score
Modified Shock Index	R	0.536
	P	<0.001

Discussion

In our study, showed significant differences in systolic blood pressure, diastolic blood pressure, mean blood pressure, and heart rate between the two groups resulting in different modified shock index values. In groups with high modified shock index values were seen to have lower SBP, DBP, and mean blood pressure, and were seen to have a faster heart rate compared to groups with low modified shock index values group. This is similar with previous studies, where in groups with a high modified shock index had lowerSBP, DBP, mean blood pressure and a faster heart rate.[2,7,8]

Another difference is also seen in the TIMI score. Patients with a high modified shock index had a higher TIMI score. Spearman correlation analysis showed that the modified shock index had a positive correlation with medium strength (r = 0.536) and significant (p <0.001) with TIMI scores. This is similar with a previous study by Gouda et al in 2016 which showed a positive correlation between the modified shock index and the TIMI score with a value of r = 0.579 and a value of p = 0.01.[2]

In STEMI patients, parameters related to the cardiovascular system such as cardiac index and stroke volume are decreased which stimulates neurohormonal reactions, where sympathetic activation is the most significant. This sympathetic activation will increase blood pressure and heart rate to compensate for the decrease in cardiac output due to myocardial infarction, so that blood pressure and heart rate after myocardial infarction can provide an integrated picture of the cardiovascular system and the neuroendocrine system and hemodynamic status.

A high modified shock index value indicates low stroke volume and peripheral vascular resistance which is a sign of hypodynamic circulation. So that the modified shock index value can be a stratification tool in predicting the severity of a disease. Where the high modified shock index value increases the probability of death.

Based on this study, it can be seen that the modified shock index has a strong relationship with the incidence of heart failure, but has no relationship with the incidence of death, cardiogenic shock, and malignant arrhythmias during treatment in STEMI patients.

After multivariate analysis, there were two independent factors that could predict MACE during hospitalization treatment in STEMI patients, TIMI Score [OR 3.93 (1.35-28.37), p = 0.002] and Modified Shock Index [OR 8.34 (5.15-34.66), p = 0.001].

Limitation of Study

The limitations of this study include the number of samples of this study is smaller than previous studies and only carried out in onecenter so that further research needs to be done with a larger number of samples and multicenter. In this study MACE observation was carried out only during hospital treatment. This study also did not compare the value of MSI in patients with acute coronary syndrome, in the future, needs to be research to find the relationship of MSI values in this population.

Conclusion

The modified shock index is a simple and easy to acquire and can be an independent factor for predicting major cardiovascular events during treatment in patients with acute myocardial infarction with ST segment elevation. The simplicity of thisproposed index makes its use accessible in large-scale clinical practicesfor risk stratification during first contact with patients.

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