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Correlation between Left Ventricular Ejection Fraction (LVEF) and six-month mortality risks after hospital discharge following myocardial infarction in patients with Non-ST-Elevation Myocardial Infarction (NSTEMI) at Prof. Dr. R. D. Kandou General Hospital, Manado, Indonesia

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ABSTRACT

Background: Reduced Left Ventricular Ejection Fraction (LVEF) is considered to worsen prognosis after an acute myocardial infarction (AMI), including Non-ST-elevation myocardial infarction (NSTEMI). This study aims to find a correlation between LVEF with mortality risk after hospital discharge following myocardial infarction using GRACE score among NSTEMI patients.
Methods: Data was collected from the iSTEMI Registry database in Prof. Dr. R. D. Kandou General Hospital from October 3rd 2018, to July 28th 2019. About 122 NSTEMI patients were collected to measure their LVEF by transthoracic echocardiography and routine clinical workup for GRACE score calculation at admission. A descriptive analysis, normality test, and bivariate correlation were applied. A p-value less than 0.05 was considered statistically significant using SPSS version 23 for Windows.
Results: The mean age of the patients was 62.07±11.11 years old and most of the study subjects were male (73%). The mean GRACE score was 118.92±33.52, whereas the mean ejection fraction was 48.76±16.32%. LVEF was negatively significant correlated with the GRACE score (p=0.017; r=-0.230).
Conclusion: Lower LVEF is correlated with increased six-month mortality risk after hospital discharge using GRACE score following myocardial infarction in a patient with Non-ST-elevation myocardial Infarction.

Keywords: Ejection Fraction, GRACE score, NSTEMI.
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INTRODUCTION

Acute Myocardial Infarction (AMI), a subset of Acute Coronary Syndrome (ACS), is the leading cause of global morbidity and mortality, causing 15% mortality each year, with a prevalence of three million people worldwide.[1-3] When a coronary artery is occluded or close to occlusion, a myocardial infarction will occur, resulting in a severe decrease in blood flow, which leads to some of the myocardium being supplied by that artery becoming infarcted.[1] Occlusion is usually the result of atherosclerosis. It causes 70% of fatal events in AMI.[2,3] AMI can be divided into ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI).[2,3] STEMI can be identified by typical ST-segment elevation. On the contrary, the absence of ST-segment elevation and elevated cardiac biomarkers (such as troponin) is classified as NSTEMI.[1]

Left ventricular ejection fraction is the most widely accepted measurement of left ventricular systolic function and is related to cardiovascular outcomes.[4,5] LVEF plays an important role in assessing the severity of decreased cardiac systolic function, making it useful for guiding the treatment of various cardiovascular diseases.[4]

The Global Registry of Acute Coronary Events (GRACE) score is one of the scores developed as a risk prediction tool to identify patients who have an increased risk of adverse events after ACS.[6] It can also estimate the cumulative 6-months mortality risk to facilitate emergency department and management of ACS patients.[6,7] GRACE score is not limited to any changes in the ST segment; hence it can be used for both STEMI and NSTEMI.[6] Until now, there are limited studies that evaluate the association between GRACE

score and LVEF In AMI patients. This study aims to find the correlation between LVEF with mortality risk after hospital discharge following myocardial infarction using GRACE score in a patient with NSTEMI.

METHODS

The data for GRACE score (age, history of heart failure, history of Acute Myocardial Infarction, Heart Rate, Systolic Blood Pressure at admission, serum creatinine, cardiac markers and history of percutaneous revascularization) in NSTEMI patients were collected from the iSTEMI Registry database, which consists of patients without a history of AMI in Prof. Dr. R. D. Kandou General Hospital. The data that was extracted was dated from October 3rd 2018 to July 28th,2019. LVEF evaluations were also collected.

The inclusion criteria in this study were patients with NSTEMI and age more than 30 years of either gender. In addition, the exclusion criteria were as follows: 1) Patients with severe valve disease; 2) Patients with congenital heart disease; 3) Patients with life-threatening co-morbidity with life expectancy <1 year; 4) Patients with second- or third-degree atrioventricular block; 5) Patients with malignancy; and 6) Patients with end-stage renal failure.

The primary outcome of this study is the correlation between LVEF and six-month mortality risk after hospital discharge. Mortality risks are calculated using the GRACE score. GRACE score parameters include heart rate, age, systolic blood pressure, cardiac arrest, Killip class, ST-segment deviation, serum creatinine and cardiac biomarker status. GRACE risk scores can be categorized as low risk with scores 0 to 108, the intermediate or medium risk with GRACE score between 108 to 140 and high risk with GRACE score >140. According to the American College of Cardiology, a normal or preserved LVEF ranges 50 to 70%. LVEF <30% is considered severe dysfunction and LVEF 30% to 49% was defined as mild-moderate dysfunction.

Statistical analysis was conducted using the Statistical Product and Service Solutions (SPSS) version 23. A descriptive analysis and bivariate correlation with the Spearman correlation test were applied. A p-value of <0.05 was considered to be statistically significant.

RESULTS

From October 3rd 2018 to July 28th 2019, we included 122 patients diagnosed with NSTEMI without prior history of AMI. Among them, 73.00% of the study subjects were male. The average age of the patients was 62.07±11.11 years (Table 1). The mean GRACE score was 118.92±33.52 (intermediate risk), whereas the mean ejection fraction was 48.76±16.32%.

Table 1. Baseline characteristics of patients.

Variable	N	Percentage (%)	Mean	SD
Age (Years)			62.07	11.11
Gender				
Male	89	73.00		
Female	33	27.00		
Bodyweight (kg)			64.35	11.52
Body height (cm)			160.90	6.87
BMI (kg/m^2)			24.76	3.76
SBP (mmHg)			135.93	31.93
DBP (mmHg)			82.29	19.77
HR (beats/minutes)			87.40	22.73
ST-segment deviation	29	23.80		
Killip classification				
I	79	64.80		
II	36	29.50		
III	6	4.90		
IV	1	0.80		
Diabetes	33	27.00		
Hypertension	82	67.20		
Dyslipidemia	40	32.80		
Current smoker	42	34.40		
Heart failure	4	3.30		
Stroke	9	7.40		
PAD	0	0.00		
Previous PCI	15	12.30		
Previous CABG	2	1.60		
History of premature CVD in family	2	1.60		
Hemoglobin (g/dL)				10.65
Hematocrit (%)			13.97	8.04
Leukocyte (mcL)			39.14	4,506.76
Lipid Profile (g/dL)			11,300.83	
Total cholesterol				56.65
HDL			184.19	10.34
LDL			36.68	51.47
Triglycerides			120.05	76.23
Serum uric acid (mg/dL)			142.37	2.74
Serum ureum (mg/dL)			8.67	44.72
Serum sodium (mEq/dL)			57,05	5.34
Serum potassium (mEq/dL)			135.00	0.65
CK-MB (U/L)			4.15	38.83
Troponin-T (ng/L)			53.85	587.00
LVEF (%)			508.49	16.31
E/A ratio			48.758	2.83
LVESD (mm)			1.31	12.33
LVEDD (mm)			36.60	13.27
TAPSE (mm)			50.36	8.53
Length of hospital stay (day)			14.61	3.89
In-hospital death	7	5.70	7.81	
GRACE score			118.92	33.52

LVEDD: Left Ventricular End Diastolic Diameter; LVEF: Left Ventricular Ejection Fraction; LVESD: Left Ventricular End Systolic Diameter; PAD: Peripheral Arterial Disease; TAPSE: Tricuspid Annular Plane Systolic Excursion; HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein; CK-MB: Creatine Kinase-Myocardial Band; GRACE: Global Registry of Acute Coronary Events; PCI: Percutaneous Coronary Intervention; SD: Standard Deviations

Table 2. Spearman correlation test to the GRACE Score.

Variable	r	p
LVEF (%)	- 0.230	0.017*

LVEF: Left Ventricular Ejection Fraction; r: coefficient correlation; *Statistically significant if p-value less than 0.05

Lower ejection fraction was significantly correlated with a higher GRACE score ($p = 0.017$; $r = - 0.230$) which means a reduction in LVEF is associated with a higher GRACE score (Table 2).

DISCUSSION

In patients with or without a history of cardiovascular disease, LVEF was an important predictor of risk stratification for multiple outcomes, including total mortality, cardiovascular death, cardiovascular hospitalizations, and hospitalizations for heart failure.[8] According to the PARADIGM-HF trial, a 5% reduction in LVEF or LVEF < 40% progressively increases the risk of death, all-cause mortality, and heart failure hospitalization.[9] A meta-analysis also had a similar result, where the adjusted mortality risk steadily increased with every 5% to 10% decrease in LVEF. However, these results were not significantly different in groups with LVEF > 40%.[10] Research by Di Tullio MR et al. also reported similar results, that LVEF was shown to be inversely associated with cardiovascular mortality up to an LVEF of 45%.[5] In the Candesartan Heart Failure Mortality Reduction (CHARM) trial, all-cause mortality increased by 39% for every 10% decrease in LVEF < 45%.[11]

A study by Kumar D et al., showed significantly higher 6-month mortality in the high-risk GRACE score compared to the intermediate-risk GRACE score, and only one patient with a low-risk GRACE score died at 6 months.[7] A retrospective study by Syyli N et al., showed that adding LVEF to GRACE score can significantly improve risk prediction of 6-month mortality after ACS.[12] The study also reported that both LVEF and GRACE score was significantly associated with 6-month mortality.[12]

In our study, reduced LVEF was significantly correlated with a higher GRACE score, therefore higher 6-month mortality risk. Toma M et al., conducted a retrospective analysis of the ASCEND trial, in which patients with higher LVEF have a lower mortality rate than those with reduced LVEF.[13] The study by Toma M et al., showed a significantly higher 180-day mortality in low ejection fraction compared to intermediate ejection fraction.[13]

A similar finding was observed by Perelshtein Brezinov O et al., where the Kaplan-Meier analysis showed that 1-year mortality rates were significantly correlated to LVEF such as 36%, 10%, and 4% are the mortality rates for patients with severe LVEF dysfunction, mild-moderate LVEF dysfunction, and preserved LVEF function respectively.[14] In addition, the study subject with severe and mild-moderate LVEF dysfunction had a 4.49- and 1.83-times greater mortality risk compared to subjects with preserved LVEF. The results were evident among both patients with STEMI and NSTEMI.[14] Another study reported that patients with preserved ejection fraction and moderately reduced ejection fraction had significantly lower mortality rates than those with reduced ejection fraction.[15]

In a previous study, mortality risks are usually modestly higher in patients with reduced ejection fraction but similar in those with moderate and preserved ejection fraction.[16] Data from the GWTG-HF trial found that patients with moderate ejection fraction had 30-day and 1-year mortality rates (8.2% and 35.1%) that were intermediate among those in preserved ejection fraction group (8.5% and 35.6%) and reduced ejection fraction (9.5% and 37.5%) groups.[17] Those results indicate that a reduced ejection fraction is correlated to the mortality risk as well as higher GRACE score as the recent study found.

CONCLUSION

Lower LVEF is correlated with increased six-month mortality risk after hospital discharge using GRACE score following myocardial infarction in a patient with non-ST elevation myocardial infarction.

CONFLICT OF INTEREST

There is no competing interest regarding this study.

ETHICS CONSIDERATION

This study was approved by Institutional Ethics Committee, Faculty of Medicine, University of Sam Ratulangi, Prof. Dr. R. D. Kandou General Hospital, Manado, Indonesia, prior to the study being conducted.

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AUTHOR CONTRIBUTION

CY, RLL and ALP were involved in the design and conceptualization of the study. CY, RLL, ALP and JP were involved in data curation and investigation. CY and ALP contributed to the statistical analysis. CY and ALP write the original draft. RLL and JP performed critical revision and editing of the manuscript.

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