



Two- Year Survival Analysis and Factors influencing Survival of Acute Myocardial Infarction

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Abstract: Background: Non-ST segment elevation myocardial infarction (NSTEMI) has less frequent complications, but has worse long-term prognosis than ST segment elevation myocardial infarction (STEMI). Mortality rates of NSTEMI were lower than STEMI but after 6 months both mortality were similar. The purpose of this study was to determine the 2-year survival in patients with acute myocardial infarction (AMI). **Method:** This cohort retrospective study included 264 AMI patients treated from January – December 2015 in H. Adam Malik Medan General Hospital. The study sample was divided based on the diagnosis of STEMI and NSTEMI. Data were obtained from medical records. All patients were contacted by phone to determine their condition 2 years after experiencing AMI. Multivariate analysis was performed to assess the factors that affect the survival. The 2-year survival of STEMI and NSTEMI was compared using the Kaplan Meier plot. **Result:** From 264 patients, there were 216 (81.8%) men with median age of 56 years. We found 147 STEMI patients and 117 NSTEMI patients. NSTEMI group tended to have history of coronary artery disease, higher blood pressure, less revascularization, longer hospitalization days and less number of post AMI complications. Survival and mortality rates in 2 years were 58% and 28%. Multivariate analysis showed higher blood pressure (OR 1.023, CI 95%, 1.003 – 1.044) dan PCI during hospitalization (OR 8.604, CI 95%, 2.264 – 32.702) showed better 2-year survival. There were no significant 2-year survival differences between the two groups (log rank 0.136). Better 2-year survival was found in patients with single vessel disease (log rank 0.001), patients who received revascularization (log rank 0.001) and patients who did not experience heart failure or cardiogenic shock during hospitalization (log rank 0.001). **Conclusion:** There was no difference in 2-year survival between STEMI and NSTEMI patients who were admitted to H. Adam Malik Medan General Hospital in 2015. The 2-year survival appeared better in patients with single vessel disease, received revascularization and did not experience heart failure or cardiogenic shock during hospitalization.

Keyword: survival, mortality, STEMI, NSTEMI.

Introduction

Cardiovascular disease (CVD) ranks the first cause of death worldwide. In 2008, 17.3 million people are estimated to have died from CVD. In Southeast Asia, the mortality rate rose to 24% and the disability rate was 26 million.¹ Eighty percent of these deaths are caused by heart attacks and strokes, and three-quarters of events occur in low-middle income countries.² As a non-communicable disease in Indonesia, coronary artery disease (CAD) is the third cause of death after stroke and diabetes mellitus (DM) at the age group of 45-54 years old.³

According to The Third Global MI Task Force, myocardial infarction is characterized by typical chest pain, electrocardiographic abnormalities, and increased cardiac enzymes.⁴ Based on these abnormalities, acute coronary syndrome (ACS) is divided into ST segment elevation myocardial infarction (STEMI), Non-ST segment elevation myocardial infarction (NSTEMI), and unstable angina pectoris.⁵ STEMI and NSTEMI are categorized as acute myocardial infarction (AMI).

TRIUMPH Registry reported the incidence of STEMI were 43 to 144 per 100,000 people per year. STEMI was often experienced by younger men and mortality was influenced by various factors, including advanced age, Killip class, time from onset of chest pain to treatment, presence of emergency systems, treatment, history of myocardial infarction, diabetes mellitus, and left ventricular ejection fraction. The morbidity was worse in patients with history of diabetes mellitus, hypertension, smoking, history of percutaneous coronary intervention / bypass surgery, kidney disorders and obesity.⁶ Meanwhile, NSTEMI occurred in 70% of all acute coronary syndrome cases and mostly experienced by older patients along with multiple comorbidities. Unlike STEMI who receive a more uniform guide to therapy, NSTEMI undergo a more diverse treatment method and inconsistent therapeutic behaviors in the use of invasive and conservative strategies that illustrate an uncertainty in the patient's initial evaluation and management.^{5,7}

SLOVAKS Registry showed a decrease in mortality from acute coronary syndrome in the last 15 years. In STEMI and NSTEMI, death during hospitalization and in 30-days were between 5.99% - 10.7% and 3.9% - 7, 65%.^{8,9} This can be caused by the transportation system, the availability of better and more modern reperfusion and pharmacotherapy therapy. In a survival analysis study conducted in Korea, the 30-days survival rate was 88%, 1-year survival was 75%, 3-years survival was 62% and 5-years survival was 40%. The highest mortality due to ACS is within the first 6 months. Initially, mortality of NSTEMI is lower than STEMI. But after 6 months, mortality both are similar and long-term mortality of NSTEMI is higher.^{5,7,10}

Most survival studies were carried out in Europe, especially in central institutions or hospitals that provide cardiology intensive care or primary coronary intervention. These data did not illustrate the complications of ACS throughout the world, where there are still many patients died before contact with health system officials. The health system level, social background and patient education seem to influence mortality in certain places¹¹. The aim of this study was to determine the 2-year survival in patients with acute myocardial infarction (AMI).

Method

Population and Design

This cohort retrospective study included 264 patients with AMI admitted to H. Adam Malik Medan General Hospital, Indonesia from January 2015 until December 2015. The inclusion criteria was AMI (STEMI and NSTEMI) patients hospitalized in H. Adam Malik General Hospital in 2015. STEMI was characterized by acute anginal chest pain, elevated cardiac enzyme, and new ST elevation at the J point in two contiguous leads with the cut-points ≥ 0.1 mV in all leads other than leads V2-V3 where the following cut points apply ≥ 0.2 mV in men ≥ 40 years; ≥ 0.25 mV in men < 40 years, or ≥ 0.15 mV in women. NSTEMI was characterized by acute anginal chest pain, elevated cardiac enzyme, and new horizontal or down-sloping ST depression ≥ 0.05 mV in two contiguous leads and/or T inversion ≥ 0.1 mV in two contiguous leads with prominent R wave or R/S ratio > 1 . The exclusion criteria were patient could not be contacted and died after 2 years due to non-cardiovascular cause. Patients who met the inclusion and exclusion criteria were recruited as subjects.

Patient's data such as profile, risk factors, previous disease, Killip class, GRACE score, ECG at admission, laboratory results, ejection fraction, angiography results, therapy, length of hospital stay, and complications were obtained from medical records. After 2 years, patients were contacted via telephone.

The patients were divided into 2 groups according to diagnosis (STEMI versus NSTEMI). Factors affecting survival was analysed. Survival after two years was compared between STEMI and NSTEMI.

Statistical Analysis

All statistical analyses were carried out using the SPSS statistical software, version 19.0. The data were presented with mean \pm 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 continuous variables compared with two free samples T test (Two Samples Independent Student's t-test) on normal distributed data or Mann Whitney U Test if the data was not normally distributed. In categorical variables, an analytical test was performed using chi squared or fisher exact tests. Data with p value < 0.25 would be included in multivariate analysis. Multivariate analysis was performed using logistic regression. The 2-year survival between STEMI and NSTEMI was compared using Kaplan Meier Plot and log rank test. The p value < 0.05 was considered as statistically significant.

Result

From January 2015 – December 2015, there were 264 AMI patients admitted to Haji Adam Malik General Hospital, consisted of 147 (55.7%) of STEMI and 117 (44.3%) of NSTEMI. A total of 216 patients were male (81.8%) with median age of 56 years old. Most common risk factor was smoking (68.9%), followed by hypertension (62.5%), dyslipidaemia (52.3%), diabetes mellitus, and history of previous coronary artery disease (17.4%). Most patients were admitted to the hospital with onset > 12 hours (75.4%) had high GRACE score (40.5%) and Killip class I-II (82.2%). Median blood pressure during admission was 130/80 mmHg. Glomerular filtration rate was normal (average 77.13 mg/ml). Troponin T level was 0.645 mg/dl and CKMB level was 58 U/L. In 89% patients, there was no arrhythmia at ECG on admission.

Coronary angiography was performed in 146 patients. Most STEMI patients had single vessel disease, while NSTEMI patient mostly presented with three-vessel disease. From 146 patients, only 76 patients underwent PCI. There was difference in inotropic and nitrate use between STEMI and NSTEMI. Enoxaparin was the anticoagulant that was mostly administered in STEMI. NSTEMI had longer hospitalization days. The most common complication after myocardial infarction was heart failure, which was higher in STEMI.

Two years following AMI, we found 153 patients alive and 75 patients died. There were 101 STEMI patients and 52 NSTEMI patients survived. We found survival and mortality rate after 2 years were 28% and 58%, respectively.

Table 1. Baseline Characteristic of Subject Study

Characteristic	AMI classification		p
	STEMI n = 147	NSTEMI n = 117	
Gender			
Male	124 (57,4%)	92 (42,6%)	0,231
Female	23 (47,9%)	25 (52,1%)	
Age (year)	56,26 \pm 0,822	58,37 \pm 0,903	0,135
Comorbidities and risk factors, yes			
Hypertension	86 (52,1%)	79 (47,9%)	0,133
Coronary artery disease	17 (37,0%)	29 (63,0%)	0,005*
Diabetes mellitus	53 (50,0%)	53 (50,0%)	0,128
Stroke	3 (27,3%)	8 (72,7%)	0,066
Chronic kidney disease	8 (32,0%)	17 (68,0%)	0,012*
Dyslipidaemia	64 (46,4%)	74 (53,6%)	0,001*
History of smoking	103 (56,6%)	79 (43,4%)	0,657.

Body mass index			
Underweight	1 (25,0%)	3 (75,0%)	0,262
Normal	46 (63,9%)	26 (36,1%)	
Overweight	59 (52,7%)	53 (47,3%)	
Obese	41 (53,9%)	35 (46,1%)	
Onset			
≤ 12 hours	36 (55,4%)	29 (44,6%)	0,956
>12 hours	111 (55,8%)	88 (44,2%)	
TIMI risk			
Low risk	84 (54,5%)	70 (45,5%)	0,660
High risk	63 (57,3%)	47 (42,7%)	
GRACE score			
Low (≤ 88)	22 (42,3%)	30 (57,7%)	
Moderate (89-118)	65 (61,9%)	40 (38,1%)	0,066
High (> 118)	60 (56,1%)	47 (43,9%)	
Killip class			
1-2	117 (53,9%)	100 (46,1%)	0,215
3-4	30 (63,8%)	17 (36,2%)	
Haemodynamic			
Heart rate, x/minute	84,176±1,707	88,247±2,319	0,576
Systolic blood pressure, mmHg	120,07±1,994	132,05±2,489	0,001*
Diastolic blood pressure, mmHg	75,714±1,236	83,076±1,365	0,001*
Laboratory			
Hemoglobin, g/dl	16,13±1,752	14,06±0,237	0,107
Creatinin, mg/ml	1,083±0,058	1,16±0,065	0,003*
Glomerular filtration rate,mg/dl	77,67±34,84	67,17±32,48	0,013*
Troponin T, ng/ml	1,04±0,083	0,63±0,075	0,001*
CKMB, U/L	133,43±14,94	61,72±8,60	0,001*
Electrocardiography at admission			
Malignant VES	4 (50,0%)	4 (50,0%)	0,130
Tachyarrhythmia	3 (33,3%)	6 (66,7%)	
Bradyarrhythmia	10 (83,3%)	2 (16,7%)	
No arrhythmia	130 (55,3%)	105 (44,7%)	
Ejection fraction			
< 40%	72 (56,3%)	56 (43,8%)	0,857
≥ 40%	75 (55,1%)	61 (44,9%)	
Coronary angiography	87 (59,6%)	59 (40,4%)	0,190
No. of affected vessel			
1VD	34 (68%)	16 (32%)	0,314
2VD	25 (62,5%)	15 (37,5%)	
3VD	19 (44,2%)	24 (55,8%)	
2VD+LM	3 (75,0%)	1 (25,0%)	
3VD+LM	3 (50,0%)	3 (50,0%)	
Not significant	3 (60,0%)	2 (40,0)	
Unknown	60 (51,7%)	56 (48,2%)	
Revascularization, yes			
PCI	49 (64,5%)	27 (35,5%)	0,004*
Fibrinolysis	8 (100,0%)	0 (0,0%)	
No reperfusion	90 (50,0%)	90 (50,0%)	
Therapy, yes			
Inotropic	44 (71,0%)	18 (29,0%)	0,006*
Aspilet	145 (56,2%)	113 (43,8%)	0,265
Clopidogrel	142 (55,3%)	115 (44,7%)	0,395
Beta Blocker	77 (52,7%)	69 (47,3%)	0,284
Nitrate	111 (50,9%)	107 (49,1%)	0,001*
ACEi/ARB	79 (55,6%)	63 (44,4%)	0,323
Statin	142 (55,5%)	114 (44,5%)	0,693

Anticoagulant			
UFH	20 (42,6%)	27 (57,4%)	0,008*
Enoxaparin	63 (60,6%)	41 (39,4%)	
Fondaparinux	55 (52,9%)	49 (47,1%)	
No anticoagulant	9 (100%)	0 (0,0%)	
Days of hospitalization, days	6,70±0,266	7,27±0,286	0,025*
Complication			
Heart failure	19 (51,4%)	18 (48,6%)	0,036*
Cardiogenic shock	14 (73,7%)	5 (26,3%)	
Bleeding	0 (0,0%)	3 (100,0%)	
Arrhythmia	11 (64,7%)	6 (35,3%)	
Stroke	0 (0,0%)	1 (100,0%)	
In-hospital death	19 (76,0%)	6 (24,0%)	
No complication	84 (51,9%)	78 (48,1%)	

After adjusting admission variables by univariate analysis, we performed multivariate analysis to find out which independent variable was the most dominant and influence the 2-year survival (Table 2). Based on the analysis, higher systolic blood pressure on admission and PCI were two of the strongest factors that influence better long-term outcome for both STEMI and NSTEMI.

Table 2. Two-year survival based on diagnosis

Diagnosis	2-year survival		Total
	Alive	Died	
STEMI	101	40	141
NSTEMI	52	35	87
Total	153	75	228

Table 3. Multivariate Analysis of Factors Influencing 2-Year Survival

Variable	B	Wald	p	OR	CI 95%
Coronary artery disease	-0,814	2,893	0,089	0,443	0,173 – 1,132
Systolic blood pressure	-0,018	5,329	0,021*	1,023	1,003 – 1,044
Revascularization					
PCI	2,152	9,981	0,002*	8,604	2,264 – 32,702
Fibrinolysis	1,380	1,140	0,286	3,976	0,316 – 50,096
Number of vessel affected					
Single vessel	-1,224	2,311	0,128	0,294	0,061 – 1,425
Multi vessel	-0,184	0,044	0,834	0,832	1,48 – 4,66
Complication					
Heart failure	22,090	0,000	0,998	39,540	0,000
Cardiogenic shock	20,776	0,000	0,998	10,735	0,000
Bleeding	20,414	0,000	0,998	73,122	0,000
Arrhythmia	23,427	0,000	0,997	14,883	0,000
Stroke	41,614	0,000	0,999	11,000	0,000

We conducted analysis survival based on diagnosis, type of revascularization, number of coronary arteries involved, and complications. STEMI patients had higher mortality rate within the first year and better survival in the second year. Conversely, patients with NSTEMI had lower mortality rates in the first year compared to STEMI but worse mortality in the following year. The difference in mortality between both groups was not significant (Log Rank 0.136). Also, patients complicated by cardiogenic shock had the highest mortality within 2 years, followed by heart failure and arrhythmia (Log Rank 0.001).

It appeared that patients with coronary angiography results showing no significant stenosis or single vessel disease had better 2-year survival. Outcomes of patients with multivessel disease improved from 0-24 months after experiencing AMI. Patients who did not undergo coronary angiography had worst survival, where the survival rate decreased in 0-3 months and continued to decline until the next 24 months. This study showed that patients with multivessel disease had higher mortality rate within 2 years (Log Rank 0.001).

Patients who did not receive reperfusion therapy had progressively lower survival rate from the first to the second year. Patients who received fibrinolysis agent had better survival rate within the first 6 months and declined steadily until the second year. Although within the first 6 months the survival rate was lower, patients treated with PCI subsequently had higher survival rates compared to fibrinolysis until the second year (Log Rank 0.001).

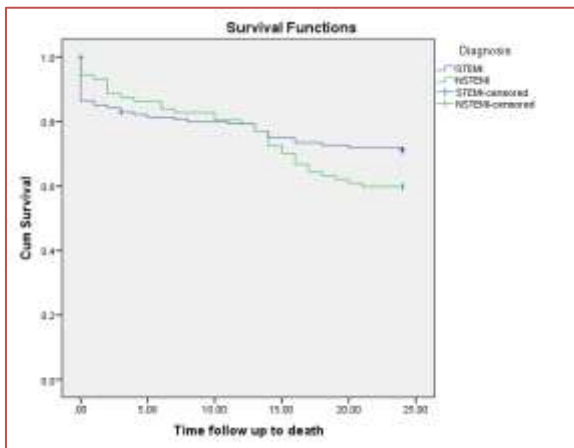


Figure 1. Kaplan Meier Curve of 2-year survival between STEMI and NSTEMI (Log Rank 0.136)

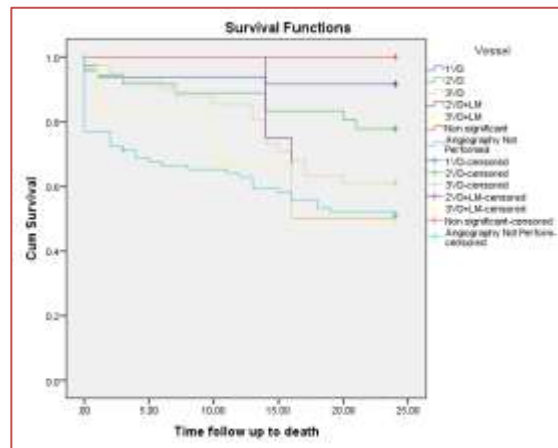


Figure 2. Kaplan Meier Curve of 2-year survival based on coronary artery lesion (Log Rank 0.001)

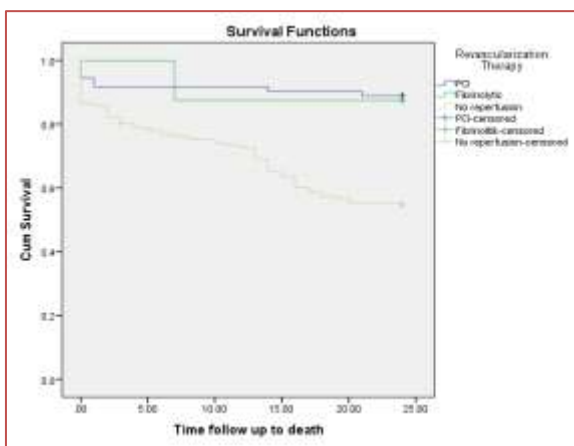


Figure 3. Kaplan Meier Curve of 2-year survival in patients treated with PCI, fibrinolytic or without reperfusion (Log Rank 0.001)

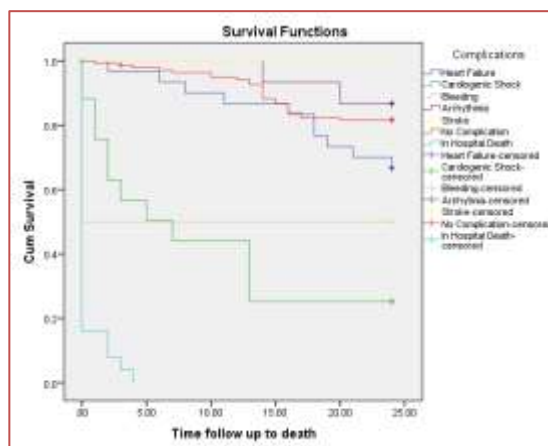


Figure 4. Kaplan Meier Curve of 2-year survival in patients with or without complications (such as heart failure, cardiogenic shock, bleeding, arrhythmia and stroke) (Log Rank 0.001).

Discussion

In 2015, there were 264 patients admitted to H. Adam Malik General Hospital due to AMI. 55.7% were diagnosed with STEMI (55.7%) and 44.3% were diagnosed with NSTEMI. In 2007, Montalescot found a higher percentage of STEMI (70.8%), mostly male with average age of 64 ± 14 years. Most common risk factors were history of smoking (68.9%), hypertension (62.5%) and dyslipidemia (52.3%). This is similar with other study in France showing the most common risk factors were dyslipidemia (49.7%), hypertension (47.1%) and smoking history (36.6%). Between STEMI and NSTEMI, there were no difference in onset of chest pain to hospital presentation, Killip class, TIMI Risk and GRACE score (p value 0.956; p value 0.215; p value 0.66; p value 0.066). This study found higher systolic and diastolic blood pressure at admission in NSTEMI (p value 0.001 and p value 0.001). Other study found only systolic blood pressure was significantly different (p value 0.001).¹²

STEMI received more revascularization (PCI and fibrinolysis) than NSTEMI (64.4% vs 35.5% and 100% vs 0%; p value 0.004). Inotropic and nitrate were more commonly administered for STEMI rather than NSTEMI (p value 0.001). This is because more STEMI patients presented with lower systolic blood pressure (Killip IV). Tarvasmäki found that STEMI was the most common cause of cardiogenic shock, but there was no difference in inotropic use between STEMI and NSTEMI.¹³

Two years follow up was conducted in 264 patients. 147 STEMI patients and 117 NSTEMI patients were alive, 36 patients were lost to follow up. STEMI had higher mortality in the first year and lower mortality in the second year. On the contrary, NSTEMI patients had lower mortality in the first year but higher mortality during the second year. The mortality rate increased in the first year, so mortality rate for STEMI and NSTEMI were almost the same, namely 8-10%. Worse long term mortality in NSTEMI might be caused by older age and comorbid factors more commonly occurred in NSTEMI patients.^{12,14,15}

Survival rate were better in patients receiving revascularization therapy (PCI or fibrinolysis). Hyunh et al found that primary PCI reduced short-term and long-term mortality of 34 % and 24%.¹⁶ WIRE Registry stated that primary PCI is the only choice of revascularization that could reduce long-term mortality rate.¹⁷ Meanwhile, STEPP-AMI trial in India failed to show different outcome in patients treated with fibrinolysis or primary PCI (3.9% vs 11.1%; p value 0.07).¹⁸

Re-infarction, stroke, cardiovascular death and long-term mortality increased according to the severity of coronary lesion. Cumulative risk after myocardial infarction was 26.4% in patients with left main artery disease. Incidence of infarction, stroke and cardiovascular death increased was worse in multiple coronary artery disease, but worse in patients who did not undergo coronary angiography.¹⁹

Cardiogenic shock and heart failure were two of the most common complications and both had low survival rate. In cardiogenic shock group, survival decreased by 50% within 2 years. Meanwhile in heart failure, reduction of survival in 2 years was 25%. Previous studies showed that 30-day and 30-day to 1-year mortality rate after AMI complicated by cardiogenic shock were 39.7% – 46.7% and 6.6% – 12.3%. Risk of death after AMI complicated by heart failure was 5.98 times higher than those without heart failure (HR 5.98; 95% CI: 5.39 – 6.64).

Limitation of Study

This has several limitations. Since this is a retrospective study, there were some difficulties faced during data collection. Number of samples was small and carried out in only one center. For comparison, further research can be continued with larger number of samples and performed in multiple centers.

Conclusions

There was no difference in 2-year survival between STEMI and NSTEMI patients who were admitted to H. Adam Malik Medan General Hospital in 2015. The 2-year survival appeared better in patients with higher blood pressure at admission, single vessel disease, received revascularization and did not experience heart failure or cardiogenic shock during hospitalization.

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