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One- and Six-month Outcomes of Patients with Non-ST Elevation Myocardial Infarction

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Abstract

Introduction: Use of risk scoring systems in patients with acute coronary syndrome helps with summarizing important prognostic data of the disease and facilitates calculating confidence limits and comparing survival rates between different treatments. In the present study, the researchers first aimed at assessing mid-term outcome of patients with non-ST elevation myocardial infarction (NSTEMI), and then determining main predictors of this outcome to improve definitive criteria for designing a risk scoring system in the population.
Methods: In a prospective cohort study, 124 patients with NSTEMI, diagnosed according to ACC/AHA guidelines and hospitalized in an academic hospital in 2013, were consecutively assessed. Baseline characteristics were collected via interviewing, physical examination, and reviewing the recorded files. All the patients were followed for one and six months to assess mid-term outcomes regarding mortality and major adverse cardiac events (MACE). MACE is defined as the occurrence of at least one of the events of death, myocardial infarction, repeated revascularization, or re-hospitalization.
Results: One-month death occurred in 3.2%, re-hospitalization in 4.0%, and myocardial infarction in none of the patients. In addition, regarding the six-month outcomes status, mortality rate was determined in 6.4%, re-hospitalization in 22.6%, and myocardial infarction in 4.8% of patients. Hence, one- and six-month MACE rates were 7.3% and 27.4%, respectively. Furthermore, three- and six-month survival rates were estimated to be 96.8% and 93.6%, respectively. According to the Cox-proportion hazard modeling, only reduced left ventricular ejection fraction (LVEF) (HR = 0.909, P = 0.017), history of chronic kidney injury (HR = 8.884, P = 0.005), and Inotrope use (HR = 35.759, P = 0.012) could predict the six-month MACE. None of the other indexes including general coronary risk factors, echocardiography parameters, and level of cardiac enzymes could predict mortality rate.
Conclusions: Patients with NSTEMI may face high six-month MACE which can be predicted by low LVEF, history of renal injury and use of inotrope. Therefore, to define risk stratification system, these indicators should be considered as well.

INTRODUCTION

The ratio of non-ST elevation myocardial infarction (NSTEMI) to ST elevation myocardial infarction (STEMI) continues to increase, and now less than one-third of myocardial infarctions (MIs) are due to STEMI [1]. Recently, the wide use of more sensitive tests such as analyzing serial high-sensitivity cardiac troponin T (hs-cTnT), which can detect even small sizes of myocardial necrosis, has increase diagnostic accuracy and led to increasing incidence of NSTEMI instead of unstable angina [2-5]. Although there have been significant improvements in the care of patients with cardiovascular disease, cardiovascular death mainly by coronary heart disease remains the leading cause of mortality worldwide [1]. Risk scores are simple, applicable and more accurate tools at risk stratification, in which prognostic value of several independent risk factors on presentation are shown. Indexes that compound several related clinical variables of

the same underlying pathophysiologic event are more powerful than any individual variable and could improve prognostic analysis in regression modeling techniques [6-8]. For instance, history of myocardial infarction, congestive heart failure, Q waves on electrocardiogram and high troponin T concentrations all represent different aspects of the extent of myocardial injury [9, 10]. In addition to the extent of myocardial injury, the extent of coronary artery disease and its resistance to management are the main prognostic determinants of acute coronary syndrome [11].

Age, heart rate, systolic blood pressure, Killip class, ST segment deviation, resuscitation from cardiac arrest, elevated cardiac enzymes and serum creatinine concentration are powerful prognostic factors in GRACE and PURSUIT scoring systems [12-14].

Seven independent predictor variables have been identified as TIMI risk factors including age > 65 years, three cardiovascular risk factors, known coronary artery disease (50% stenosis), severe angina symptoms, use of aspirin in the last seven days, ST segment deviation > 0.05 mV, and elevated serum cardiac markers of necrosis [15, 16]

Use of risk scoring systems in patients with acute coronary syndrome helps to summarize important prognostic data of the disease and facilitates comparing survival rate between different treatments [17, 18].

In the present study, we aimed to first assess mid-term outcome of patients with NSTEMI, and then determine main predictors of this outcome.

METHODS

In a prospective cohort study, 124 patients with diagnosed NSTEMI according to ACC/AHA guidelines, who were hospitalized at Modarres hospital between March 2012 and September 2013, were consecutively included. Baseline characteristics were collected via interviewing, physical examination, and reviewing the recorded files including demographic characteristics, medical history, medication, previous cardiac intervention, laboratory parameters, and functional class status.

Patients were also assessed using two-dimensional echocardiography to determine structural and functional parameters such as left ventricular ejection fraction, end systolic and diastolic diameters, and also diastolic functional indexes. They also underwent coronary angiography to determine presence and severity of coronary arteries involvement.

To assess mid-term outcomes of NSTEMI, all the patients were followed for one and six months to evaluate mid-term outcomes regarding mortality and major adverse cardiac events (MACE), defined as the occurrence of at least one of the events of myocardial infarction, repeated revascularization, or re-hospitalization.

Results were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by frequency (%) for categorical variables. Continuous variables were compared using t-test or non-parametric Mann-Whitney U test, whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the two study groups. Categorical variables were, on the other hand, compared using chi-squared test or Fisher's exact test when more than 20% of cells with expected count of less than five were observed. Cox proportional hazard model was used to determine main correlates of MACE. Statistical analysis was performed by SPSS version 21.0 (SPSS Inc., Chicago, IL). P values of 0.05 or less were considered statistically significant.

RESULTS

Totally, 124 patients were included in the study. The mean age of patients was 62.40 ± 11.07, ranging 35 to 93 years. Baseline demographic and clinical characteristics of patients are shown in Table 1.

Table1: Baseline Demographical and Clinical Characteristics in Patients with Non-ST Elevation Myocardial Infarction

Variables	Amount
Demographics	
Age (y)	62.4 ± 11.7
BMI (k/m^2)	26.28 ± 2.95
Male sex (%)	72.9
Medical History (%)	
Hypertension	56.5
Diabetes mellitus	33.9
Hyperlipidemia	50.8
Obesity (BMI > 30 kg/m^2)	29.8
Current smoking	34.9
Prior CABG	15.3
Prior PCI	12.1
Peripheral arterial disease	11.3
Prior heart failure	27.4
Prior cerebrovascular events	8.1
Prior renal failure	12.1
Chronic lung disease	15.3
Previous Aspirin use	52.4
Recent Function Class	
I	38.7
II	44.4
III	16.1
IV	0.8
Presentation Features	
Typical chest pain (%)	65.3
Chest pain + Dyspnea (%)	33.1
Atypical chest pain (%)	1.6
Initial heart rate (beats/min)	85.02 ±1.49
Initial systolic BP (mm Hg)	130.85 ± 26.22
ECG Findings (%)	
Pathologic Q wave	7.0
ST depression	68.5
Transient ST elevation	4.0
Laboratory Results	
Peak Troponin (µg/l)	3.08 ± 2.48
Peak CPK (IU/L)	631 ± 5.00
Peak CK.MB (IU/L)	87.06 ± 6.83
Hemoglobin (g/dL)	14.07 ± 1.68
Serum creatinine (mg/dL)	1.25 ± 0.32
TIMI Risk Score (%)	
Low risk (score 0-2)	6.5
Intermediate risk (score 3-4)	56.5
High risk (5-7)	37.1

Values are presented as percentages or mean± SD.

BP: Blood pressure; BMI: Body mass index; CABG: Coronary artery bypass grafting; ECG: Electrocardiogram; TIMI: Thrombolysis in Myocardial Infarction; PCI: Percutaneous coronary intervention.

The most common traditional cardiovascular risk factors were hypertension (56.5%), followed by hyperlipidemia, current smoking, diabetes mellitus, and obesity. Nearly one third of patient (27.8%) had history of coronary revascularization, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG); about half had history of previous aspirin administration. Medical treatments during hospitalization, echocardiography and angiography findings are demonstrated in Table 2. Only a few patients (0.8%) received low molecular weight heparin instead of unfractionated heparin.

Approximately 96% of the patients underwent cardiac catheterization (37.1% within 24 hours from index admission and 58.1% after 24 hours), whereas 62.2% experienced percutaneous coronary intervention, 15.3% endured bypass surgery, and 22.5% were treated conservatively.

Based on the angiography report, three coronary vessel involvements were the most frequent results, followed by two vessel diseases (VD), one VD and left main disease (Table 2).

Regarding the one-month outcomes, one-month death occurred in 3.2%, re-hospitalization in 4.0%, CABG in 0.8%, and myocardial infarction in none of the patients. In addition, regarding the six-month outcomes, mortality rate was determined in 6.4%, re-hospitalization in 22.6%, CABG in 3.2%, and myocardial infarction in 4.8% of patients. Hence, one- and six-month MACE rates were 7.3% and 27.4%, respectively; survival rates at one and six months were 96.8% and 93.6%, respectively.

According to univariate analysis, different variants predict six-month MACE (Table 3); however, based on the Cox-proportion hazard modeling, only reduced left ventricular ejection fraction (LVEF) (HR = 0.909, P = 0.017), history of chronic kidney injury (HR = 8.884, P = 0.005), and Inotrope usage (HR = 35.759, P = 0.012) could predict six-month MACE.

In this context, none of the indexes including general coronary risk factors, echocardiography parameters, and level of cardiac enzymes could predict mortality rate.

DISCUSSION

According to the increasing trend of the overall incidence of NSTEMI compared with other components of acute coronary syndrome, the assessment of this ischemic event and also determining its related determinants are necessary. Besides, designing a risk stratification system to determine the level of risk in patients with NSTEMI can lead to better clinical management of these patients and also to schedule appropriate treatment programs for these patients.

In the present study, we first attempted to determine mid-term outcomes of patients with NSTEMI and then aimed to assess main predictors of NSTEMI outcomes in the study population. Based on observation, the mean age of patients NSTEMI was 62.40 ± 11.07 years, consistent with those of Korea Acute Myocardial Infarction Registry (KAMIR) (63.6 ± 12.2 years) [19]; but, they were younger than patients with NSTEMI in Malopolska Registry of Acute Coronary Syndromes performed by Dziewierz et al. (70.2 ± 11.6 years) [20]. The most frequent cardiovascular risk factor was hypertension, consistent with most NSTEMI studies [19-21]; however, smoking and hyperlipidemia were more common in a cohort study [22].

In this study, the mid-term mortality rate in patients with NSTEMI was 6.4%. Furthermore, one- and six-month MACE rates were 7.3% and 27.4%, respectively. On the other hand, although patients with NSTEMI had an acceptable mortality rate, they experienced a high mid-term MACE rate; among every four patients, one faced with cardiac morbidities in a mid-term period.

In one report, 458 patients without persistent ST segment elevation acute coronary syndrome were assigned to early invasive strategy. Hospital and overall mortality rates were 3.3% and 4.8%; respectively. MACE was observed in 20.3% of patients within six months [23].

Moreover, for the patient who had been referred for catheterization and the ones who underwent conservative strategy, Khalill et al. reported one-year mortality rate of 4% and 10%; respectively [24]. In another study performed by Park HW et al., the MACE rates for early term (one month) and late-term (one year) were 6.9% and 8.0%; respectively [25].

Table 2: In Hospital Medication, Echocardiography and Angiography Findings in Patients with Non-ST Elevation Myocardial Infarction

Variables	Amounts
Hospital Medication (%)	
UFH	99.2
LMWH	0.8
Aspirin + clopidegrol	67.7
Aspirin + clopidegrol + eptifibatide	32.3
Inotrope	5.6
Statin	100
Beta blockers	89.5
Calcium blockers	2.4
Echocardiography Parameters	
LVEF (%)	43.61 ± 11.35
LVEDD (cm)	5.34 ± 0.64
RVEDD (cm)	3.05 ± 0.28
Ea/Ee	12.44 ± 4.40
TAPSE (cm)	1.89 ± 0.27
MR (%)	
Mild	39.5
Moderate	19.4
Severe	2.4
Angiography Results (%)	
SVD	12.9
2VD	29.8
3VD	33.9
LMD	6.5

Values are presented as percentages or mean ± SD.
LMD: Left main disease; LMWH: Low-molecular-weight heparin; LVEF: Left ventricular ejection fraction; LVEDD: Left ventricular end diastolic diameter; MR: Mitral regurgitation; RVEDD: Right ventricular end diastolic diameter; SVD: Single vessel disease; 2VD: Two vessel disease; 3VD: Three vessel disease; TAPSE: Tricuspid annular plane systolic excursion; UFH: Unfractionated heparin.

Table 3: Comparison of Patients with NSTEMI according to 6-months MACE

Characteristics	MACE (+), (n = 34)	MACE (-), (n = 90)	P value
Male gender	27 (79.4)	63 (70)	0.295
Age (y)	66.41 ± 10.64	60.88 ± 10.90	0.013
BMI (kg/m2)	25.56 ± 2.31	26.55 ± 3.13	0.097
Hypertension	23 (67.6)	43 (47.8)	0.122
Diabetes mellitus	12 (35.3)	30 (33.3)	0.837
Current Smoking	16 (47.1)	27 (30.0)	0.032
Hyperlipidemia	16 (47.1)	47 (52.2)	0.608
Prior CABG	9 (26.5)	17 (18.9)	0.019
Prior PCI	4 (11.8)	11 (12.2)	0.889
Prior heart failure	19 (55.9)	15 (16.0)	< 0.001
Prior renal failure	9 (26.5)	6 (6.7)	0.003
Prior cerebrovascular events	3 (8.8)	7 (7.8)	0.849
Peripheral arterial disease	6 (17.6)	8 (8.9)	0.169
Opium	7 (20.6)	7 (7.8)	0.132
LVEF	34.44 ± 13.30	47.08 ± 8.61	< 0.001
LVEDD	5.77 ± 0.78	5.18 ± 0.49	< 0.001
RVEDD	3.12 ± 0.31	3.03 ± 0.26	0.066
TAPSE	1.7 ± 0.3	1.93 ± 0.2	0.005
Ea/Ee	13.7 ± 4.7	11.9 ± 4.3	0.060
MR			
Mild	12 (35.3)	37 (41.1)	0.149
Moderate	14 (41.2)	10 (11.1)	0.001
Severe	1 (2.9)	2 (2.2)	0.889
TIMI Score	4.7 ± 1.2	3.9 ± 1.2	0.001
ACC/AHA high risk	21 (63.6)	26 (28.5)	0.001
ACC/AHA moderate risk	11 (33.3)	58 (63.7)	0.004
ACC/AHA low risk	1 (3.0)	7 (7.6)	0.32
Previous Aspirin usage	20 (60)	45 (49)	0.185
Drugs in hospitalization			
Aspirin + Clopidegrol	27 (79.4)	57 (63.3)	0.251
Aspirin + Clopidegrol + Eptifibatide	7 (20.6)	33 (36.7)	0.095
UFH	34 (100)	89 (98.9)	0.537
Inotrope	6 (17.6)	1 (1.1)	0.002
Beta blockers	24 (70.6)	87 (96.7)	0.226
Pathologic Q wave	4 (11.8)	0	0.005
ST-T change	27 (79.4)	58 (64.4)	0.001
Angiography within 24h	7 (21.2)	39 (43.3)	0.035
Angiography results			
SVD	1 (3.1)	15 (17.2)	0.005
2VD	7 (20.6)	30 (34.5)	0.021
3VD	15 (46.9)	27 (31.0)	0.001
LMD	3 (9.4)	5 (5.7)	0.445

Values are presented as n (%) or mean ± SD.
Abbreviations are as in Tables 1 and 2. MACE: Major adverse cardiac events.

From the CRUSADE registry, one-year mortality rate in older patients with NSTEMI (aged ≥ 65 years) was 24.4%, and age was the most significant predictor of mortality [21]. Recently, Kim et al. reported a six-months MACE ranging from 12.4% to 23.1% based on TIMI risk score for low- to high-risk patients with NSTEMI, respectively, in KAMIR [19].

In the second step of study, we found that patients with MACE were older and more likely to be current smokers, have a history of CHF, CABG, CKD, pathologic Q wave, ST-segment changes, LV and RV dysfunction, moderate MR, catheterization after 24 hours, and inotrope usage during hospitalization; however, the correlation of severe MR and MACE was not statistically significant, which may be due to insufficient total number of severe MRs. The TIMI risk score (TRS) system

had a good correlation with MACE for patients in the high-risk group. By Cox-proportion hazard analysis, we could introduce reduced LVEF, history of chronic kidney injury, and Inotrope use as major factors triggering mid-term MACE in patients with NSTEMI.

In KAMIR by Kim et al., Killip class above III, the presence of heart failure or cardiogenic shock and NT-ProBNP demonstrated good correlations with MACE, and the TRS system had a good correlation with MACE for patients in the low and intermediate groups [19].

On the other hand, demographic parameters, echocardiography indexes and also increased level of cardiac enzymes were not correlated with poor mid-term outcome in those patients.

It seems that the type of predictors of NSTEMI consequences can be different in various populations depending on characteristics of population, diagnostic criteria of MACE, follow-up time, and number of patients included.

This study revealed that in a limited portion of the Iranian population, only three factors including reduced LVEF, history of chronic kidney injury, and Inotrope usage could predict six-month MACE, suggesting that the abovementioned parameters are probably more significant than other prognostic factors reported.

Limitations of this study can be discussed from various points. First, a small number of participants was used; thus, the findings should be treated with care. Second, other variables could provide novel prognostic results. Third, further studies need to be accomplished to achieve verification of new scoring systems.

In conclusion, patients with NSTEMI may face high six-month MACE, which can be predicted by low LVEF, history of renal injury, and use of inotrope.

Therefore, defining a risk stratification system should be considered in these patients.

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CONFLICTS OF INTEREST

There is no conflict of interest for the present study.

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