A trend of Japanese Acute Myocardial Infarction Patients: Development of Prognostic Prediction Rules

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Abstract

Acute myocardial infarction is still one of the serious diseases with a high mortality rate. The aim of this study is to explore the prognostic predictors for the outcome of acute myocardial infarction patients. A total of 457 acute myocardial infarction patients admitted to Nihon University Itabashi Hospital between 2014 and 2017 were analyzed in this study. The primary endpoint of this study was a 30-day mortality. The secondary endpoint was a major adverse event: all-cause death, non-fatal myocardial infarction, hospitalization due to heart failure, stroke, bleeding and repeat percutaneous coronary intervention. Forty-two patients died within 30 days after acute myocardial infarction. There were 123 patients who had major adverse event within the 1 year. Multiple Poisson regression model was used to identify the most important predicting factors for 30-day mortality

after acute myocardial infarction, which were higher Killip classification (risk ratio [RR]: 4.17, 95% confidence interval [CI]: 1.74-9.95), history of stroke (RR: 3.79, 95% CI: 1.59-9.01), maximum creatine kinase level more than 1500 IU/L (RR: 3.02, 95% CI: 1.25-7.31), age (RR: 1.04, 95% CI: 1.01-1.08), and heart rate (RR: 1.02, 95% CI: 1.01-1.03). The classification and regression trees analysis identified Killip classification as the most important factor for 30-day mortality. However, the Killip classification (RR: 1.91, 95% CI: 1.09-3.42) and the use of beta-blockers (RR: 1.68, 95% CI: 1.11-2.53) were found to be significant predictors for the one-year major adverse event. The initial profiles except for the Killip classification were not associated with the one-year outcome. These findings are expected to improve clinical outcomes of Japanese patients with acute myocardial infarction.

I Introduction

Acute myocardial infarction (AMI) is defined as myocardial cell death due to prolonged myocardial ischemia (Libby, 2013). Clinically AMI is diagnosed with rising cardiac biomarkers such as creatine kinase or cardiac troponin and the ST-T change in an electrocardiogram. It is the most frequent condition responsible for heart disease, which is the second leading cause of death. The number of AMI patients increased from 7.4% to 27.0% during the last 30 years (Takii et al., 2010). Primary percutaneous coronary intervention (PCI) is an established revascularization strategy for AMI, and can reduce mortality up to 10% after AMI (Hochman et al., 1999) compared to thrombolysis or coronary artery bypass grafting (CABG). Furthermore, the use of drug-eluting stent (DES), which is a metallic stent coated with drugs suppressing cell proliferation was released around 2000. It has dramatically reduced the target lesion revascularization (TLR) compared to bare metal stent (BMS) implantation. Nonetheless, the in-hospital mortality rate for AMI is still around 10%

(Miyachi et al., 2016; Nabel & Braunwald, 2012) and the adverse cardiovascular event one year after AMI is about 20% (Miyamoto et al., 2017; Stone et al., 2011).

I-1 Problem Statement

Japan is one of the countries with a rapidly growing aging population; one-third of the Japanese population is expected to be over 65 years old by the year 2035 and the number of elderly patients with cardiovascular disease will increase. It is reported that the mortality in the elderly AMI patients is higher than that in the non-elderly patients (Kojima et al., 2018). Stratifying the risk of AMI patients to provide precise treatment is necessary. The CADILLAC risk score (Halkin et al., 2005), GRACE risk score (Granger et al., 2003), TIMI risk score (Sabatine et al., 2004), and PURSUIT risk score (Boersma et al., 2000) were established as a prognostic scoring system for AMI. The GRACE score was validated using in Japanese data (Fujii et al., 2014; Komiyama et al., 2018). However, these scoring systems are not widely used in Japan because there are too complicated to apply in clinical settings. More studies are needed to identify important predictors to improve the outcome of Japanese AMI patients.

I-2 Objectives

The aims of this study were to identify the prognostic factors of Japanese AMI patients and also to develop simple statistical models to improve the prognosis of elderly AMI patients in the future.

II. Methodology

II-1 Data source and study population

This study consisted of a retrospective cohort design. The patients' records were collected

from the electronic medical record database of the coronary care unit of Nihon University Itabashi Hospital, Tokyo, Japan. Clinical information was obtained from a review of patients' electronic records. AMI patients who were admitted to Nihon University Itabashi Hospital between 2014 and 2017 were serially recruited. Patients admitted before 2013 could not be recruited because their records were stored in the paper-based medical charts. Inclusion criteria were: AMI, 20 years old or more, did or did not undergo primary PCI; and AMI patients with cardiac arrest: at arrival to hospital, walk-in admissions, arrival in ambulance, onset at hospital, and onset outside of the hospital such as home.

II-2 Definition of variables

AMI consisted of two types. ST-elevation myocardial infarction (STEMI) was defined as chest compression with persistent ST-segment elevation in the electrocardiogram, and non- ST-elevation myocardial infarction (NSTEMI) was defined as chest compression without persistent ST-segment elevation in ECG. Killip classification was used as a severity classification of AMI. Killip et al. (1967) classified AMI into four groups based on physical findings such as pulmonary congestion and cardiogenic shock. According to the report, the mortality rate of AMI is 6% in Group I, 17% in Group II, 38% in Group III, and 81% in Group IV.

II-3 Measures

The data were collected on demographics (age, gender, and body mass index), comorbidity (prior MI, stroke, heart failure, renal dysfunction received hemodialysis, hypertension, hyperlipidemia, diabetes mellitus, and smoking history), vital signs (blood pressure (BP), heart rate (HR), left ventricular ejection fraction (LVEF)), time course (transfer time, door-to-balloon (D2B) time, length of stay in hospital), initial laboratory data (hemoglobin, serum creatinine, creatine kinase

(CK), cardiac troponin T, N-terminal pro-brain natriuretic peptide (NT-proBNP), lipid profiles, and glucose profiles), intervention profiles (culprit vessels, primary PCI, the use of mechanical support devices such as intra-aortic balloon pumping or percutaneous cardiopulmonary support, and the use of respirator devices), and medication at discharge.

II-4 Outcome measurement and grouping

The primary outcome of interest was the 30-day mortality. The Mortality group consisted of the patients who died within 30 days and the Survivor group consisted of the patients without a fatal event within 30 days. The secondary outcome included major adverse event (MAE) such as all-cause death, non-fatal MI, stroke, heart failure, repeat PCI, and bleeding defined by the Thrombolysis In Myocardial Infarction classification as none, minor, or major (Cannon et al., 2001) within one year from the date of admission.

II-5 Statistical analysis

Continuous variables were presented in terms of mean ± standard deviation or median with interquartile range, and categorical variables were presented as numbers and percentages. Student t-test or Mann-Whitney U test was used to test whether the mean or median of a continuous variable was different between the event and event-free groups and chi-squared test or Fisher's exact test to assess the association between the categorical variables. To predict 30-day mortality and MAE within one year after AMI, we employed a Poisson regression model. Likelihood-ratio-test-based stepwise forward selection was performed to identify potential variables to apply to Poisson regression analysis, the variables with a *P* value less than .2 were chosen as the stepwise candidates. Also, the Classification And Regression Trees (CART) analysis (Breiman et al., 1984) was performed to identify the best predictors of 30-day mortality and develop the risk stratification model.

CART is one of the useful methods for predicting an outcome with explanatory variables. When the outcome was a discrete variable, we applied the classification tree to the analysis. However, when the outcome was a continuous variable, we used the regression tree for the analysis. In this study, the main outcome was death within 30-days, which is a discrete variable. Therefore, using the classification tree method, a prediction model was conducted in the same way of using a logistic or Poisson regression analysis. All statistical analyses were performed with RStudio (Version 1.1.463, RStudio, Inc., Boston, MA, USA), which is an integrated development environment for R (Version 3.5.2, The R Foundation for Statistical Computing, Vienna, Austria). All CART analyses were performed using the recursive partitioning (rpart) package in the R statistical computing environment.

II-6. Ethical Statement

This study was conducted in accordance with the Declaration of Helsinki. The protocol was reviewed and approved by the Institutional Review Board of Nihon University Itabashi Hospital (RK-180612-04).

III. Results

III-1. Patient cohort characteristics

A total of 457 AMI patients were analyzed. The patient characteristics are summarized in Table 1. The mean age was 67.7 years, 79.2% were male, and 73.3% were STEMI. In this cohort, 42 patients (9.2%) died within 30 days after AMI. Features of the Mortality group were more elderly (72.6 years vs. 67.2 years, $P = 0.012$), lower hyperlipidemia (21.4% vs. 45.5%, $P = 0.014$) and more history of stroke (26.2% vs. 5.8%, $P < 0.001$). In the Mortality group, there were more patients with cardiac arrest (31.0% vs. 4.8%, $P < 0.001$) and cardiogenic shock (42.9% vs. 4.6%, $P < 0.001$) at arrival. The Killip classification was higher in the Mortality group than in the Survivor group.

Hemoglobin (12.3 g/dL vs. 13.4 g/dL, $P = 0.002$) and lipids levels were lower, and serum creatinine (median 1.14 mg/dL vs. 0.86 mg/dL, $P < 0.001$), NT-proBNP (median 1035.0 pg/mL vs. 638.0 pg/mL, $P = 0.037$), and blood glucose (241.3 mg/dL vs. 168.1 mg/dL, $P < 0.001$) levels were higher in the Mortality group compared to the Survivor group. In the interventional profiles, culprit vessel was more severe in the Mortality group, and mechanical support devices (76.2% vs. 26.7%, $P < 0.001$) and respirator (88.1% vs. 15.2%, $P < 0.001$) were more used in the mortality group. The maximum CK levels were higher in the Mortality group (median 5241.0 IU/L vs. 1332.5 IU/L, $P < 0.001$).

III-2 Prediction model for 30-day mortality

Table 2 shows the list of potential predictors for 30-day mortality, which were considered for the Poisson regression model. Simple Poisson regression models revealed 23 variables as significant, in the profiles at arrival, a 30-day mortality was strongly associated with higher Killip classification (RR: 11.3, 95% CI: 6.17-20.7, $P < 0.001$), cardiogenic shock at arrival (RR: 8.51, 95% CI: 4.62-15.7, $P < 0.001$), cardiac arrest at arrival (RR: 5.76, 95% CI: 2.99-11.1, $P < 0.001$), history of stroke (RR: 4.84, 95% CI: 2.40-9.76, $P < 0.001$), and elder people of 65 years or more (RR: 3.02, 95% CI: 1.40-6.53). On the other hand, in the intervention profiles, a 30-day mortality was strongly associated with the use of respirator (RR: 26.4, 95% CI: 10.4-67.2, $P < 0.001$), the use of mechanical support device (RR: 7.03, 95% CI: 3.45-14.3, $P < 0.001$), LMT as a culprit vessel (RR: 6.87, 95% CI: 2.91-16.2, $P < 0.001$), and maximum CK levels more than 1500 IU/L (RR: 2.65, 95% CI: 1.32-5.32, $P = 0.006$). As the result of putting the reasonable variables of the above into the stepwise selection, a multiple Poisson regression model identified the most significant mortality risk predictors as: Killip classification (adjusted RR: 4.17, 95% CI: 1.74-9.95), history of stroke (adjusted RR: 3.79, 95% CI: 1.59-9.01), maximum CK level more than 1500 IU/L (adjusted RR: 3.02, 95% CI: 1.25-7.31), age

(adjusted RR: 1.04, 95% CI: 1.01-1.08), and HR (adjusted RR: 1.02, 95% CI: 1.01-1.03).

The classification tree obtained by the above CART setting and pruning is shown in Figure 1. The CART method identified the variable "Killip classification" as the most important variable. The cutoff point value was 3.5 on the "Killip classification". Therefore, to predict the death event within 30-days, we needed to firstly focus on the information of the "Killip classification". If the patient's value of "Killip classification" is observed as 1, 2, or 3, we should predict no death event within 30-days. Yet, if the value of "Killip classification" is observed as 4, we need to predict the death event within 30-days. The next best predictor of 30-day mortality in the higher Killip group was maximum CK levels at a discrimination level of more than 4815 IU/L and furthermore, in the maximum CK levels of less than 4815 IU/L patients, the age of more than 72 years as was tertiary predictor. In the lower Killip group, systolic BP of less than 81 mmHg was the secondary predictor.

III-3 Major adverse event in one year

In the subset of the patients without 30-day mortality, a total of 123 MAE (29.6%) occurred within one year: 9 all-cause death; 6 recurrent non-fatal MI; 59 repeat PCI; 24 re-hospitalizations due to heart failure; 14 bleeding; 14 stroke (Table 3). The Killip classification was higher, initial LVEF was lower (47.2% vs. 50.6%, $P = 0.035$) and maximum CK level was higher (median 1734.0 IU/L vs. 1277.5 IU/L, $P = 0.026$) in the MAE group (see Table 4). However, the D2B time was shorter (median 54.0 min vs. 68.5 min, $P = 0.049$) and there were more beta-blockers administrated at discharge (75.6% vs. 60.5%, $P = 0.003$) in the MAE group. Simple Poisson regression model identified higher Killip classification (RR: 1.84, 95% CI: 1.03-3.07) and the use of beta-blockers (RR: 1.66, 95% CI: 1.10-2.50) as a potential risk factor. The above variables and the variables, which had a reasonable difference between the two groups, were entered into a stepwise selection model. Those additional variables were: age of 65 years or more, male, LVEF, serum creatinine level, high-

density lipoprotein cholesterol level, initial CK level, maximum CK levels more than 1500 IU/L, D2B time, primary PCI, duration of hospital stay, and the use of beta-blockers. As a result, the use of beta-blockers, primary PCI and Killip classification were chosen as the potential factors.

Finally, the multiple Poisson regression model revealed two predictors. A higher Killip classification (RR: 1.92, 95% CI: 1.08-3.42), and the use of beta-blockers (RR: 1.68, 95% CI: 1.11-2.53) were significant predictors for the one-year MAE after AMI (Table 5).

IV. Discussions

In the present study, the features of AMI in the Tokyo area were studied. Multiple Poisson regression model identified Killip classification, history of stroke, maximum CK level, age and, HR as significant predictors, and the CART analysis revealed Killip classification as a most important predictor for 30-day mortality. Interestingly, the initial profiles, except for Killip classification and beta-blocker, medications at discharge were not associated with a one-year MAE after AMI.

Globally, AMI remains one of the most serious diseases despite improvement of treatment strategies or the development of novel devices. Because of that, physicians are often wondering what should they deal with those patients after the acute phase treatment such as primary PCI. There are some risk stratification systems such as the GRACE risk score, which are absolutely reasonable. However, it is not convenient to apply these scoring systems directly for treatment strategy in clinical settings and the risk scoring may not be one more thing to improve the patient's prognosis. The purpose of this study was to explore novel prognostic factors easily applying to treatment strategy. The present study demonstrated the features of AMI patients with 30-day mortality in the Tokyo area, Japan. There are some large Japanese AMI registry data such as JROD-DPC and JAMIR (Kojima et al., 2018; Yasuda et al., 2016) and the background of AMI patients in the present study was very similar to the registry data and the mortality rate was also similar. By contrast, the transfer time and

door-to-balloon time were shorter compared to the JAMIR data. This means that the distance between in study hospital located in an urban area, and the onset place might be shorter than those in the area where the JAMIR data was collected. In addition, the data in this study examined laboratory values; therefore the predictors were analyzed in more detail. There were some differences in the initial laboratory levels between the Mortality group and the Survivor group, but none of these were related to the outcome in the present cohort. The AMI Kyoto Multi-Center Risk Study revealed that a laboratory stratification model could predict mortality after AMI (Yanishi et al., 2016). Researchers need to validate whether the present data fits the above stratification model. In the present cohort, multiple Poisson regression models identified Killip classification, history of stroke, maximum CK levels, age, and HR as significant predicting factors. Since the CART analysis also identified Killip, maximum CK level, and age as important predictors, these variables can be considered as robust predictors. The association between mortality of AMI and Killip classification is well established (Killip & Kimball, 1967) and Killip, age, and HR have already been applied as predicting factors in some stratification systems (Granger et al., 2003; Sabatine et al., 2004). Furthermore, because Komiyama et al. (2018) reported that the GRACE score was validated in Japanese AMI patients, the present results are reasonable. Elevation of CK reflects cardiac damage due to AMI, therefore it is reasonable that is related to mortality after AMI (Halkin et al., 2006). Moreover, in the present study, AMI patients with stroke had 3.8 times higher risk of mortality than those without stroke, which is consistent with the Brammås et al. (2013) report. Although these risk factors are similar, the reason why stoke is involved in the prognosis of myocardial infarction is still unclear.

The CART analysis is an empirical, statistical method. Unlike a multiple regression model, it is suitable for generating clinical decision rules by statistically examining variables from the most important to the least. As a result, CART model constructs decision trees that are easy to interpret and may be applied in clinical settings. CART analysis constructs decision trees, but when trees are

too busy, it becomes a non-generalized model. In the present study, trees were pruned by one-sigma rule, finally CART analysis identified Killip classification, maximum CK level, and age as important factors for 30-day mortality. As mentioned above, these are the same predicting values identified by multiple Poisson regression model. These variables can be considered as robust factors.

While the aim of this study was to identify the prognostic factors of Japanese AMI patients and also develop simple statistical models to improve the prognosis of elderly AMI patients in the future, it is important to consider whether there are interventions for the identified predictors. It may be hard to decrease the Killip classification value. Although there are no drugs to prevent CK elevation or cardiac dysfunction after AMI, a novel LV unloading device, IMPELLA, may improve CK elevation and LV dysfunction (Saku et al., 2018). In the Mortality group, the initial HR was higher than that in the Survivor group. This seemed to be due to activation of sympathetic nerve or compensation for the blood pressure reduction. This finding is consistent with the previous evidence that the early use of beta-blockers was associated with a reduction of 30-day mortality in patients with AMI (Puymirat et al., 2016). Therefore, the administration of beta-blocker may be effective.

In the present study, no significant predictors except the Killip severity and the use of beta-blocker for one-year MAE were found. Particularly, initial demographic, vital and laboratory data were not related to one-year MAE. Miyamoto et al. (2017) discovered that LVEF at discharge was one of the independent predictors of one-year outcome. This suggests that optimal secondary treatment and prevention, not primary treatment, might be more important for the one-year outcome. However, in the present study, as physiological and laboratory data at discharge were not collected, it is still unclear which factors at discharge are associated with the adverse event one year after AMI. The use of beta-blockers was a negative predictor for the one-year adverse event in the present study. Previous studies found that the prolonged use of beta-blockers was not associated with the long-term outcome after AMI (Puymirat et al., 2016) nor was use of beta-blockers associated with any

reduction in cardiovascular morbidity or mortality in non-MI patients and preserved cardiac function in patients without a prior history of AMI (Motivala et al., 2016).

V Limitation

There are some limitations to this study. Although this study was a single-center, retrospective cohort study, these results might be applicable to the treating AMI in urban areas. However, because the sample size was small, these results should not be generalized to other areas. It can be compared with the data from other areas. In this study, the differences in the patient background by such factors as area, socio-economic status, types of medical insurance, and family composition were not evaluated and cognitive function or frailty of patients was also not evaluated; it is still unclear whether these factors affected the outcome. Some patients' data were missing because they were transferred to the other hospitals, clinics or nursing homes. The present cohort data revealed some predicting variables, but they were not validated in the other cohort. Although there are some risk scoring systems, they were not applied in the present cohort. Future research should compare the present results with other valid scoring systems. Because as the various stent types such as BMS, 2nd generation, and 3rd generation DES were not identified, the association between stent type and repeat PCI is still unclear. As the laboratory data and physiological data at discharge were not collected, the association between discharge condition and the one-year outcome is also unclear.

VI. Conclusion

The features of AMI in the Tokyo area were studied in the present study. Killip classification, maximum CK level, age and heart rate were identified as the significant predictor for 30-day mortality after AMI statistically. Killip classification and the use of beta blocker may be predictors for one-year MAE.

VII Acknowledgement

The author really thanks Prof. Mahbub Latif for helpful discussion and suggestions about this study, Dr. Kuniyoshi Hayashi for helpful support for statistical analysis, and Dr. Daiki Kobayashi for discussing this project.

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Figure legend

Figure 1. Decision tree model predicting 30-day mortality after acute myocardial infarction.

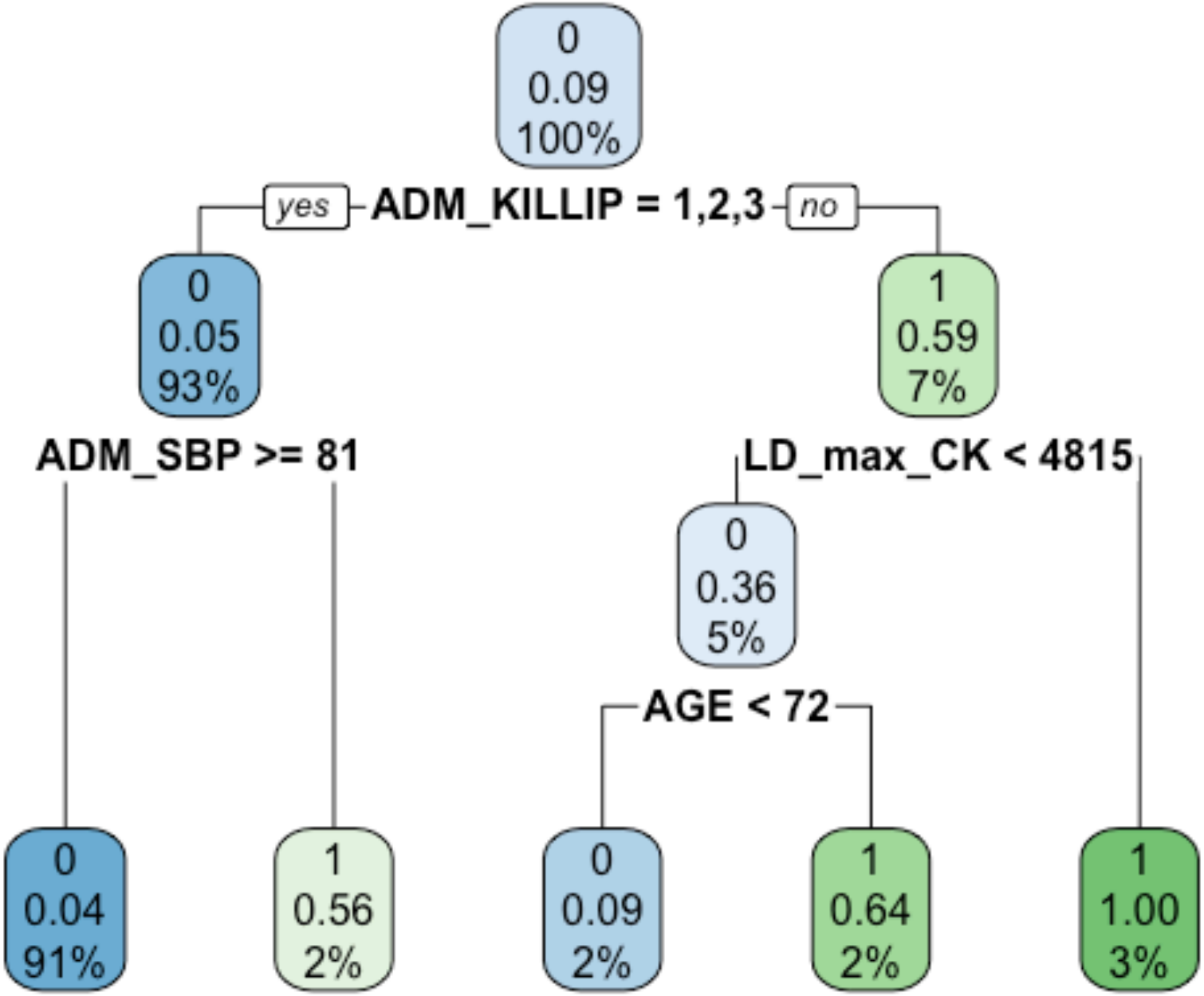
0
0.09
100%
yes
ADM_KILLIP = 1,2,3
no
0
0.05
93%
1
0.59
7%
ADM_SBP >= 81
LD_max_CK < 4815
0
0.36
5%
AGE < 72
0
0.04
91%
1
0.56
2%
0
0.09
2%
1
0.64
2%
1
1.00
3%

Table 1. Baseline patient characteristics with and without 30-day mortality

	Overall n = 457	Survivor n = 415	Moratlity n = 42	*P* value
Demographic data				
Age (years)	67.7 ± 13.3	67.2 ± 13.2	72.6 ± 13.2	0.012
Male, n (%)	362 (79.2)	328 (79.0)	34 (81.0)	0.927
BMI (kg/m^2)	23.5 ± 3.6	23.5 ± 3.6	22.9 ± 3.5	0.273
Medical history				
Hypertension, n (%)	274 (60.8)	257 (61.9)	17 (40.5)	0.052
Diabetes, n (%)	138 (30.6)	127 (30.6)	37 (26.2)	0.963
Hyperlipidemia, n (%)	198 (43.9)	189 (45.5)	59 (21.4)	0.014
Smoking, n (%)	287 (65.4)	267 (64.3)	20 (47.6)	0.683
Prior MI, n (%)	43 (9.5)	37 (8.9)	6 (14.3)	0.241
Hemodialysis, n (%)	26 (5.8)	22 (5.3)	4 (9.5)	0.261
Heart failure, n (%)	7 (1.6)	6 (1.4)	1 (2.4)	0.462
Stroke, n (%)	35 (7.8)	24 (5.8)	11 (26.2)	< 0.001
Profiles at arrival				
Ambulance use, n (%)	270 (59.1)	240 (57.8)	30 (71.4)	0.123
Transfer time (min)	35.4 ± 9.5	35.4 ± 9.5	35.4 ± 9.3	0.986
STEMI, n (%)	337 (73.7)	302 (72.8)	35 (83.3)	0.194
Cardiac arrest, n(%)	33 (7.2)	20 (4.8)	13 (31.0)	< 0.001
Cardiogenic shock, n (%)	37 (8.1)	19 (4.6)	18 (42.9)	< 0.001
Killip class I	373 (81.6)	357 (86.0)	16 (38.1)	< 0.001
Killip class II	38 (8.3)	33 (8.0)	5 (11.9)	
Killip class III	12 (2.6)	11 (2.7)	1 (2.4)	
Killip class IV	34 (7.4)	14 (3.4)	20 (47.6)	
sBP (mmHg)	135.2 ± 31.2	137.2 ± 30.4	110.0 ± 31.6	< 0.001
dBP (mmHg)	82.8 ± 21.2	83.6 ± 21.3	72.3 ± 17.7	0.003
HR (beat/min)	84.0 ± 25.2	82.3 ± 23.9	103.9 ± 31.6	< 0.001
LVEF (%)	48.6 ± 12.9	49.6 ± 12.4	35.0 ± 12.2	< 0.001
Laboratory data				
WBC (/μL)	9400 (7300-12000)	9400 (7300-11950)	10000 (7700-14600)	0.152
Hb (g/dL)	13.3 ± 2.2	13.4 ± 2.2	12.3 ± 2.6	0.002
Cr (mg/dL	0.87 (0.72-1.13)	0.86 (0.71-1.07)	1.14 (0.80-1.64)	< 0.001
CK (IU/L)	248 (117.8-671.8)	246 (117.5-665.0)	375 (122.0-1137.0)	0.219
NT-proBNP (pg/mL)	682 (165.5-2624.5)	638 (152.0-2497.8)	1035 (520.5-3444.3)	0.037
Glucose (mg/dL)	174.7 ± 78.1	168.1 ± 68.5	241.3 ± 125.1	< 0.001
HbA1c (%)	6.4 ± 1.2	6.4 ± 1.3	6.1 ± 0.8	0.092
TC (mg/dL)	183.9 ± 53.1	187.9 ± 52.0	143.6 ± 47.1	< 0.001
HDL-C (mg/dL)	42.0 ± 12.4	42.5 ± 12.2	36.6 ± 13.5	0.003
LDL-C (mg/dL)	113.0 ± 43.0	115.7 ± 42.9	86.3 ± 34.8	< 0.001
Triglyceride (mg/dL)	89.5 (56.0-154.5)	93.0 (57.0-155.5)	78.0 (47-109.0)	0.027
Intervention profile				
Culprit vessel				< 0.001
LAD	216 (48.0)	196 (47.8)	20 (50.0)	
LCX	68 (15.1)	63 (15.4)	5 (12.5)	
RCA	155 (34.4)	147 (35.9)	8 (20.0)	
LMT	11 (2.4)	4 (1.0)	7 (17.5)	
Primary PCI, n (%)	429 (93.9)	392 (94.5)	37 (88.1)	0.164
D2B time (min)	62 (38.3-113.5)	62.5 (39.0-116.0)	51.0 (33.5-104.3)	0.132
Mechanical support use, n (%)	143 (31.3)	111 (26.7)	32 (76.2)	< 0.001
Respirator use, n (%)	100 (21.9)	63 (15.2)	37 (88.1)	< 0.001
Max CK (IU/L)	1438.0 (599.0-3286.0)	1332.5 (577.3-2927.8)	5241.0 (1378.5-9771.0)	< 0.001

Data are expressed as mean ± SD, median (interquartile range), or number (%). The differences between the two groups were compared using a t-test, Mann-Whitney U test, chi-squared test, Fisher's exact test as appropriate. BMI, body mass index; MI, myocardial infarction; STEMI, ST-elevation myocardial infarction; sBP, systolic blood pressure; dBP, diastolic blood pressure; HR, heart rate; LVEF, left ventricular ejection fraction; WBC, white blood cells; Hb, hemoglobin; Cr, serum creatinine; CK, creatine kinase; NT-proBNP, N-terminal pro-brain natriuretic peptide; HbA1c, hemoglobin A1c; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol, LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; LMT, left main tract coronary artery; PCI, percutaneous coronary intervention; D2B, door-to-balloon.

Table 2. Predictive value of potential risk for 30-day mortality by Poisson regression analysis

	Crude			Adjusted		
Variables	RR	95% CI	*P* value	RR	95% CI	*P* value
Age, per year	1.03	1.01-1.06	0.018	1.04	1.01-1.08	0.024
Male	1.12	0.52-2.41	0.781			
BMI, per kg/m^2	0.95	0.87-1.04	0.294			
Hypertension, yes	0.52	0.28-0.99	0.047			
Diabetes, yes	0.92	0.46-1.86	0.825			
Hyperlipidemia, yes	0.40	0.19-0.84	0.015			
Smoking, yes	0.81	0.41-1.64	0.565			
Prior MI, yes	1.78	0.74-4.25	0.195			
Hemodialysis, yes	1.92	0.68-5.42	0.216			
Heart failure, yes	1.71	0.24-12.5	0.595			
Stroke, yes	4.84	2.40-9.76	< 0.001	3.79	1.59-9.01	0.003
Ambulance use, yes	1.73	0.89-3.38	0.108			
Transfer time, per min	1.00	0.96-1.04	0.986			
STEMI, yes	1.78	0.79-4.01	0.164			
Cardiac arrest, yes	5.76	2.99-11.1	< 0.001			
Shock, yes	8.51	4.62-15.7	< 0.001			
Killip IV vs I-III	11.3	6.17-20.7	< 0.001	4.17	1.74-9.95	0.001
sBP, per mmHg	0.97	0.96-0.98	< 0.001			
HR, per beat/min	1.02	1.01-1.03	< 0.001	1.02	1.01-1.03	0.001
LVEF, per %	0.93	0.91-0.96	< 0.001			
WBC (/μL)	1.00	1.00-1.00	0.051			
Hb, per g/dL	0.83	0.73-0.94	0.004			
Cr, per mg/dL	1.11	0.98-1.25	0.091			
CK, per IU/L	1.00	1.00-1.00	0.002			
NT-proBNP, per pg/mL (log)	1.18	1.00-1.39	0.043			
Glucose, per mg/dL	1.01	1.00-1.01	< 0.001			
TC per mg/dL	0.98	0.97-0.99	< 0.001			
HDL-C, per mg/dL	0.96	0.93-0.99	0.005			
LDL-C, per mg/dL	0.98	0.97-0.99	< 0.001			
Triglyceride, per mg/dL	0.99	0.99-1.00	0.032			
Culprit vessel, reference LAD						
LCX	0.79	0.30-2.12	0.645			
RCA	0.56	0.25-1.27	0.162			
LMT	6.87	2.91-16.2	< 0.001			
Primary PCI, yes	0.48	0.19-1.23	0.127			
Max CK level, per IU/L	1.00	1.00-1.00	< 0.001			
Max CK > 1500 IU/L	2.65	1.32-5.32	0.006	3.02	1.25-7.31	0.014
D2B time, per min	1.00	0.99-1.00	0.295			
Mechanical support use, yes	7.03	3.45-14.3	< 0.001			
Respirator use, yes	26.4	10.4-67.2	< 0.001			

RR, risk ratio; CI, confidence interval; BMI, body mass index; MI, myocardial infarction; STEMI, ST-elevation myocardial infarction; sBP, systolic blood pressure; HR, heart rate; LVEF, left ventricular ejection fraction; WBC, white blood cells; Hb, hemoglobin; Cr, serum creatinine; CK, creatine kinase; NT-proBNP, N-terminal pro-brain natriuretic peptide; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol, LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; LMT, left main tract coronary artery; PCI, percutaneous coronary intervention; D2B, door-to-balloon.

Table 3. Clinical outcomes during follow-up

Outcome	n (%)
30-day clinical follow-up (457 patients)	
Mortality	42 (9.2)
1-year clinical follow-up (415 patients)	
Any MAE	123 (29.6)
All-cause death	19 (4.6)
Recurrent MI	6 (1.4)
Repeat PCI	59 (14.2)
Heart failure hospitalization	24 (5.8)
Bleeding	14 (3.4)
Stroke	14 (3.4)

MAE, major adverse event; MI myocardial infarction; PCI, percutaneous

Table 4. Patient characteristics with and without 1-year adverse event

	Overall n = 415	No-MAE n = 291	MAE n = 123	*P* value
Demographic data				
Age (years)	67.2 ± 13.2	67.7 ± 13.8	65.9 ± 11.8	0.191
Male, n (%)	328 (79.0)	224 (77.0)	104 (84.6)	0.109
BMI (kg/m^2)	23.5 ± 3.6	23.6 ± 3.5	23.4 ± 3.9	0.691
Medical history				
Hypertension, n (%)	257 (61.9)	179 (61.9)	78 (63.4)	0.863
Diabetes, n (%)	127 (30.6)	86 (29.8)	40 (32.5)	0.660
Hyperlipidemia, n (%)	189 (45.5)	129 (44.6)	60 (48.8)	0.506
Smoking, n (%)	267 (64.3)	184 (64.3)	103 (67.8)	0.540
Prior MI, n (%)	37 (8.9)	24 (8.3)	13 (10.6)	0.584
Hemodialysis, n (%)	22 (5.3)	14 (4.8)	8 (6.5)	0.481
Heart failure, n (%)	6 (1.4)	5 (1.7)	1 (0.8)	0.674
Stroke, n (%)	24 (5.8)	18 (6.2)	6 (4.9)	0.760
Profiles at arrival				
Ambulance use, n (%)	240 (57.8)	167 (57.4)	72 (58.5)	0.915
Transfer time (min)	35.4 ± 9.5	35.2 ± 9.0	36.1 ± 10.5	0.497
STEMI, n (%)	302 (72.8)	210 (72.2)	92 (74.8)	0.667
Cardiac arrest, n(%)	20 (4.8)	11 (3.8)	9 (7.3)	0.137
Shock, n (%)	19 (4.6)	14 (4.8)	5 (4.1)	0.999
Killip class I	357 (86.0)	253 (86.9)	103 (83.7)	0.007
Killip class II	33 (8.0)	26 (8.9)	7 (5.7)	
Killip class III	11 (2.7)	8 (2.7)	3 (2.4)	
Killip class IV	14 (3.4)	4 (1.4)	10 (8.1)	
sBP (mmHg)	137.2 ± 30.4	137.6 ± 30.4	136.6 ± 30.4	0.781
dBP (mmHg)	83.6 ± 21.3	83.8 ± 21.4	83.3 ± 21.0	0.807
HR (beat/min)	82.3 ± 23.9	81.9 ± 23.7	83.1 ± 24.4	0.652
LVEF (%)	49.6 ± 12.4	50.6 ± 12.0	47.2 ± 13.2	0.035
Laboratory data				
WBC (/μL)	9400 (7300-11950)	9400 (7300-11750)	9400 (7150-12350)	0.532
Hb (g/dL)	13.4 ± 2.2	13.5 ± 2.1	13.4 ± 2.3	0.699
Cr (mg/dL	0.86 (0.71-1.07)	0.86 (0.72-1.03)	0.87 (0.68-1.18)	0.503
CK (IU/L)	246 (117.5-665.0)	230.0 (114.5-614.5)	260.0 (124.5-665.5)	0.607
NT-proBNP (pg/mL)	638 (152.0-2497.8)	638 (113.8-2460.8)	616.0 (263.0-2509.0)	0.240
Glucose (mg/dL)	168.1 ± 68.5	165.8 ± 67.1	170.6 ± 64.2	0.501
HbA1c (%)	6.4 ± 1.3	6.4 ± 1.1	6.4 ± 1.5	0.328
TC (mg/dL)	187.9 ± 52.0	189.8 ± 52.6	183.4 ± 50.6	0.268
HDL-C (mg/dL)	42.5 ± 12.2	43.2 ± 12.5	41.0 ± 11.3	0.110
LDL-C (mg/dL)	115.7 ± 42.9	115.8 ± 43.9	115.6 ± 40.5	0.955
Triglyceride (mg/dL)	93 (57.0-155.5)	92.5 (55.5-155.0)	94.0 (61.5-155.0)	0.706
Intervention profile				
Culprit vessel				0.598
LAD	196 (47.8)	141 (49.1)	55 (44.7)	
LCX	63 (15.4)	45 (15.7)	18 (14.6)	
RCA	147 (35.9)	99 (34.5)	48 (39.0)	
LMT	4 (1.0)	2 (0.7)	2 (1.6)	
Primary PCI, n (%)	392 (94.5)	272 (93.5)	120 (97.6)	0.145
D2B time (min)	62.5 (39.0-116.0)	68.5 (41.0-119.0)	54.0 (36.0-103.3)	0.049
Mechanical support use, n (%)	111 (26.7)	73 (25.1)	38 (30.9)	0.272
Respirator use, n (%)	63 (15.2)	42 (14.4)	21 (17.1)	0.594
Max CK (IU/L)	1332.5 (577.3-2927.8)	1277.5 (500.3-2676.8)	1734.0 (737.0-3608.5)	0.026
Medications at discharge				
Aspirin, n (%)	411 (99.0)	288 (99.0)	123 (100)	0.999
ACE-I/ARB, n (%)	309 (74.5)	218 (74.9)	91 (74.0)	0.805
Beta-blocker, n (%)	269 (64.8)	176 (60.5)	93 (75.6)	0.003
Ca channel blocker, n (%)	74 (17.8)	54 (18.6)	20 (16.3)	0.674
Diuretics, n (%)	92 (22.2)	68 (23.4)	24 (19.5)	0.438
MRA, n (%)	42 (9.9)	31 (10.7)	11 (8.9)	0.722
Nitrate/nitrite, n (%)	48 (11.6)	36 (12.4)	12 (9.8)	0.504
Statin, n (%)	338 (81.4)	238 (81.8)	101 (82.1)	0.999
Insulin, n (%)	36 (8.7)	28 (9.6)	8 (6.5)	0.345

Data are expressed as mean ± SD, median (interquartile range), or number (%). The differences between the two groups were compared using a t-test, Mann-Whitney U test, chi-squared test, Fisher's exact test as appropriate. MAE, major adverse event; BMI, body mass index; MI, myocardial infarction; STEMI, ST-elevation myocardial infarction; sBP, systolic blood pressure; dBP, diastolic blood pressure; HR, heart rate; LVEF, left ventricular ejection fraction; WBC, white blood cells; Hb, hemoglobin; Cr, serum creatinine; CK, creatine kinase; NT-proBNP, N-terminal pro-brain natriuretic peptide; HbA1c, hemoglobin A1c; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol, LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; LMT, left main tract coronary artery; PCI, percutaneous coronary intervention; D2B, door-to-balloon; ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; MRA, mineral corticoid receptor antagonist.

Table 5. Predictive value of potential risk for 1-year adverse event by Poisson regression analysis

	Crude			Adjusted		
Variables	RR	95% CI	*P* value	RR	95% CI	*P* value
Age, per year	0.99	0.98-1.01	0.272			
Age > 65 years	0.77	0.54-1.10	0.151			
Male	1.44	0.88-2.34	0.148			
BMI, per kg/m2	0.99	0.94-1.04	0.738			
Hypertension, yes	1.05	0.72-1.51	0.813			
Diabetes, yes	1.09	0.75-1.60	0.641			
Dyslipidemia, yes	1.12	0.79-1.60	0.518			
Smoking, yes	1.16	0.79-1.71	0.454			
Prior MI, yes	1.20	0.67-2.13	0.538			
Hemodialysis, yes	1.23	0.60-2.53	0.566			
History of HF, yes	0.55	0.08-3.97	0.557			
History of stroke, yes	0.83	0.37-1.88	0.654			
Ambulance use	1.03	0.72-1.48	0.856			
Transfer time, per min	1.01	0.98-1.03	0.569			
STEMI, yes	1.10	0.73-1.65	0.644			
Killip III-IV vs I-II	1.84	1.03-3.27	0.038	1.92	1.08-3.42	0.026
Cardiac arrest, yes	1.56	0.79-3.07	0.202			
Shock, yes	0.88	0.36-2.16	0.781			
sBP, per mmHg	1.00	0.99-1.01	0.797			
HR, per beat/min	1.00	0.99-1.01	0.704			
LVEF, per %	0.99	0.97-1.00	0.074			
WBC, per log(/μL)	1.11	0.68-1.80	0.681			
Hb, per g/dL	0.99	0.91-1.07	0.745			
Cr, per mg/dL	1.06	0.98-1.15	0.175			
CK, per IU/L	1.04	0.89-1.21	0.619			
NT-proBNP, per pg/mL (log)	1.05	0.96-1.15	0.283			
Glucose, per mg/dL	1.00	1.00-1.00	0.572			
HDL-C, per mg/dL	0.99	0.97-1.00	0.178			
Triglyceride, per mg/dL	1.04	0.80-1.34	0.792			
Culprit vessel, reference LAD						
LCX	1.02	0.60-1.73	0.947			
RCA	1.16	0.79-1.71	0.443			
LMT	1.78	0.43-7.30	0.422			
Primary PCI, yes	2.24	0.71-7.06	0.166	2.01	0.64-6.32	0.232
Max CK level, per IU/L	1.16	0.98-1.36	0.079			
Max CK > 1500 IU/L	1.41	0.99-2.01	0.059			
D2B time, per min	1.00	1.00-1.00	0.147			
Mechanical support use, yes	1.22	0.83-1.79	0.307			
Respirator use, yes	1.15	0.72-1.83	0.567			
Hospital stay, per days	1.01	1.00-1.02	0.179			
ACE-I/ARB, yes	0.96	0.64-1.43	0.831			
Beta blocker, yes	1.66	1.10-2.50	0.016	1.68	1.11-2.53	0.014
Ca blocker, yes	0.90	0.55-1.45	0.652			
Diuretics, yes	0.85	0.54-1.32	0.462			
MRA, yes	0.87	0.47-1.61	0.653			
Nitrate/nitrite, yes	0.82	0.45-1.49	0.513			
Statin, yes	1.01	0.63-1.59	0.987			
Insulin, yes	0.73	0.36-1.49	0.386			

RR, risk ratio; CI, confidence interval; BMI, body mass index; MI, myocardial infarction; STEMI, ST-elevation myocardial infarction; sBP, systolic blood pressure; HR, heart rate; LVEF, left ventricular ejection fraction; WBC, white blood cells; Hb, hemoglobin; Cr, serum creatinine; CK, creatine kinase; NT-proBNP, N-terminal pro-brain natriuretic peptide; HDL-C, high-density lipoprotein cholesterol; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; LMT, left main tract coronary artery; PCI, percutaneous coronary intervention; D2B, door-to-balloon; ACE-I, angiotensin converting enzyme inhibitor; MRA mineral conrticoid receptor antagonist.