Factors Associated with In-Hospital Death in Patients with Killip Class 3 Acute Myocardial Infarction

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Summary
The clinical outcomes in acute myocardial infarction (AMI) patients with Killip class 3 are often inconsistent with those in the literature, and the factors associated with poor outcomes have not been sufficiently investigated. The purpose of this study was to identify factors associated with in-hospital death in AMI patients with Killip class 3. We included 205 AMI patients with Killip class 3, and divided them into a survived group (n = 189) and in-hospital death group (n = 16). The primary objective was to identify factors associated with in-hospital death using multivariate analysis. Age was significantly younger in the survived group than in the in-hospital death group (73.1 ± 11.2 versus 83.2 ± 6.2 years, P < 0.001). Systolic blood pressure (SBP) was significantly higher in the survived group than in the in-hospital death group (150.0 ± 31.2 versus 124.8 ± 25.3 mmHg, P = 0.002). The prevalence of TIMI thrombus grade ≥ 2 was significantly greater in the in-hospital death group than in the survived group (56.3 versus 22.2%, P = 0.005). In multivariate logistic regression analysis, in-hospital death was significantly associated with age [odds ratio (OR) 1.168, 95% confidence interval (CI) 1.061-1.287, P = 0.002] and TIMI thrombus grade ≥ 2 (versus ≤ 1: OR 5.743, 95% CI 1.717-19.214, P = 0.005), and inversely associated with SBP on admission (per 10 mmHg increase: OR 0.764, 95% CI 0.613-0.953, P = 0.017). In conclusion, in-hospital death was associated with age and coronary thrombus burden, and was inversely associated with SBP on admission in patients with Killip class 3. It may be important to recognize these high risk features to improve the clinical outcomes of patients with Killip class 3.

Key words: Pulmonary edema, Percutaneous coronary intervention, Thrombus

Acute myocardial infarction (AMI) is the leading cause of death in developed as well as developing countries.1-3 Since AMI has a wide variety of presentations from minor high-sensitivity troponin elevation without myocardial damage to severe cardiogenic shock caused by pump failure,4-6 several classifications for the risk stratification of patients with AMI have been developed.7-9 Of those classifications, the Killip classification has been used in clinical practice for more than 50 years.10 It is well known that Killip class 4 (cardiogenic shock) is closely associated with poor clinical outcomes in patients with AMI.10 It is also known that Killip class ≤ 2 is associated with favorable clinical outcomes in patients with AMI.11,12 However, the clinical outcomes in patients with Killip class 3 were not consistent among different reports,13-15 suggesting that the severity of Killip class 3 varies widely from simple pulmonary edema to pulmonary edema complicated with a pre-shock state. Moreover, the clinical factors associated with poor clinical outcomes have not been sufficiently investigated in AMI patients with Killip class 3. The purpose of this study was to identify factors associated with in-hospital death in AMI patients with Killip class 3.

Methods

Study design: We reviewed all AMI patients treated at our institution (Saitama Medical Center, Jichi Medical University) between January 2009 and December 2019. The inclusion criterion was (1) patients with AMI. The exclusion criteria were (1) patients with shock at admission, (2) patients without pulmonary edema at admission, and (3) patients who did not undergo coronary angiography during hospitalization. The final study population was divided into a survived group and an in-hospital death group. The diagnosis of pulmonary edema was retrospectively performed by reviewing initial chest X-rays. The first author (MH) reviewed the chest X-rays of all cases, and divided them into cases with obvious pulmonary edema and cases with borderline pulmonary edema. MH and a senior author (KS) reviewed the chest X-rays of borderline cases together, and finalized the cases with pul-
monary edema. The primary interest for this study was to identify factors associated with in-hospital death using multivariate logistic regression analysis. This study was approved by the institutional review board of Saitama Medical Center, Jichi Medical University (S20-153), and written informed consent was waived because of the retrospective study design. The data collection and storage were performed anonymously, according to Japanese Ministry of Health, Labour and Welfare guidelines.

**Definitions:** Acute myocardial infarction (AMI) was defined according to the universal definition.\(^6\,17\) Diagnostic ST elevation was defined as new ST elevation at the J point in at least two contiguous leads of 2 mm (0.2 mV), and AMI patients with ST elevation were diagnosed as ST elevation myocardial infarction (STEMI).\(^18\) Hypertension was defined as systolic blood pressure (SBP) > 140 mmHg or medical treatment for hypertension.\(^19\) Diabetes mellitus was defined as hemoglobin A1c ≥ 6.5% (national glycolhemoglobin standardization program (NGSP) value) or treatment for diabetes mellitus.\(^20\,22\) Dyslipidemia was defined as total cholesterol ≥ 220 mg/dL, low-density lipoprotein cholesterol ≥ 140 mg/dL, or treatment for dyslipidemia.\(^23\) We used the laboratory data at admission. Since we could not measure some laboratory data such as HbA1c or low-density lipoprotein (LDL) cholesterol levels during off hours (night or holidays), we substituted the earliest HbA1c or LDL cholesterol levels since admission for the laboratory data at admission.\(^20\) Left ventricular ejection fraction (LVEF) was measured by transthoracic echocardiography during the index hospitalization. LVEF was calculated using either the modified Simpson’s method, Teichholz method, or eyeball estimation. The Teichholz method was adopted only when the modified Simpson’s method was not available. An eyeball estimation was adopted only when these 2 methods were not available. We also calculated estimated glomerular filtration rate (eGFR) using serum creatinine (Cr), age, weight, and gender according to the following formula: eGFR = 194 × Cr\(^{-1.094}\) × age\(^{-0.287}\) × 0.739 (female).\(^23\) Chronic kidney disease was defined as an estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m\(^2\) including patients on chronic dialysis.\(^24\) The initial thrombolysis in myocardial infarction (TIMI) flow grade, final TIMI flow grade, and TIMI thrombus grade were recorded from coronary angiography.\(^11,25\)

**Statistical analysis:** Data are expressed as the mean ± SD or percentage. Categorical variables are presented as numbers (percentages) and were compared using Fisher’s exact test. For continuous variables, the Shapiro-Wilk test was performed to determine whether the continuous variables were normally distributed or not. Normally distributed continuous variables were compared using the Student t-test. Otherwise, continuous variables were compared using the Mann-Whitney U test. Multivariate logistic regression analysis was performed to identify factors associated with in-hospital death. In this model, in-hospital death was adopted as a dependent variable. In the multivariate stepwise logistic regression model, the selection of independent variables was derived from the results of univariate comparison between the survived and in-hospital death groups (\(P < 0.05\) in univariate analysis). However, variables with missing values were not included in the model. Moreover, when there were ≥ 2 similar variables, only one variable was entered into the multivariable logistic model to avoid multi-collinearity. In the multivariable stepwise logistic regression analysis, likelihood ratio statistical criteria using the backward elimination method were obtained. The odds ratio (OR) and the 95% confidence interval (CI) were also calculated. A \(P\) value < 0.05 was considered statistically significant. We analyzed all data by SPSS ver. 24 for Windows (SPSS, Inc., Chicago, IL, USA).

**Results**

From January 2009 to December 2019, a total of 2418 AMI patients were admitted to our medical center. After excluding 2213 patients who were compatible with the exclusion criteria, the final study population consisted of 205 AMI patients who were divided into the survived group (\(n = 189\)) and the in-hospital death group (\(n = 16\)) (Figure). The in-hospital mortality of the study population was 7.8%. The details of the in-hospital death group are shown in Table I.

A comparison of the patient characteristics between the survived and in-hospital groups is shown in Table II. Age was significantly younger in the survived group (73.1 ± 11.2 years) than in the in-hospital death group (83.2 ± 6.2 years) (\(P < 0.001\)). Systolic blood pressure (SBP) was significantly higher in the survived group (150.0 ± 31.2 mmHg) than in the in-hospital death group (124.8 ± 25.3 mmHg) (\(P = 0.002\)). Heart rate was significantly faster in the survived group (104.5 ± 21.6 bpm) than in the in-hospital death group (84.9 ± 26.8 bpm) (\(P = 0.006\)). Table III shows comparisons of the angiographic and procedural findings between the 2 groups. The prevalence of TIMI thrombus grade ≥ 2 was significantly greater in the in-hospital death group (56.3%) than in the survived group (22.2%) (\(P = 0.005\)). The final TIMI flow grade was greater in the survived group than in the in-hospital death group (\(P = 0.029\)).

Table IV shows a comparison of the clinical outcomes between the 2 groups. The incidence of intubation was significantly greater in the in-hospital death group (56.3%) than in the survived group (16.9%) (\(P = 0.001\)). Catecholamine use was more common in the in-hospital death group (56.3%) than in the survived group (11.6%) (\(P < 0.001\)). Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was more frequently used in the in-hospital death group (18.8%) than in the survived group (2.6%) (\(P = 0.017\)). The details of patients with VA-ECMO are shown in the Supplemental Table. Both peak creatine kinase and peak creatine kinase-myocardial band were significantly greater in the in-hospital death group than in the survived group.

Table V shows the results of multivariate logistic regression analysis. The initial model included the following variables: age, SBP on admission, heart rate on admission, TIMI thrombus grade ≥ 2, and final TIMI flow grade 3. In-hospital death was significantly associated with age (OR 1.168, 95% CI 1.061-1.287, \(P = 0.002\)) and TIMI thrombus grade ≥ 2 (versus ≤ 1: OR 5.743, 95% CI 2.516-12.26).
Acute myocardial infarction from January 2009 to December 2019 (n = 2418)

Shock at admission (n = 271)

Without pulmonary edema (n = 1936)

Coronary angiography was not performed (n = 6)

Acute myocardial infarction with pulmonary edema (n = 205)

In-hospital death?

Survived group (n = 189)

In-hospital death group (n = 16)

**Figure.** Study flowchart.

**Table I.** Details of the Patients Who Died During the Index Hospitalization

| Patient No. | Age | Sex  | Infarct-related artery        | Number of disease vessels | Cause of in-hospital death       |
|-------------|-----|------|-------------------------------|---------------------------|---------------------------------|
| 1           | 90  | Male | Left anterior descending artery | Double                    | Cardiac death                  |
| 2           | 87  | Female | Right coronary artery           | Triple                    | Cardiac death                  |
| 3           | 93  | Female | Left anterior descending artery | Single                    | Pneumonia                      |
| 4           | 89  | Male | Left main trunk                | Triple                    | Cardiac death                  |
| 5           | 81  | Male | Left anterior descending artery | Single                    | Pneumonia                      |
| 6           | 81  | Female | Left anterior descending artery | Single                    | Cardiac death                  |
| 7           | 75  | Male | Left circumflex artery         | Single                    | Cardiac death                  |
| 8           | 87  | Female | Left circumflex artery         | Single                    | Cardiac death                  |
| 9           | 85  | Male | Left anterior descending artery | Single                    | Acute renal failure            |
| 10          | 75  | Male | Left anterior descending artery | Single                    | Cerebral hemorrhage            |
| 11          | 77  | Male | Left circumflex artery         | Triple                    | Cardiac death                  |
| 12          | 83  | Male | Left anterior descending artery | Double                    | Cardiac death                  |
| 13          | 88  | Male | Left anterior descending artery | Triple                    | Cardiac death                  |
| 14          | 80  | Male | Left circumflex artery         | Single                    | Cardiac death                  |
| 15          | 88  | Male | Left anterior descending artery | Double                    | Pneumonia                      |
| 16          | 72  | Male | Right coronary artery          | Single                    | Pneumonia                      |

1.717-19.214, *P = 0.005), and inversely associated with SBP on admission (per 10 mmHg increase: OR 0.764, 95% CI 0.613-0.953, *P = 0.017*).

**Discussion**

The present study included 205 AMI patients with Killip class 3 who were divided into a survived group (n = 189) and in-hospital death group (n = 16). The incidences of intubation and catecholamine use were both significantly greater in the in-hospital death group than in the survived group. The multivariate logistic model revealed that in-hospital death was associated with age and TIMI thrombus grade, and inversely associated with SBP on admission. Age is a well-known strong predictor of poor clinical outcomes in patients with AMI. Our results suggest that intra-coronary thrombus and SBP on admission may be useful to find the highest risk group among AMI
patients with Killip class 3.

We should discuss why TIMI thrombus grade ≥ 2 was associated with in-hospital death. First, a large thrombus burden in initial angiography is reported to be associated with slow flow in primary percutaneous coronary intervention (PCI). Since slow flow in patients with AMI is a predictor of poor clinical outcomes, patients with TIMI thrombus grade ≥ 2 might have insufficient coronary reperfusion. However, in our multivariate stepwise model, final TIMI flow grade was eliminated from the model, suggesting that final TIMI flow grade was not associated with in-hospital death. Therefore, our data would not support this hypothesis. Second, a high thrombus burden itself might be a predictor of poor outcomes irrespective of coronary reperfusion. Zalewski, et al. reported that residual thrombus burden was associated with a worse outcome at 90 days. Moreover, a large thrombus burden might reflect a poor general status or severity of AMI such as higher peak CK-MB or longer pain to balloon time. Our data would support this second hypothesis.

The reason why SBP on admission was associated with in-hospital death should be noted. Since we excluded patients with Killip class 4 at admission, SBP on admission might reflect a poor general status or severity of AMI. Moreover, a large thrombus burden might reflect a poor general status or severity of AMI such as higher peak CK-MB or longer pain to balloon time. Our data would support this second hypothesis.

**Table II.** Comparison of Patient’s Characteristics Between the Survived and In-Hospital Death Groups

| Variable                                           | All (n = 205) | Survived group (n = 189) | In-hospital death group (n = 16) | P value |
|----------------------------------------------------|--------------|--------------------------|---------------------------------|---------|
| Age (years)                                        | 73.9 ± 11.2  | 73.1 ± 11.2              | 83.2 ± 6.2                      | <0.001  |
| Male sex, n (%)                                    | 134 (65.4)   | 122 (64.6)               | 12 (75.0)                       | 0.585   |
| ST elevated myocardial infarction, n (%)           | 103 (50.2)   | 91 (48.1)                | 12 (75.0)                       | 0.066   |
| Non-ST elevated myocardial infarction, n (%)       | 102 (49.8)   | 98 (51.9)                | 4 (25.0)                        | 0.066   |
| Body mass index (kg/m²)                            | 22.9 ± 4.0   | 23.0 ± 4.0               | 21.4 ± 2.7                      | 0.100   |
| Hypertension, n (%)                                | 165 (80.5)   | 153 (81.0)               | 12 (75.0)                       | 0.522   |
| Diabetes mellitus, n (%)                           | 112 (54.6)   | 104 (55.0)               | 8 (50.0)                        | 0.796   |
| Dyslipidemia, n (%)                                | 116 (56.6)   | 110 (58.2)               | 6 (37.5)                        | 0.122   |
| Current smoker, n (%)                              | 118 (57.6)   | 109 (57.7)               | 9 (56.3)                        | 1.000   |
| Chronic kidney disease, n (%)                      | 64 (31.2)    | 62 (32.8)                | 2 (12.5)                        | 0.157   |
| Hemodialysis, n (%)                                | 20 (9.8)     | 20 (10.6)                | 0 (0)                           | 0.375   |
| History of previous acute myocardial infarction, n (%) | 36 (17.6)  | 34 (18.0)               | 2 (12.5)                        | 0.743   |
| History of previous CABG, n (%)                    | 12 (5.9)     | 11 (5.8)                 | 1 (6.3)                         | 1.000   |
| History of cerebrovascular disease, n (%)          | 89 (43.4)    | 83 (43.9)                | 6 (37.5)                        | 0.794   |
| Peripheral artery disease, n (%)                   | 19 (9.3)     | 19 (10.1)                | 0 (0)                           | 0.372   |
| Systolic blood pressure on admission (mmHg)         | 148.0 ± 31.4 | 150.0 ± 31.2             | 124.8 ± 25.3                    | 0.002   |
| Heart rate on admission (bpm)                      | 103.0 ± 22.6 | 104.5 ± 21.6             | 84.9 ± 26.8                     | 0.006   |
| Ejection fraction on admission (%)                 | 38.2 ± 10.7  | 38.0 ± 10.8              | 41.3 ± 9.4                      | 0.236   |
| Laboratory data at admission                       |              |                          |                                 |         |
| Total cholesterol (mg/dL)                          | 179.7 ± 42.6 (197/205) | 180.7 ± 43.2 (184/189) | 166.1 ± 30.6 (13/16) | 0.249   |
| Triglycerides (mg/dL)                              | 100.4 ± 68.3 (199/205) | 102.1 ± 69.9 (186/189) | 75.4 ± 31.6 (13/16) | 0.152   |
| Hemoglobin Alc (%)                                 | 6.7 ± 1.4 (196/205) | 6.8 ± 1.5 (184/189)     | 6.6 ± 1.2 (12/16) | 0.833   |
| White blood cell count (μL)                        | 12430 ± 9065 | 12329 ± 9365             | 13629 ± 4079                    | 0.096   |
| Hemoglobin (g/dL)                                  | 12.2 ± 2.5   | 12.2 ± 2.5               | 12.2 ± 2.6                     | 0.957   |
| C-reactive protein (mg/dL)                         | 3.5 ± 5.0    | 3.1 ± 4.5                | 7.2 ± 8.6                      | 0.117   |
| Serum creatinine (mg/dL)                           | 2.0 ± 2.6    | 2.1 ± 2.7                | 1.5 ± 0.9                      | 0.190   |
| eGFR (mL/minute/1.73 m²)                           | 52.2 ± 44.2  | 52.9 ± 45.0              | 44.0 ± 32.7                    | 0.121   |
| Brain natriuretic peptide, (pg/mL)                 | 1150.9 ± 979.9 (198/205) | 1177.0 ± 986.3 (184/189) | 806.7 ± 849.1 (16/16) | 0.109   |

Data are expressed as the mean ± SD or number (percentage). Student’s t test or Mann-Whitney U test was used for continuous variables, and Fisher’s exact test was used for categorical variables. CABG indicates coronary artery bypass graft surgery; and eGFR, estimated glomerular filtration rate.
sion of endogenous catecholamine, which might increase SBP spontaneously. If we treated pulmonary edema adequately, such overexpression of endogenous catecholamine might resolve, which decreased SBP. Although we excluded patients who required catecholamine at admission in the present study, we used catecholamines in approximately 15% of the study population during hospitalization, which suggests the presence of potential cardiogenic...
because some patients died in the very early phase. More-
ases. It was inevitable that several values were missing,
retrospective study, there are some inherent selection bi-
Study limitations:
the patient’s hemodynamics in emergency rooms or cathe-
case scenario.
class 3 shows relatively low SBP at hospital presentation,
be a potential choice, considering the high mortality of
sent study, which is considerably higher than other AMI
mortality of patients with Killip class 3.

dated SBP may be a potential target to improve the

tical circulatory support may be needed to stabilize

t to improve the overall mortality of patients with Killip class 3.
The clinical implications of the present study should
Patients with a high thrombus burden should be
had been reported. Moreover, approximately 30% of
population required intra-aortic balloon pumping, and approxi-
20% of the in-hospital death group required veno-
membrane oxygenation in the present study, which is consid-
erably higher than other AMI populations.39) We speculate that Killip class 3 with bor-
SBP might be a potential target to improve the overall mortal-
ality of patients with Killip class 3.
The clinical implications of the present study should
be noted. Patients with a high thrombus burden should be
treated carefully. Although the effectiveness of distal pro-
tection devices was found to be inconsistent among sev-
eral randomized studies,34–36 a distal protection device may
be a potential choice, considering the high mortality of
patients with Killip class 3. When a patient with Killip
class 3 shows relatively low SBP at hospital presenta-
tion, we should consider the possibility that the patient is in a
pre-shock state. Prompt catecholamine support or me-
chanical circulatory support may be needed to stabilize
the patient’s hemodynamics in emergency rooms or cathe-
ter laboratories. Thus, we should prepare for the worst

case scenario.

**Study limitations:** Since this study was a single-center,
retrospective study, there are some inherent selection bi-
ases. It was inevitable that several values were missing,
because some patients died in the very early phase. More-
over, we could not provide initial blood gas data in the
emergency room due to many missing values, partly be-
cause we needed to avoid puncturing an artery for blood
gas sampling in the emergency room before reaching the
catheter laboratory. Because the study period was long
(from 2009 to 2019), the treatment strategy for patients
with AMI might not be consistent, which may have af-
fected the clinical outcomes. As compared to earlier stud-
ies,13–15 the in-hospital mortality (7.8%) was low, which
made the number of patients in the in-hospital death
group small. This small number of events limited the
number of independent variables in the multivariate logistic

Conclusions

In AMI patients with Killip class 3, in-hospital death
was associated with older age and coronary thrombus bur-
den, and was inversely associated with SBP on admission.
It is important to recognize these high risk features in or-
der to improve clinical outcomes in AMI patients with
Killip class 3.

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Table IV. Comparison of Clinical Outcomes Between the Survived and In-Hospital Death Groups

|                          | All (n = 205) | Survived group (n = 189) | In-hospital death group (n = 16) | P value |
|--------------------------|--------------|-------------------------|---------------------------------|---------|
| Intubation for respirator, n (%) | 41 (20.0)    | 32 (16.9)               | 9 (56.3)                        | 0.001   |
| Use of non-invasive positive pressure ventilation, n (%) | 111 (54.1)   | 105 (55.6)              | 6 (37.5)                        | 0.196   |
| Use of catecholamine, n (%) | 31 (15.1)    | 22 (11.6)               | 9 (56.3)                        | < 0.001 |
| Use of intra-aortic balloon pumping, n (%) | 65 (30.8)    | 60 (31.7)               | 5 (31.3)                        | 1.000   |
| Use of veno-arterial extracorporeal membrane oxygenation, n (%) | 8 (3.9)      | 5 (2.6)                 | 3 (18.8)                        | 0.017   |
| Peak creatine kinase (IU/L) | 1722.6 ± 2720.3 | 1587.4 ± 2562.5   | 3388.6 ± 3890.6                  | 0.002   |
| Peak creatine kinase-myocardial band (IU/L) | 139.4 ± 217.0 | 132.8 ± 220.4         | 249.4 ± 183.7                   | 0.003   |
| Length of CCU stay (days) | 6.8 ± 7.4    | 6.5 ± 7.2               | 9.8 ± 8.3                       | 0.156   |
| Length of hospital stay (days) | 21.13 ± 31.0 | 21.4 ± 32.1            | 17.6 ± 13.5                     | 0.888   |

Data are expressed as the mean ± SD or number (percentage). Student’s t test or the Mann-Whitney U test was used for continuous variables, and Fisher’s exact test was used for categorical variables. CCU indicates coronary care unit.

Table V. Univariate and Multivariate Logistic Regression Analysis to Identify Factors Associated with In-Hospital Death

| Independent variables | Univariate analysis | Multivariate analysis |
|-----------------------|---------------------|----------------------|
|                       | Odds ratio          | 95% confidence interval | P value | Odds ratio          | 95% confidence interval | P value |
| Age                   | 1.157               | 1.058-1.264           | 0.001   | 1.168               | 1.061-1.287             | 0.002   |
| SBP on admission (per 10 mmHg) | 0.726               | 0.591-0.892           | 0.002   | 0.764               | 0.613-0.953             | 0.017   |
| Heart rate on admission | 0.962               | 0.940-0.985           | 0.001   |                   |                       |         |
| TIMI thrombus grade ≥ 2 (versus ≤ 1) | 4.500               | 1.582-12.803          | 0.005   | 5.743               | 1.717-19.214            | 0.005   |
| Final TIMI flow grade 3 (versus ≤ TIMI2) | 0.259               | 0.074-0.901           | 0.034   |                   |                       |         |

SBP indicates systolic blood pressure; and TIMI, thrombolysis in myocardial infarction. Multivariate logistic regression analysis with likelihood ratio statistical criteria using backward elimination method was performed.
References

1. Rao HB, Sastry BK, Korabathina R, Raju KP. Sudden cardiac death after acute ST elevation myocardial infarction: insight from a developing country. Heart Asia 2012; 4: 83-9.
2. Chehab O, Qannus AS, Eldirani M, Hassan H, Tamim H, Dakik HA. Predictors of In-Hospital Mortality in Patients Admitted with Acute Myocardial Infarction in a Developing Country. Cardiol Res 2018; 9: 293-9.
3. Krumholz HM, Normand ST, Wang Y. Twenty-Year Trends in Outcomes for Older Adults With Acute Myocardial Infarction in the United States. JAMA Netw Open 2019; 2: e191938.
4. Neumann JT, Twerenbold R, Ojeda F, et al. Cardiogenic shock and cardiac arrest complicating ST-segment elevation myocardial infarction in the United States, 2000-2017. Resuscitation 2020; 155: 55-64.
5. Yamamoto K, Sakakura K, Akashi N, et al. Clinical outcomes after acute myocardial infarction according to a novel stratification system linked to a rehabilitation program. J Cardiol 2018; 72: 227-33.
6. Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: A method for prognostication and therapeutic decision making. JAMA 2000; 284: 835-42.
7. Braidshaw PJ, Ko DT, Newman AM, Donovan LR, Tu JV. Validity of the GRACE (Global Registry of Acute Coronary Events) acute coronary syndrome prediction model for six month post-discharge death in an independent data set. Heart 2006; 92: 905-9.
8. Killip T 3rd, Kimball JT. Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. Am J Cardiol 1967; 20: 457-64.
9. Hochman JS, Boland I, Slepper LA, et al. Current spectrum of cardiogenic shock and effect of early revascularization on mortality. Results of an International Registry. SHOCK Registry Investigators. Circulation 1995; 91: 873-81.
10. Tsukui T, Sakakura K, Taniguchi Y, et al. Factors associated with poor clinical outcomes of ST-elevation myocardial infarction in patients with door-to-balloon time <90 minutes. PLoS One 2020; 15: e0241251.
11. Cepas-Guillem PL, Borrego-Rodriguez J, Flores-Umanzor E, et al. Outcomes of Nonagenarians With ST Elevation Myocardial Infarction. Am J Cardiol 2020; 125: 11-8.
12. Jinnouchi K, Sakakura K, Yamamoto K, et al. Further Validation of a Novel Acute Myocardial Infarction Risk Stratification (nARS) System for Patients with Acute Myocardial Infarction. Int Heart J 2020; 61: 463-9.
13. Mizzuto Y, Sakakura K, Yamamoto K, et al. Determinants of Permanent Coronary Artery Stenosis After Primary Percutaneous Coronary Intervention. JACC Cardiovasc Interv 2019; 12: 2316-24.
14. Lee WC, Chen TY, Chen CJ, et al. Impact of age on management and outcome of acute coronary syndrome: observations from the Global Registry of Acute Coronary Events (GRACE). Am Heart J 2005; 149: 67-73.
15. Anderson JL, Karagounis LA, Becker LC, Sorensen SG, Menlovice RL. TIMI perfusion grade 3 but not grade 2 results in improved outcome after thrombolysis for myocardial infarction. Ventriculographic, enzymatic, and electrocardiographic evidence from the TEAM-3 Study. Circulation 1993; 87: 1829-39.
16. Sawano S, Sakakura K, Adachi Y, et al. In-hospital outcomes of acute myocardial infarction with cardiogenic shock caused by right coronary artery occlusion vs. left coronary artery occlusion. Cardiovasc Interv Ther 2018; 33: 338-44.
17. Avezum A, Makiide M, Spencer F, et al. The effect of complete revascularization and long door-to-balloon time in current primary percutaneous coronary interventions. Heart Vessels 2018; 33: 498-506.
18. Sawano S, Sakakura K, Yamamoto K, et al. Determinants of short and long door-to-balloon time in current primary percutaneous coronary interventions. Heart Vessels 2018; 33: 498-506.
19. Sawano S, Sakakura K, Yamamoto K, et al. Contemporary use and trends in percutaneous coronary intervention in Japan: an outline of the J-PCI registry. Cardiovasc Interv Ther 2020; 35: 218-26.
20. Tsukui T, Sakakura K, Taniguchi Y, et al. Determinants of short and long door-to-balloon time in current primary percutaneous coronary interventions. Heart Vessels 2018; 33: 498-506.
21. Sawano S, Sakakura K, Yamamoto K, et al. Contemporary use and trends in percutaneous coronary intervention in Japan: an outline of the J-PCI registry. Cardiovasc Interv Ther 2020; 35: 218-26.
22. Seguchi M, Sakakura K, Tsukui T, et al. Determinants of In-Hospital Death Among the Very Elderly with Acute Myocardial Infarction. Int Heart J 2020; 61: 879-87.
23. Matsu S, Imai E, Horio M, et al. Revised equations for estimated GFR from serum creatinine in Japan. Am J Kidney Dis 2009; 53: 982-92.
24. Taniguchi Y, Sakakura K, Adachi Y, et al. In-hospital outcomes of acute myocardial infarction with cardiogenic shock caused by right coronary artery occlusion vs. left coronary artery occlusion. Cardiovasc Interv Ther 2018; 33: 338-44.
25. Gibson CM, de Lemos JA, Murphy SA, et al. Combination therapy with abciximab reduces angiographically evident thrombus in acute myocardial infarction: a TIMI 14 substudy. Circulation 2001; 103: 2530-4.
tion in primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: 15-month follow-up of the DEDICATION (Drug Elution and Distal Protection in ST Elevation Myocardial Infarction) trial. J Am Coll Cardiol 2010; 55: 867-71.

35. Stone GW, Webb J, Cox DA, et al. Distal microcirculatory protection during percutaneous coronary intervention in acute ST-segment elevation myocardial infarction: a randomized controlled trial. JAMA 2005; 293: 1063-72.

36. Hibi K, Kozuma K, Sonoda S, et al. A Randomized Study of Distal Filter Protection Versus Conventional Treatment During Percutaneous Coronary Intervention in Patients With Attenuated Plaque Identified by Intravascular Ultrasound. JACC Cardiovasc Interv 2018; 11: 1545-55.

**Supplemental Files**

Supplemental Table
Please see supplemental files; https://doi.org/10.1536/ihj.21-078