Impact of Door-to-Balloon Time Reduction Depending on the Killip Classification in Patients with ST-Segment Elevation Myocardial Infarction Transported by Emergency Medical Services

Acute Myocardial Infarction-Kyoto Multi-Center Risk Study Group

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Summary

The coronavirus disease 2019 pandemic occurred in several countries, making the conventional medical system difficult to maintain. Recent recommendations aim to prevent nosocomial infections and infections among health care workers. Therefore, establishing a cardiovascular medical system under an emergency for patients with ST-segment elevation myocardial infarction (STEMI) is desired. This study aimed to determine the relationship between prognosis and door-to-balloon time (DBT) shortening based on the severity on arrival.

This retrospective, multi-center, observational study included 1,127 consecutive patients with STEMI. Patients were transported by emergency medical services and underwent primary percutaneous coronary intervention. Patients were stratified according to the Killip classification: Killip 1 (n = 738) and Killip ≥ 2 (n = 389) groups.

Patients in the Killip ≥ 2 group were older, with more females, and more severity on arrival than those in the Killip 1 group. The 30-day mortality rate in the Killip 1 and Killip ≥ 2 groups was 2.2% and 18.0%, respectively. The Killip ≥ 2 group had a significant difference in the 30-day mortality between patients with DBT ≤ 90 minutes and those with DBT > 90 minutes; however, this did not occur in the Killip 1 group. Furthermore, multivariate analysis revealed that DBT ≤ 90 minutes was not a significant predictive factor in the Killip 1 group; however, it was an independent predictive factor in the Killip ≥ 2 group.

DBT shortening affected the 30-day mortality in STEMI patients with Killip ≥ 2, although not those with Killip 1.

Key words: Myocardial infarction, Early reperfusion therapy, Primary percutaneous coronary intervention, Severity, In-hospital mortality, Coronavirus disease 2019 pandemic, Polymerase chain reaction testing

Early reperfusion therapy by the primary percutaneous coronary intervention (PCI) reportedly reduced in-hospital mortality in patients with ST-segment elevation myocardial infarction (STEMI).1,2 For patients with STEMI, international guidelines have emphasized the significance of early reperfusion and the necessity of performing primary PCI within 12 hours from the onset of symptom. Furthermore, reducing door-to-balloon time (DBT), particularly to ≤ 90 minutes, is one of the most important aspects of early reperfusion therapy that could decrease in-hospital mortality.3,4 Conversely, some studies indicated that DBT shortening had no significant impact on mortality. In low-risk patients with STEMI, delays in DBT had a lower impact on mortality. Even with longer delays in DBT, transfer to a primary PCI-capable hospital might be the optimal reperfusion option.5,6 Kodama, et al. reported that DBT shortening had no clinical effect on mortality in all patients with STEMI using self-transport (e.g., taxi, public transportation, private car, or walking).7 Using self-transport, patients with STEMI may have more time available for further examinations or diagnosis. Additionally, the peak creatinine phosphokinase (CPK) value, which indicates the infarct size or long-term outcome, was significantly independent of DBT reduction.8,9 These results suggest that DBT’s prognostic importance may vary depending on the severity in patients with STEMI.

Coronavirus disease 2019 (COVID-19) has been...
spreading in Japan since 2020. The infection’s rapid spread worldwide has restricted normal hospital functions in several countries. The disease has affected routine medical care and caused delays in treating acute diseases because of difficulties maintaining the conventional emergency medical services (EMS) system. The number of asymptomatic COVID-19-infected individuals is higher than expected, contributing to the transmission of the virus. There is a possibility that some emergency patients, including those with STEMI, may be asymptomatic carriers of COVID-19. Moreover, recent studies revealed that COVID-19 patients often suffer from myocardial infarction due to plaque rupture, arterial thrombosis via endothelial dysfunction, and a rapid increase in oxygen consumption.

Some patients with STEMI have asymptomatic COVID-19 and nosocomial infection. Thus, infections among health care workers (HCWs) may become a major problem. Therefore, it is necessary to perform rapid COVID-19 antigen or polymerase chain reaction (PCR) testing or chest computed tomography (CT) imaging at the time of initial treatment of STEMI. This may result in delays in the treatment for STEMI. However, to achieve DBT ≤ 90 minutes, reperfusion therapy would be required under protective clothing without waiting for the test results. Therefore, it is necessary to develop a modified strategy that considers the safety of HCWs and prevents nosocomial infections. With limited healthcare resources, improving traditional strategies and further stratifying emergency patients is important to utilize medical resources and maintain the healthcare system.

We aimed to investigate the relationship between the prognosis and DBT reduction based on the severity on arrival for patients with STEMI transported by EMS and establish the emergency systems under the COVID-19 pandemic for patients with STEMI.

### Methods

#### Ethics approval and consent to participate:

The ethics committee of Kyoto Prefectural University of Medicine as a general organization (reference number: RBMR-E-190) and the ethics committees of each participating institution approved this study in 2009 (Appendix). We provided enrolled patients with an opt-out option because this study used existing data from medical records. We included all informed consent records in the electronic medical record system. All authors read and agreed to the article as written.

#### Patient population:

The AMI-Kyoto Multi-Center Risk Study was a retrospective, multi-center, observational study that included patients with acute myocardial infarction (AMI). From January 2009 to December 2015, 3,428 consecutive patients diagnosed with AMI, who were admitted to 20 participating institutions (AMI-Kyoto Multi-Center Risk Study Group institutions), enrolled in this study. Initially, 81 patients with cardiopulmonary arrest on hospital arrival and 688 patients with non-STEMI were excluded. Subsequently, 685 patients arrived at the hospitals using self-transport (e.g., a taxi, public transportation, private car, or walking), 92 patients who had in-hospital symptom onset, and 561 patients who transferred from another hospital were excluded. Next, 80 patients who were admitted over 24 hours after symptom onset were excluded because primary PCI within 24 hours after symptom onset was recommended by the American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the management of STEMI. Furthermore, patients who had an unknown symptom onset time (n = 73), did not undergo primary PCI (n = 31), and had erroneous data (n = 10) were excluded from this study. The final study population comprised 1,127 STEMI patients transported by the EMS and underwent primary PCI within 24 hours from symptom onset (Figure 1).

We stratified all enrolled STEMI patients using the Killip classification, a standard classification of severity for STEMI. We evaluated the impact of DBT shortening in the Killip 1 and Killip ≥ 2 groups.

#### Definitions:

The diagnosis of AMI required the presence of at least two of the following three criteria: (1) characteristic clinical history of ischemic-type chest pain lasting for > 20 minutes; (2) serial changes on electrocardiogram (ECG) suggestive of myocardial infarction (Q waves) or myocardial injury/ischemia (ST-segment elevation); and (3) transient increase in CPK and troponin levels to more than two-folds above the normal laboratory value.

Coronary flow and coronary artery stenosis were evaluated using the Thrombolysis in Myocardial Infarction (TIMI) classification and AHA classification, respectively. Significant coronary artery stenosis was defined as ≥ 75% reduction in the internal diameter of the right, left anterior descending, or left circumflex coronary arteries and their major branches, or ≥ 50% reduction in the internal diameter of the left main trunk (LMT). Multivessel involvement was defined as simultaneous thrombosis of multiple coronary arteries or of an undetermined culprit artery in the presence of multiple stenotic vessels, as observed on initial coronary angiography. The TIMI risk score for STEMI was reported as one of the risk stratification tools for patients with STEMI in 2000. With a total score of 14 points, the score can predict 30-day mortality at the time of the hospital visit in the patients with STEMI. It consists of the following eight factors: age, medical history of diabetes mellitus/hypertension or angina, systolic blood pressure (SBP) < 100 mmHg, heart rate (HR) > 100 beats/minute (bpm), Killip classes II-IV, bodyweight < 67 kg, ECG changes indicating anterior ST-segment elevation or left bundle branch block, and time to treatment (> 4 hours). Onset time was when the patient experienced initial myocardial ischemia-related symptoms. Door time referred to when the patient’s arrival at the primary PCI-capable hospital was recorded. The attending cardiologist determined primary PCI and other treatment strategies. We established the cut-off point of 90 minutes for DBT based on the recommendation by the ACC/AHA guidelines for the management of STEMI. Balloon time pertained to the time at which a revascularization device, including a thrombus aspiration catheter or a coronary balloon, reached the causative lesion for the first time. Thirty-day mortality was defined as all-cause death within 30 days after hospitalization, and in-hospital mortality was defined as all-cause death during hospitalization.

#### Statistical analysis:

All in-hospital data were transmitted
to the Department of Cardiovascular Medicine center in the Kyoto Prefectural University of Medicine for analysis. Continuous variables were presented as mean and standard deviation or median and interquartile range (IQR), whereas categorical variables were presented as numbers and percentages. The Chi-square test was used when appropriate, and Fisher’s exact test compared categorical variables. The Student’s t-test or Mann-Whitney U-test was performed to compare continuous variables based on data distribution. Univariate analysis revealed the odds ratio (OR) and 95% confidence interval (CI) of 30-day mortality in each group. Additionally, the multivariate logistic regression analysis was performed to explore independent prognostic factors using some variables in each group. Statistical analyses were performed using SPSS, version 23 (IBM Corp., Armonk, NY, USA). A P value < 0.05 was considered statistically significant.

Results
Baseline and lesion characteristics: The Killip ≥ 2 group patients were significantly older than those in the Killip 1 group (71.5 ± 11.9 years versus 68.0 ± 12.1 years, P < 0.05). The Killip ≥ 2 group had significantly higher frequencies of patients aged ≥ 65 years, female, and conventional major risk factors, such as hypertension and diabetes mellitus, than the Killip 1 group (all, P < 0.05). There were no significant differences in cardiovascular medical history between the two groups. The Killip ≥ 2 group had significantly higher proportions of patients with SBP < 100 mmHg and HR ≥ 100 bpm than the Killip 1 group (P < 0.05). The mean TIMI risk score on arrival was significantly higher in the Killip ≥ 2 group than in the Killip 1 group (P < 0.05).

The culprit vessels were more likely to be the LMT or proximal lesion in the left anterior descending artery (LAD) in the Killip ≥ 2 group than those in the Killip 1 group (P < 0.05). The Killip ≥ 2 group had more multivessel diseases than the Killip 1 group. The proportions of patients with pre-TIMI 0 and post-TIMI < 3 were significantly higher in the Killip ≥ 2 group than those in the Killip 1 group. The Killip ≥ 2 group patients were treated with support devices more frequently than those in the Killip 1 group (Table I).

Time interval from symptom onset: Table II shows the time interval from symptom onset in the two groups. Onset-to-door time showed no significant difference between the two groups. The Killip ≥ 2 group had a significantly longer DBT than the Killip 1 group (91 [IQR, 70-124] versus 85 [IQR, 68-111] minutes, P < 0.05), and the proportion of patients in whom DBT ≤ 90 minutes was achieved was significantly lower in the Killip ≥ 2 group than that in the Killip 1 group (P < 0.05). Consequently, the onset-to-balloon time (OBT) was significantly longer in the Killip ≥ 2 group; however, OBT ≤ 3 hours did not show a significant difference between the two groups.

Clinical outcomes: Table III shows the clinical outcomes of the patients with STEMI with EMS. The 30-day mortality rate in all patients with STEMI with EMS was 7.6%, and the Killip ≥ 2 group had a significantly higher 30-day mortality rate than the Killip 1 group (18.0% versus 2.2%, P < 0.05). The in-hospital mortality rate in all patients with STEMI with EMS was 8.7%. The Killip ≥ 2 group had a significantly higher in-hospital mortality rate than the Killip 1 group (21.1% versus 2.2%, P < 0.05). The rate of complications after primary PCI was signifi-
### Table 1. Baseline and Lesion Characteristics in All STEMI Patients with EMS

| Characteristic                        | All (n = 1,127) | Killip 1 (n = 738) | Killip ≥ 2 (n = 389) | P value |
|--------------------------------------|-----------------|-------------------|----------------------|---------|
| Age, years                           | 69.2 ± 12.2     | 68.0 ± 12.1       | 71.5 ± 11.9          | < 0.05  |
| Age ≥ 65 years, n (%)                | 738 (35.8)      | 458 (62.1)        | 280 (72.0)           | < 0.05  |
| Female, n (%)                        | 281 (24.9)      | 171 (23.2)        | 110 (28.3)           | 0.05    |
| Weight < 67 kg, n (%)                | 784 (69.6)      | 519 (70.3)        | 265 (68.1)           | 0.45    |
| Hypertension, n (%)                  | 652 (57.9)      | 429 (58.1)        | 223 (57.3)           | < 0.05  |
| Hyperlipidemia, n (%)                | 473 (42.0)      | 330 (44.7)        | 143 (36.8)           | < 0.05  |
| Diabetes mellitus, n (%)             | 310 (27.5)      | 187 (25.3)        | 123 (31.6)           | < 0.05  |
| Smoking, n (%)                       | 470 (41.7)      | 340 (45.4)        | 130 (33.2)           | < 0.05  |
| Family history, n (%)                | 76 (6.7)        | 57 (7.7)          | 19 (4.9)             | < 0.05  |
| Prior MI, n (%)                      | 106 (9.4)       | 73 (9.9)          | 33 (8.5)             | 0.39    |
| Previous PCI, n (%)                  | 137 (12.2)      | 83 (11.2)         | 54 (13.9)            | 0.36    |
| Prior CABG, n (%)                    | 10 (0.9)        | 5 (0.7)           | 5 (1.3)              | 0.75    |
| Previous stroke, n (%)               | 68 (6.0)        | 40 (5.4)          | 28 (7.2)             | 0.48    |
| Physical examination on arrival      |                 |                   |                      |         |
| Systolic BP < 100 mmHg, n (%)        | 211 (18.7)      | 82 (11.1)         | 129 (33.2)           | < 0.05  |
| HR ≥ 100 bpm, n (%)                  | 119 (10.6)      | 39 (5.3)          | 80 (20.6)            | < 0.05  |
| TIMI risk score on arrival           | 5.1 ± 2.7       | 4.0 ± 2.0         | 7.4 ± 2.3            | < 0.05  |
| Laboratory data on arrival           |                 |                   |                      |         |
| Hb, g/dL                             | 14.2 (12.7–15.4)| 14.4 (12.9–15.5) | 13.7 (12.1–15.3)     | < 0.05  |
| CRP, mg/dL                           | 0.12 (0.06–0.34)| 0.10 (0.06–0.25) | 0.20 (0.08–0.66)     | < 0.05  |
| WBC, × 10³ μg/dL                     | 9.4 (7.4–11.8)  | 9.1 (7.3–11.3)    | 10.0 (7.9–12.9)      | 0.95    |
| Cr, mg/dL                            | 0.87 (0.71–1.09)| 0.84 (0.70–1.02)  | 0.93 (0.76–1.23)     | < 0.05  |
| BS, mg/dL                            | 160 (134–214)   | 152 (131–191)     | 189 (143–266)        | < 0.05  |
| Culprit lesions, n (%)               |                 |                   |                      |         |
| LMT                                  | 44 (3.9)        | 11 (1.5)          | 33 (8.5)             | < 0.05  |
| LAD                                  | 541 (48.0)      | 335 (45.4)        | 206 (53.0)           | < 0.05  |
| LAD proximal                         | 317 (28.1)      | 184 (24.9)        | 133 (34.2)           | < 0.05  |
| LAD mid                              | 197 (17.5)      | 133 (18.0)        | 64 (16.5)            | 0.51    |
| LAD distal or Diagonal               | 27 (2.4)        | 18 (2.4)          | 9 (2.3)              | 0.90    |
| RCA                                  | 483 (42.9)      | 338 (45.8)        | 145 (37.3)           | < 0.05  |
| LCX                                  | 104 (9.2)       | 60 (8.1)          | 44 (11.3)            | 0.08    |
| Multi-vessel diseases, n (%)         | 428 (38.0)      | 260 (35.2)        | 168 (43.2)           | < 0.05  |
| Pre TIMI 0, n (%)                    | 683 (60.6)      | 419 (56.8)        | 264 (67.9)           | < 0.05  |
| Pre TIMI < 3, n (%)                  | 992 (88.0)      | 634 (85.9)        | 358 (92.0)           | < 0.05  |
| Post TIMI < 3, n (%)                 | 95 (8.4)        | 42 (5.7)          | 53 (13.6)            | < 0.05  |
| Primary PCI procedures, n (%)        |                 |                   |                      |         |
| Thrombectomy                         | 809 (71.8)      | 546 (74.0)        | 263 (67.6)           | < 0.05  |
| Ballooning                           | 811 (72.0)      | 541 (73.3)        | 270 (69.4)           | 0.17    |
| Stenting, n (%)                      | 1018 (90.3)     | 675 (91.5)        | 343 (88.2)           | 0.08    |
| Bare Metal Stent                     | 329 (29.2)      | 210 (28.5)        | 119 (30.6)           | 0.45    |
| Drug Eluting Stent                   | 697 (61.8)      | 467 (63.3)        | 230 (59.1)           | 0.17    |
| Support devices, n (%)               |                 |                   |                      |         |
| Temporary pacing                     | 174 (15.4)      | 97 (13.1)         | 77 (19.8)            | < 0.05  |
| IABP                                 | 192 (17.0)      | 51 (6.9)          | 141 (36.2)           | < 0.05  |
| Respirator                           | 99 (8.8)        | 4 (0.5)           | 95 (24.4)            | < 0.05  |
| PCPS                                 | 36 (3.2)        | 2 (0.3)           | 34 (8.7)             | < 0.05  |
| CHDF                                 | 53 (2.9)        | 4 (0.5)           | 49 (12.9)            | < 0.05  |

Data are presented as n (%), mean (standard deviation), or median (interquartile ranges). MI indicates myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; BP, blood pressure; HR, Heart rate; Hb, hemoglobin; CRP, C-reactive protein; WBC, white blood cell; Cr, creatinine; BS, blood sugar; TIMI, thrombolysis in myocardial infarction; LMT, left main trunk; LAD, left anterior descending branch; RCA, right coronary artery; LCX, left circumflex branch; IABP, intra-aortic balloon pumping; PCPS, percutaneous cardiopulmonary support; and CHDF, continuous hemodiafiltration. For each variable, the percentages reflect the total number of patients whose data are available. The P value was compared with the Killip 1 and Killip ≥ 2 groups.

Significantly higher in the Killip ≥ 2 group than that in the Killip 1 group (P < 0.05). The Killip ≥ 2 group had higher complications after primary PCI, such as cardiac rupture, refractory ventricular tachycardia/ventricular fibrillation, and surgery than the Killip 1 group (all, P < 0.05). Furthermore, the peak CPK value was significantly higher in the Killip ≥ 2 group than in the Killip 1 group (P < 0.05). Impact of DBT ≤ 90 minutes in the low- and high-risk
In the Killip group, there was no significant difference in the peak CPK value, mortality was significantly lower in patients with DBT ≤ 90 minutes (1.4% and 3.2%, respectively; P = 0.10), and there was no significant difference in the peak CPK value (Figure 2). Conversely, in the Killip ≥ 2 group, 30-day mortality was significantly lower in patients with DBT ≤ 90 minutes than in those with DBT > 90 minutes (13.3% versus 22.8%, P < 0.05). No significant difference was noted in the peak CPK value between patients with DBT ≤ 90 minutes and DBT > 90 minutes (Figure 2).

We evaluated the predictive factor for 30-day mortality by using the univariate and multivariate analyses with age, female, culprit lesion (LMT or LAD proximal), DBT ≤ 90 minutes, pre-TIMI 0, and post-TIMI < 3, which were general prognostic factors. In the Killip 1 group, DBT ≤ 90 minutes was not a significant predictive factor for 30-day mortality (OR = 0.49; 95% CI: 0.17-1.42; P = 0.19). Pre-TIMI 0 and post-TIMI < 3 were strong predictive factors for 30-day mortality (P < 0.05) (Table IV). Conversely, in the Killip ≥ 2 group, DBT ≤ 90 minutes was a significant predictive factor for 30-day mortality (OR = 0.56; 95% CI: 0.32-0.99; P < 0.05). Moreover, age and post-TIMI < 3 were strong predictive factors for 30-day mortality (P < 0.05) (Table IV).

**Discussion**

This study showed that DBT ≤ 90 minutes was an independent predictive factor for the 30-day mortality in STEMI patients transported by the EMS with Killip ≥ 2, although not those with Killip 1. Additionally, DBT ≤ 90 minutes did not affect the peak CPK value, indicating the two groups’ infarct size.

In-hospital mortality in AMI patients has decreased worldwide due to the increased use of ambulance services and reperfusion therapy. Primary PCIs are conventional reperfusion strategies in patients with STEMI; they reportedly reduce in-hospital mortality in these patients. The 2017 ESC guidelines or the 2013 ACC/AHA guidelines for the management of STEMI recommended DBT ≤ 90 minutes for patients who initially arrive at a PCI-capable hospital. In Japan, there are several PCI-capable hospitals, and primary PCI is performed in each hospital to achieve DBT shortening as much as possible. However, some studies have not closely correlated DBT reduction with prognosis. We have previously reported that DBT shortening had no clinical effect on mortality in all patients with STEMI using self-transport and did not affect in-hospital prognosis. Moreover, the peak CPK value, which indicates the infarct size or long-term outcome, was significantly independent of DBT reduction. This study suggested that DBT might impact in-hospital outcomes in high-risk STEMI patients, although there was no impact in the low-risk STEMI patients. Furthermore, this study indicated that post-TIMI < 3 was a strong predictive factor for 30-day mortality. We suggest that the reliable achievement of post-TIMI 3 is more important than DBT shortening in the low-risk STEMI patients. According to

| Table II | Time Intervals in All STEMI Patients with EMS |
|----------|---------------------------------------------|
|          | All (n = 1,127) | Killip 1 (n = 738) | Killip ≥ 2 (n = 389) | P value |
| ODT, minutes | 70 (44–137) | 70 (42–135) | 72 (44–145) | 0.27 |
| ODT > 12 hours, n (%) | 32 (2.8) | 16 (2.2) | 16 (4.1) | 0.06 |
| DBT, minutes | 86 (68–114) | 85 (68–111) | 91 (70–124) | < 0.05 |
| DBT ≤ 90 minutes, n (%) | 622 (55.2) | 426 (57.7) | 196 (50.4) | < 0.05 |
| OBT, minutes | 176 (130–263) | 171 (128–255) | 180 (135–272) | < 0.05 |
| OBT ≤ 3 hours, n (%) | 584 (52.7) | 389 (52.7) | 195 (50.1) | 0.41 |

Data are presented as n (%) or median (first to third quartile range). ODTS indicates on-set-to-door time; DBT, door-to-balloon time; and OBT, on-set-to-balloon time. For each variable, the percentages reflect the total number of patients whose data are available. P value was compared with the Killip 1 and Killip ≥ 2 groups.

| Table III | Clinical Outcomes in All STEMI Patients with EMS |
|----------|-----------------------------------------------|
|          | All (n = 1,127) | Killip 1 (n = 738) | Killip ≥ 2 (n = 389) | P value |
| 30-day mortality, n (%) | 86 (7.6) | 16 (2.2) | 70 (18.0) | < 0.05 |
| In-hospital mortality, n (%) | 98 (8.7) | 16 (2.2) | 82 (21.1) | < 0.05 |
| Complications, n (%) | 85 (7.5) | 27 (3.7) | 56 (14.4) | < 0.05 |
| Cardiac rupture | 16 (1.4) | 5 (0.7) | 11 (2.8) | < 0.05 |
| Subacute thrombosis | 12 (1.1) | 8 (1.1) | 4 (1.0) | 0.61 |
| Refractory VT/VF | 27 (2.4) | 6 (0.8) | 21 (5.4) | < 0.05 |
| Stroke | 15 (1.3) | 7 (0.9) | 8 (2.1) | 0.11 |
| Surgery | 24 (2.1) | 5 (0.7) | 19 (4.9) | < 0.05 |
| Peak CPK, mg/dL | 2,115 (982–3,906) | 1,863 (864–3,377) | 2,636 (1,229–5,228) | < 0.05 |

Data are presented as n (%) or median (first to third quartile range). VT/VF indicates ventricular tachycardia/ventricular fibrillation; and CPK, creatinine phosphokinase. For each variable, the percentages reflect the total number of patients whose data are available. P value was compared with the Killip 1 and Killip ≥ 2 groups.
Figure 2. The 30-day mortality rate, in-hospital mortality rate, and peak CPK value for patients with STEMI receiving emergency medical services stratified by DBT ≤ 90 minutes and DBT > 90 minutes. TIMI indicates thrombolysis in myocardial infarction; DBT, door-to-balloon time; and CPK, creatinine phosphokinase.

Table IV. Univariate and Multivariate Analyses for 30-Day Mortality in the Killip 1 and Killip ≥ 2 Groups

|                        | Killip 1 group (n=738) | Killip ≥2 group (n=389) | Killip 1 group (n=426) | Killip ≥2 group (n=193) |
|------------------------|------------------------|-------------------------|------------------------|-------------------------|
| 30-day mortality, %    | 1.4 (1.06–1.76)        | 13.3 (7.06–25.2)        | 1.4 (1.06–1.76)        | 22.8 (13.1–38.4)        |
| In-hospital mortality, %| 1.4 (1.06–1.76)        | 16.8 (10.0–27.9)        | 1.4 (1.06–1.76)        | 25.4 (15.3–42.3)        |
| Peak CPK, mg/dl         | 1,861 (856–3,393)      | 2,039 (1,140–3,696)     | 1,861 (856–3,393)      | 2,438 (1,188–4,737)     |

LMT indicates left main trunk; LAD, left anterior descending branch; DBT, door-to-balloon time; TIMI, thrombolysis in myocardial infarction; OR, odds ratio; and CI, confidence interval.
these results, we speculated that low-risk STEMI patients with Killip 1 may have a grace period to confirm antigen and PCR test results until the primary PCI. The improvement of pre-hospital care led to a decrease in out-of-hospital mortality in patients with STEMI, and the incidence of heart failure on arrival has been increasing. By contrast, in-hospital heart failure has improved due to the development of acute treatment, including primary PCI. The complication of heart failure on arrival has recently been indicated as an important prognostic factor in patients with STEMI. This study believed that early reperfusion therapy with DBT ≤ 90 minutes may have improved the 30-day mortality in STEMI patients with Killip ≥ 2 due to early stabilization of heart failure. Particularly, in STEMI patients with cardiogenic shock, early reperfusion therapy may be recommended for STEMI patients with Killip ≥ 2 because early stabilization of heart failure or peripheral circulation may improve mortality. Furthermore, some reports indicated that several confounding factors, such as older age, culprit lesion, and post-TIMI, are affected with peak CPK. DBT reduction is not the only factor affected with peak CPK after primary PCI. Therefore, in this study, we speculated that peak CPK had no significant difference between each DBT group in STEMI patients with Killip 1 and Killip ≥ 2. However, a long-term survey is desired in the future because long-term prognosis or chronological ejection fraction has not been evaluated in this study. According to these results, we suggest that high-risk patients with STEMI classified as Killip ≥ 2 should require revascularization as quickly as possible, as in the past reports.

We investigated the knowledge, perception, and confidence level regarding COVID-19 care among HCWs involved in cardiovascular medicine at 35 hospitals in 2020. The result revealed a lack of knowledge about optimal infection-prevention measures for COVID-19, such as using PPE, isolating patients with COVID-19, and preventing infection during aerosol-generating procedures. Most HCWs (especially non-physician HCWs) showed low confidence toward COVID-19 care, and the lack of knowledge about infection-prevention measures was associated with poor confidence. Therefore, several HCWs experienced anxiety and stress due to the possibility of infection. Further aggravation of this situation could disrupt the healthcare system and adversely affect cardiovascular emergency care, including primary PCI for patients with STEMI. Therefore, establishing the emergency systems during the COVID-19 pandemic is desirable for patients with STEMI. Primary triage using the Killip classification is important to ascertain patients with STEMI who require DBT shortening quickly. We speculate that this result may help reshape the treatment strategies for STEMI in situations wherein the normal medical regimen is unsustainable, such as the COVID-19 pandemic or major earthquakes. During the COVID-19 pandemic, it is important to prevent nosocomial infection among HCWs, and statements about such prevention have been announced by various societies. However, the transmission dynamics of COVID-19 remains not fully understood. The fact that there are more asymptomatic COVID-19-infected individuals than expected makes it difficult to prevent the infection. There is a statement that primary PCI should remain the default strategy for diagnosed STEMI patients during the COVID-19 pandemic. We hope that this simple triage using the Killip classification will help save time to prioritize antigen-antibody testing or CT scanning, especially for low-risk patients with subjective symptoms of fever and cough. Several past reports show that patients with Killip 1 are the most low-risk among all patients with STEMI, consistent with that in Japan. Therefore, we believe that the Killip classification can provide time to reduce the risk of widespread disease in cases of low triage levels and will lead to a reduction in unexpected infections to HCWs and nosocomial infections. On the other hand, early reperfusion therapy with as much infection prevention as possible is desirable for STEMI patients with Killip ≥ 2.

We believe that the Killip classification helps distinguish between low- and high-risk patients with STEMI based on their bedside information. Additionally, we expect that primary triage using the Killip classification will help establish cardiovascular emergency systems for patients with STEMI during the COVID-19 pandemic.

Study limitations: This study had some limitations. First, this was a retrospective, observational study. Therefore, the effect of confounding factors that were not analyzed should be considered. Moreover, blood examinations were taken only on arrival. Thus, the dietary conditions before arrival and the effect of dehydration might change blood examination values. Second, reperfusion therapy was performed by primary PCI without transvenous fibrinolytic therapy in all patients with STEMI, and TIMI grade 3 coronary flow was achieved in > 90% of the patients after primary PCI, which is similar to that in the clinical setting. Third, all facilities participating in this registry were PCI-capable hospitals. Nevertheless, there may be delays in treatment response for patients with STEMI, depending on the size of the participating facilities. Fourth, this registry was recorded under the usual medical system and did not reflect the impact of COVID-19 on the medical system. Finally, this study did not evaluate long-term outcomes after hospital discharge, including death, cardiovascular events, and heart failure. Therefore, it is important to further evaluate the long-term outcomes in patients with STEMI in the future.

Conclusions

This study indicated that DBT ≤ 90 minutes affected the 30-day mortality in STEMI patients transported by EMS with Killip ≥ 2, although not those with Killip 1. During the COVID-19 pandemic, especially in STEMI patients with Killip 1, there may be a grace period to confirm antigen and PCR test results to prevent the spread of infection. On the other hand, early reperfusion therapy should be performed as quickly as possible in STEMI patients with Killip ≥ 2.

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of the institutes that participated in the AMI-Kyoto Multi-Center Risk Study Group (Appendix).

Disclosure

Conflicts of interest: The authors declare no conflict of interest.

Appendix

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