Impact of the SARS-CoV-2 Pandemic on Primary Percutaneous Coronary Intervention for Patients with ST-Elevation Myocardial Infarction
A Japanese Multicenter Study

Yuki Matsubara,1 MD, Takuya Izumikawa,2 MD, Soichiro Washimi,1 MD, Takeshi Yamada,1 MD, Sho Hashimoto,1 MD, Norimasa Taniguchi,1 MD, Shunsuke Nakajima,1 MD, Tetsuya Hata,1 MD and Akihiko Takahashi,1 MD

Summary
During the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, patients with ST-elevation myocardial infarction (STEMI) should be treated as possibly infected individuals. Therefore, more time is considered necessary to conduct primary percutaneous coronary intervention (PCI). In this study, we sought to evaluate the impact of the SARS-CoV-2 pandemic on primary PCI for STEMI. Between March 2019 and March 2021, 259 patients with STEMI underwent primary PCI. Patients were divided into 2 groups: the pre-pandemic group (March 2019-February 2020) and the pandemic group (March 2020-February 2021). The patient demographics, reperfusion time including onset-to-door time, door-to-balloon time (DTBT), computed tomography (CT), peak creatinine phosphokinase (CPK), and 30-day mortality rate were investigated. The mean age of the patients was 70.4 ± 12.9 years, and 71.6% were male. There were 117 patients before the pandemic and 142 during the pandemic. The median DTBT was 29 (21.25-41.25) minutes before the pandemic and 48 minutes (31-73 minutes) during the pandemic (P < 0.001). The median door-to-catheter-laboratory time was 13.5 (10-18.75) minutes before the pandemic and 29.5 (18-47.25) minutes during the pandemic (P < 0.001). CT evaluation was performed before PCI in 39 (33.3%) patients and 63 (44.4%) patients (P = 0.08); their peak CPK levels were 1480 (358-2737.5) IU and 1363 (621-2722.75) IU (P = 0.56), and the 30-day mortality rates were 4.3% and 2.1% (P = 0.48), respectively. The SARS-CoV-2 pandemic changed the diagnostic procedure in the emergency department and affected the DTBT in patients with STEMI. Nonetheless, no adverse effects on the 30-day mortality rate were observed.

Key words: Door-to-balloon time, Pandemic

Since the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection emerged in December 2019,1 the subsequent global pandemic has imposed difficulties on health care delivery in addition to the detrimental effects of SARS-CoV-2 on patients with heart disease. In particular, medical interventions requiring time-sensitive procedures such as cardiac emergencies have been greatly affected.2

In the treatment of ST-segment elevation myocardial infarction (STEMI), door-to-balloon time (DTBT) is a key performance quality metric. Recent studies have reported that patients with a DTBT over 90 minutes have a significant increase in mortality compared with those with a DTBT of ≤ 90 minutes.3-5 Accordingly, the current guidelines for STEMI recommend that recanalization should be accomplished within 90 minutes,6-9 and to date, higher proportions of patients with STEMI have been treated according to the guidelines.4-9

However, the SARS-CoV-2 pandemic adversely affects the revascularization procedure. This is because regardless of the absence of SARS-CoV-2 symptoms, additional procedures are required to prepare for the potential risk of infection. These additional procedures include providing personal protective equipment (PPE) in both the emergency department and catheter laboratories, taking chest CT in SARS-CoV-2-suspected cases, and performing polymerase chain reaction (PCR) tests. Furthermore, these changes in the percutaneous coronary intervention (PCI) procedure may have adverse effects on the prognosis. However, little is known about the impact of the SARS-CoV-2 pandemic on the revascularization time and the prognosis of patients with STEMI in Japan.

In this study, we sought to evaluate the impact of the SARS-CoV-2 pandemic on the DTBT and clinical out-
comes in patients with STEMI in the hospital, where the distal radial artery was used as the primary vascular access site.

Methods

Study design and population: This was a retrospective study of 259 consecutive patients with STEMI who underwent primary PCI between January 2019 and March 2021 in two Japanese primary PCI-capable hospitals, where inpatient treatment for SARS-CoV-2 pneumonia also had been conducted. The patients were divided into two groups: before the pandemic (March 2019-February 2020) and during the pandemic (March 2020-February 2021). Patients with cardiopulmonary arrest on arrival and an onset-to-door time of ≥ 24 hours during the study period were excluded. Furthermore, to evaluate the impact of the fluctuation of the pandemic on the revascularization time, the pandemic period was divided into two phases, namely, the early phase (first wave, March 2020-August 2020) and the late phase (second and third waves, September 2020-February 2021), and indices including DTBT, door-to-cardiac-catheter-laboratory (CCL) time, onset-to-door time, and number of PCR tests performed and positive results were compared.

Diagnosis, reperfusion, and clinical indices: The diagnosis of STEMI was based on the European Society of Cardiology/American College of Cardiology Foundation/American Heart Association/World Heart Federation universal definition of MI. STEMI is defined as myocardial enzyme elevation and an electrocardiogram showing ST-segment elevation in at least two contiguous leads or a new left bundle branch block. Reperfusion was achieved at the time of the first balloon inflation or the first manual thrombus aspiration, if performed. The follow-up period for the acute results was 30 days. The following clinical indices were also studied: patient characteristics, lesion, and procedural characteristics, coronary risk factors, previous MI, coronary artery bypass grafting, serum creatinine level, hemoglobin level, manner of presentation to the hospital, onset-to-door time, DTBT, use of intra-aortic balloon pump (IABP), and/or extracorporeal membrane oxygenation (ECMO). The findings of thrombolyis in myocardial infarction (TIMI) flow before and after PCI and the final blush grade were also investigated.

Diagnostic and PCI Procedure: Since all emergency cases were treated as potential SARS-CoV-2-infected cases, medical staff in the emergency department prepared PPE including an N-95 respirator, eye protection, gloves, and protective clothing. For patients with a high suspicion of infection, CT examination was routinely conducted before PCI. Furthermore, swab tests for PCR were performed after the real-time PCR test became available in each hospital during the study period.

Ethical Considerations: This study was performed following the principles of the Declaration of Helsinki, and ethical approval was obtained from the institutional review boards of the participating hospitals.

Statistical analyses: All categorical data were analyzed with the chi-squared test or Fisher’s exact test, as appropriate according to the sample size. All continuous vari-ables were tested for normal distribution with the Kolmogorov-Smirnov test: if normally distributed, they are expressed as the mean ± standard deviation; otherwise, they are given as a median and interquartile range. The Wilcoxon rank-sum test was used to analyze continuous variables. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University; http://www.jichi.ac.jp/saitama-sct/SaitamaHP.files/statmedEZR.html), which is a graphical user interface for R (The R Foundation for Statistical Computing, version 2.13.0). More precisely, it is a modified version of R commander (version 1.6-3) that was designed to add statistical functions that are frequently used in biostatistics. Significance was set at P < 0.05.

Results

Patient characteristics: The mean age of the patients was 72.7 ± 13.8 years, and 64.4% were male. The mean height was 160.1 ± 10.1 cm, and the mean weight was 59.1 ± 14.2 kg. In this study, 12 (4.6%) patients had a history of MI. There were 30 walk-in patients (11.6%) (Table I). The culprit lesion was located in the right coronary artery in 39.0% of the patients, left anterior descending artery in 44.8%, left circumflex artery in 13.1%, and left main trunk in 3.1% (Table II).

PCI procedure: Primary PCI was performed within the distal radial approach in 80.7% of the patients, conventional radial approach in 10.8%, and femoral approach in 2.3%. IABP and ECMO were used in 53 (20.5%) patients and 4 (1.5%) patients, respectively (Table II). The proportion of the index TIMI coronary flow detected by coronary angiography was not significantly different before and during the pandemic period. Final TIMI flow rates of 0, 1, 2, and 3 were 0%, 0%, 1.7%, and 98.3% and 0.7%, 2.1%, 0.7%, and 96.5% before and during the pandemic, respectively (Table III). Similarly, no significant difference was found between the two groups. CT examination before PCI was conducted in 33.3% and 44.4% of the patients before and during the pandemic (P = 0.08) (Table IV).

Revascularization time and mortality: The DTBT was 29 (21.3-41.25) minutes before the pandemic. The DTBT during the pandemic period was significantly longer at 48 (18-47.25) minutes. Further, the onset-to-door time during the pandemic was significantly longer than that before the pandemic at 83 minutes (51-141) versus 153 minutes (87-251) (P < 0.001). Moreover, the door-to-CCL time was significantly longer during the pandemic (P < 0.001), while there was no significant difference in the CCL-balloon time (Table IV). The peak CK levels were 1480 (358-2737.5) IU and 1363 (621-2722.75) IU before and during the pandemic, respectively (P = 0.56). The 30-day mortality rate was 4.3% before the pandemic and 2.1% during the pandemic (P = 0.47). With regard to the impact of the fluctuation of the pandemic on the revascularization procedure, the door-to-CCL time during the late pandemic phase was significantly longer than that during the early pandemic phase (P = 0.049). No patient underwent nasal swab tests for PCR during the early pandemic phase while 24 patients (28.2%) did during the late pandemic phase (P < 0.001). No patient showed a positive result for SARS-CoV-2 AND DOOR-TO-BALLOON TIME
Table I. Patient Characteristics

|                      | Overall (n = 259) | Before Pandemic (n = 117) | During pandemic (n = 142) | P value |
|----------------------|-------------------|---------------------------|---------------------------|---------|
| Age, years           | 72.7 ± 13.8       | 72.3 ± 12.4               | 73.0 ± 14.2               | 0.62    |
| Male                 | 167 (64.4%)       | 73 (62.4%)                | 94 (66.2%)                | 0.60    |
| Height, cm           | 160.1 ± 10.1      | 159.4 ± 9.60              | 160.6 ± 10.6              | 0.30    |
| Weight, kg           | 59.1 ± 14.2       | 59.4 ± 12.3               | 58.9 ± 15.8               | 0.96    |
| Hypertension         | 151 (58%)         | 62 (53%)                  | 89 (62.7%)                | 0.13    |
| Diabetes mellitus    | 75 (29.0%)        | 34 (28.9%)                | 41 (29.1%)                | 1.00    |
| Hyperlipidemia       | 123 (47.5%)       | 63 (53.8%)                | 60 (42.3%)                | 0.08    |
| Smoking              | 123 (47.5%)       | 51 (43.6%)                | 72 (51.1%)                | 0.26    |
| OMH                  | 12 (4.6%)         | 4 (3.4%)                  | 8 (3.4%)                  | 0.56    |
| CABG                 | 2 (0.7%)          | 1 (0.9%)                  | 1 (0.7%)                  | 1.00    |
| Serum creatinine, g/dL | 0.8 [0.7-1.1]   | 0.8 [0.7-1.1]             | 0.9 [0.7-1.1]             | 0.56    |
| Hemoglobin, g/dL     | 13.6 [12.18-15.1] | 13.9 [12.15-15.05]        | 13.5 [12.15-15.2]         | 0.87    |
| Walk-in patients     | 30 (11.6%)        | 13 (11.1%)                | 17 (12.0%)                | 0.85    |

OMI indicates old myocardial infarction, and CABG, coronary artery bypass grafting. Values represent mean ± SD or number (%).

Table II. Culprit Lesion and PCI Procedure

| Culprit lesion | Overall (n = 259) | Before pandemic (n = 117) | During pandemic (n = 142) | P value |
|----------------|-------------------|---------------------------|---------------------------|---------|
| RCA            | 101 (39.0%)       | 39 (33.3%)                | 62 (43.7%)                | 0.10    |
| LAD            | 116 (44.8%)       | 61 (52.1%)                | 55 (38.7%)                | 0.03    |
| LCX            | 34 (13.1%)        | 14 (12%)                  | 20 (14.1%)                | 0.71    |
| LMT            | 8 (3.1%)          | 3 (2.6%)                  | 5 (3.5%)                  | 0.73    |
| Access site    |                   |                           |                           |         |
| Distal radial approach | 209 (80.7%)  | 102 (87.2%)               | 107 (75.4%)               | 0.02    |
| Conventional radial approach | 28 (10.8%) | 19 (7.7%)                | 9 (13.4%)                 | 0.16    |
| Femoral approach | 6 (2.3%)         | 1 (0.9%)                  | 5 (3.5%)                  | 0.27    |
| IABP           | 53 (20.5%)        | 24 (20.5%)                | 29 (20.4%)                | 1.00    |
| ECMO           | 4 (1.5%)          | 2 (1.7%)                  | 2 (1.4%)                  | 1.00    |

RCA indicates right coronary artery; LAD, left anterior descending artery; LCX, left circumflex artery; LMT, left main trunk; IABP, intra-aortic balloon pumping; and ECMO, extracorporeal membrane oxygenator.

Table III. TIMI Flow Value Before and After PCI

|                     | Overall (n = 259) | Before pandemic (n = 117) | During pandemic (n = 142) | P value |
|---------------------|-------------------|---------------------------|---------------------------|---------|
| Before PCI          |                   |                           |                           | 0.59    |
| TIMI 0              | 179 (69.1%)       | 84 (71.8%)                | 95 (66.9%)                |         |
| TIMI 1              | 59 (22.8%)        | 25 (21.4%)                | 34 (23.9%)                |         |
| TIMI 2              | 18 (6.9%)         | 6 (5.1%)                  | 12 (8.5%)                 |         |
| TIMI 3              | 4 (1.5%)          | 2 (1.7%)                  | 2 (0.7%)                  |         |
| After PCI           |                   |                           |                           | 0.37    |
| TIMI 0              | 1 (0.3%)          | 0 (0%)                    | 1 (0.7%)                  |         |
| TIMI 1              | 3 (1.2%)          | 0 (0%)                    | 3 (2.1%)                  |         |
| TIMI 2              | 3 (1.2%)          | 2 (1.7%)                  | 1 (0.7%)                  |         |
| TIMI 3              | 252 (97.3%)       | 115 (98.3%)               | 137 (96.5%)               |         |

TIMI indicates thrombolysis in myocardial infarction; and PCI, percutaneous coronary intervention.

CoV-2 during both the early and late pandemic periods (Table V).

Discussion

In this study, we demonstrated that (1) the onset-to-door time and DTBT during the SARS-CoV-2 pandemic is significantly longer than that before the pandemic. (2) Delayed DTBT is attributed to the longer door-to-CCL time, which may reflect additional procedures including the use of PPE, chest CT examination, and swab examination for PCR. (3) A longer revascularization time did not
contribute to the 30-day mortality rate. (4) Fluctuation of the pandemic situation is considered to affect the door-to-CCL time during the pandemic.

Since the emergence of SARS-CoV-2 in December 2019, the virus has spread quickly across the globe. In Japan, the first infected patient was reported on January 17, 2020, who had returned home from Wuhan. To date, in Japan 463,000 people have been infected, and 9,000 people have died. Under such unprecedented circumstances, the delivery of health care faced difficulties beyond the spread of the disease itself, particularly in fields where medical intervention is time-sensitive.

The prominent adverse effect of the pandemic on the treatment of patients with STEMI was a late presentation to the hospital. Several reports have suggested that the time it took patients with STEMI to present to a hospital was significantly longer after the SARS-CoV-2 virus pandemic. These delays are attributed to misled altruistic behavior not to overburden the health care system, stay-at-home orders, as well as social containment mandates, and SARS-CoV-2 iatrophobia (fear of contagion). Similarly, the present study indicated that the onset-to-door time during the pandemic was significantly longer than that before the pandemic.

Delayed reperfusion after admission was another adverse effect on the treatment of STEMI during the pandemic. There is an increasing possibility that asymptomatic patients with SARS-CoV-2 may present to the hospital with STEMI. A study on asymptomatic patients among real-time PCR-positive cases in Japan showed that 30.8-56.5% of the patients were asymptomatic. Thus, substantial attention should be paid to patients presenting with cardiac emergencies, even though the patient was asymptomatic. As the management of MI is time-sensitive, an expert team wearing PPE should provide primary PCI in a timely fashion in a dedicated CCL room. To achieve this, it is pertinent to mandate additional on-the-job training. Further, the present study indicated that fluctuations in the pandemic situation influenced the procedure before PCI. In the late pandemic phase, the number of infected patients increased dramatically in the second and third waves of the pandemic compared with that in the first wave. The elongation of the door-to-CCL time in the late pandemic phase may reflect the fact that the medical staff took more precautions when attending to patients with STEMI. Therefore, the learning curve effect was not observed in the light of shortening the revascularization time. We consider that the learning curve effect, if any, was offset by the fact that emergency staff were overwhelmed by the unprecedented increase in the number of cases during the late phase of the pandemic.

A fibrinolysis-based strategy should be considered an alternative revascularization strategy during this pandemic. It may be applicable in non-PCI-capable referral hospitals, specifically where primary PCI cannot be executed or is not deemed as the best option. During the early pandemic period in Wuhan, a fibrinolysis-based strategy was applied. In that study, 17 patients with STEMI treated with fibrinolysis achieved comparable in-hospital and 30-day rates to those treated with PCI in the same period. The reason for this paradoxical outcome, which did not match the previous data regarding PCI and fibrinolysis, is attributed to the fact that primary PCI patients showed longer onset of first medical contact (FMC) time, longer

| Table IV. Revascularization Time and Clinical Outcome |
|-----------------------------------------------|
| | Overall | Before pandemic | During pandemic |
| | (n = 259) | (n = 117) | (n = 142) |
| Door-to-Balloon Time | 38 [27-61] | 29 [21.25-41.25] | 48 [31-73] |
| Door-to-CCL Time | 19 [12-37] | 13.5 [10-18.75] | 29.5 [18-47.25] |
| CCL-to-Balloon Time | 16 [11-22] | 13 [10-19] | 18 [13-25] |
| Onset-to-Door-Time | 120 [67-192] | 83 [51-141] | 153 [87-251] |
| Peak CK Value | 1396.5 [502.3-2695.3] | 1480 [358-2737.5] | 1363 [621-2722.8] |
| 30-day mortality | 8 (3.1%) | 5 (4.3%) | 3 (2.1%) |
| CT evaluation before PCI | 102 (39.4%) | 39 (33.3%) | 63 (44.4%) |

CCL indicates cardiac catheterization laboratory; CK, creatine kinase; CT, computed tomography; and PCI, percutaneous coronary intervention.

| Table V. Comparison of the Revascularization Time Between Early and Late Phase of the Pandemic |
|-----------------------------------------------|
| | Pandemic phase | Early Phase* (n = 57) | Late Phase** (n = 85) |
| | | Door-to-balloon time, minutes | 46 [32-58.5] | 55 [31-79.5] |
| | | Door-to-CCL time, minutes | 26 [17-35] | 33 [18.5-55] |
| | | CCL-to-balloon time, minutes | 18 [14-22] | 18 [12.5-27] |
| | | Onset-to-door-time, minutes | 146 [86.25-257] | 155 [94-237] |
| | | Nasal swab sampling for PCR | 0 (0%) | 24 (28.2%) |
| | | Positive for SARS-CoV-2 | 0 (0%) | 24 (28.2%) |
| | | CT examination | 23 (40.4%) | 40 (47.1%) |

PCL indicates cardiac catheterization laboratory; and PCR, polymerase chain reaction.

*March 2020-August 2020; **September 2020-February 2021.
FMC-to-wire time, significantly increased number and length of stents, and much worse TIMI flow.\[16\]

In the present study, the peak CK level and 30-day mortality rate did not differ between before and during the pandemic, despite the significantly longer revascularization time during the pandemic period. However, as primary PCI remains the standard of care for patients with STEMI at PCI-capable hospitals, a dedicated workflow for the “new normal” to expedite the diagnostic and therapeutic procedure should be established in each primary PCI-capable hospital.

**Limitations:** This study has several limitations. First, this was a multicenter retrospective study with historical control data. Second, the number of patients was quite small; therefore, the results may suffer from selection bias. Third, the results may reflect the potential learning curve for pandemic-dedicated PCI procedures. Fourth, other potential confounders that could affect the DTBT, such as the mode of arrival to the emergency department (walk-in versus ambulance), presence of accompanying family members, frailty, and severity of a hemodynamic condition, were not fully investigated. Finally, the local area where the two participating primary PCI hospitals are located may not represent the typical pandemic situation in Japan; therefore, the results of the current study may not be applicable as a Japanese standard.

**Conclusions**

The SARS-CoV-2 pandemic affects the treatment of patients with STEMI. Although the time delay in the presentation and revascularization was significantly longer, no adverse effects on the 30-day prognosis, peak cardiac enzyme, and final TIMI coronary flow were observed. To improve DTBT, the workflow of primary PCI should be reconsidered in the new normal brought about by the pandemic. Furthermore, the involvement of health care professionals in public relations is considered important to encourage early presentation to the hospital.

**Disclosure**

**Conflicts of interest:** All authors have no potential conflicts of interest for this work.

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