



The influence of COVID-19 pandemic on management of acute myocardial infarction in Japan; Insight from the Miyagi AMI Registry Study

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ABSTRACT

Background: Due to the coronavirus disease 2019 (COVID-19) pandemic, the first state of emergency had been declared from April 7 to May 25, 2020, in Japan. This pandemic might affect the management for patients with acute myocardial infarction (AMI). **Method and Results:** To evaluate the critical care and outcomes of AMI patients during the COVID-19 outbreak, we examined the patients with AMI hospitalized in 2020 ($n = 1186$) and those in 2017–2019 ($n = 4877$) using a database of the Miyagi AMI Registry Study. The door-to-device time under the emergency declaration became longer as compared with that of the same period in 2017–2019 [83 (65–111) vs 74(54–108) min, $p = 0.04$]. Importantly, the time delay was noted in only patients with Killip class I on arrival, but not in those with Killip class II–IV. Meanwhile, there were no significant changes in the duration from the symptom onset to hospital arrival, the use rate of ambulance and the performance rate of primary percutaneous coronary intervention before and after the COVID-19 outbreak. Eventually, in-hospital mortality had not deteriorated under the state of emergency (6.7 vs 7.8 %, $P = 0.69$). **Conclusion:** The emergence of the COVID-19 outbreak seemed to affect AMI management and highlight understanding the barriers to cardiovascular critical care.

1. Introduction

Coronavirus disease (COVID-19) has been widespread worldwide, and the World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020 [1]. Also in Japan, due to the first wave of the COVID-19 pandemic, the government declared the first state of emergency for metropolitan areas including Tokyo, Osaka, Hyogo and Fukuoka prefectures on April 7, 2020, and expanded its application scope to the entire country on April 16. Then on May 25, the declaration was discontinued due to improved infectiousness [2]. This pandemic has brought a change to the healthcare setting for not only chronic conditions but also acute illness including acute myocardial infarction (AMI) by the increasing needs to allocate limited medical resources to the treatment of COVID-19 patients [3]. Indeed, in Europe, Latin America, South East Asia and North Africa, the COVID-19 pandemic has been shown to have affected on the emergent care for ST-segment elevation myocardial infarction (STEMI) with a reduction in the executing rate of primary percutaneous coronary intervention (PCI), a significant delay in

the establishment of coronary reperfusion, and a resultant increase in in-hospital mortality [4,5]. In Japan which has a high rate of primary PCI [6,7], several studies have demonstrated that the frequency of primary PCI has been declining [8–11]. However, limited data about the treatment delay was available in a few retrospective single-center studies with a small number of subjects in Japan [10,11]. In the present study, we therefore aimed to evaluate the benchmark timelines and outcomes of AMI patients during the first state of emergency due to the COVID-19 pandemic in Japan using a prospective, multicenter data from the Miyagi AMI Registry Study.

2. Methods

This study was approved by the Institutional Review Board of Tohoku University Graduate School of Medicine (2019-1-838) and all personal data were protected at all times.

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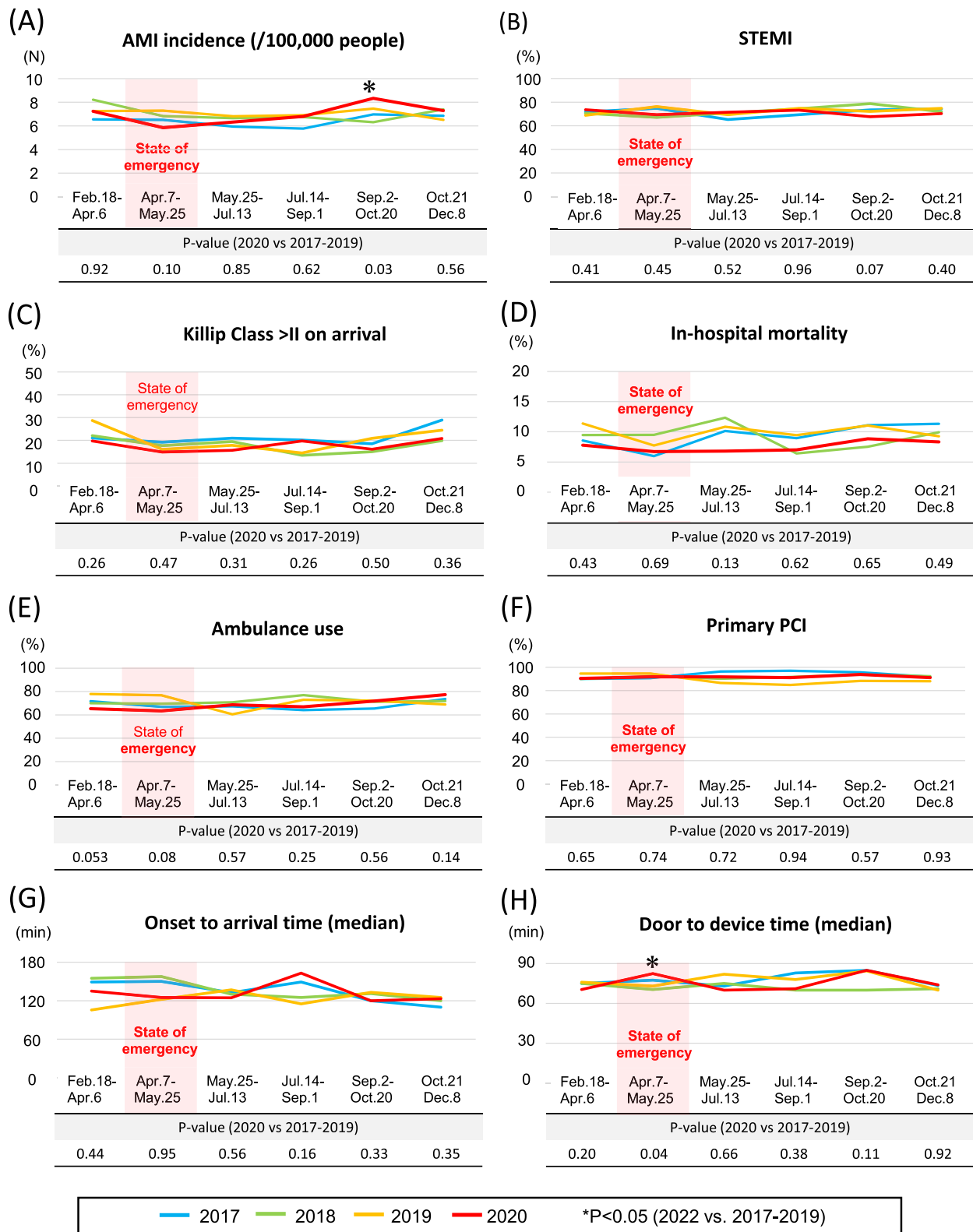


Fig. 1. Clinical characteristics, treatment delay, and outcome of AMI patients during the State of emergency for COVID-19 pandemic in 2020 as compared with those in 2017–2019. AMI, acute myocardial infarction; STEMI, ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention.

2.1. The Miyagi AMI registry study

Miyagi Prefecture is located in northeastern Japan, with a population of about 2.31 million and an area of 7,282 km² [15]. The Miyagi AMI Registry is a prospective, multicenter and observational study and has

been conducted for 42 years [6,12–14]. All 45 hospitals with a cardiac care unit and/or cardiac catheterization facility in Miyagi Prefecture have been participating (Supplementary Appendix) [6,12–14], and thus almost all AMI patients in Miyagi Prefecture are transferred to one of the participating hospitals via emergency medical service. In the present

Table 1
Influence of state of emergency for COVID-19 pandemic on treatment delay and in-hospital mortality of AMI patients.

	Feb. 18–Apr. 6 (Before the state of emergency)			Apr. 7–May 25 (Under the state of emergency)			May 26–Dec. 8 (After the state of emergency)		
	2020	2017–2019	P value	2020	2017–2019	P value	2020	2017–2019	P value
Door-to-device time (median, min)									
Over-all	71 (50–113)	76 (55–119)	0.20	83 (65–111)	74 (54–74)	0.04	75 (56–120)	75 (55–115)	0.71
Ambulance use	61 (47–92)	71 (53–110)	0.03	77 (59–99)	69 (52–98)	0.20	70 (53–100)	70 (53–101)	0.98
No ambulance use	105 (60–165)	104 (62–156)	0.98	102 (77–134)	89 (63–151)	0.57	109 (70–173)	96 (66–153)	0.30
STEMI	61 (47–93)	70 (52–105)	0.82	80 (63–105)	71 (52–102)	0.73	70 (53–102)	70 (53–102)	0.77
Non-STEMI	142 (72–199)	118 (73–176)	0.79	104 (68–206)	85 (63–154)	0.15	99 (68–175)	106 (70–161)	0.68
Killip class I	67 (48–115)	76 (54–120)	0.17	83 (64–116)	72 (54–108)	0.03	75 (56–120)	73 (54–110)	0.33
Killip class II–IV	77 (53–105)	73 (58–118)	0.98	78 (66–91)	80 (55–117)	0.81	74 (60–111)	89 (60–131)	0.22
Onset-to-arrival time (median, min)									
Over-all	135 (65–322)	139 (67–400)	0.44	125 (74–325)	140 (62–350)	0.95	130 (65–334)	125 (61–315)	0.73
Ambulance use	124 (64–302)	125 (61–343)	0.78	108 (66–283)	115 (59–293)	0.97	110 (60–276)	111 (60–246)	0.42
No ambulance use	170 (77–434)	240 (103–669)	0.11	225 (92–448)	278 (115–645)	0.27	223 (112–390)	218 (94–525)	0.48
STEMI	115 (63–280)	125 (60–339)	0.59	123 (61–302)	125 (60–339)	0.73	120 (61–298)	117 (60–276)	0.67
Non-STEMI	230 (86–665)	240 (104–677)	0.76	180 (91–346)	192 (84–390)	0.93	175 (74–364)	180 (80–441)	0.41
Killip class I	140(69–356)	140 (65–431)	0.53	128(69–347)	150(67–372)	0.59	140(70–351)	131(63–336)	0.34
Killip class II–IV	129(53–272)	134 (70–356)	0.56	121(89–283)	102(50–237)	0.29	80(50–208)	100(58–239)	0.16.
In-hospital mortality									
Over-all	7.8 % (13/167)	9.8 % (50/509)	0.43	6.7 % (9/134)	7.8 % (37/477)	0.69	7.8 % (52/664)	9.9 % (184/1859)	0.12
Ambulance use	11.0 % (12/109)	11.8 % (44/372)	0.82	7.1 % (6/79)	7.4 % (25/340)	0.93	9.1 % (43/431)	11.3 % (147/1297)	0.17
No ambulance use	4.4 % (6/137)	1.7 % (1/58)	0.36	6.1 % (3/49)	8.8 % (12/137)	0.56	4.7 % (9/190)	6.6 % (37/562)	0.36
STEMI	7.3 % (9/123)	8.9 % (32/358)	0.58	5.4 % (5/93)	7.2 % (25/347)	0.53	7.9 % (37/468)	9.9 % (133/1348)	0.21
Non-STEMI	9.1 % (4/44)	11.9 % (18/151)	0.60	9.8 % (4/41)	9.2 % (12/130)	0.92	7.7 % (15/196)	10.0 % (51/511)	0.34
Killip class I	3.0 % (4/134)	5.2 % (20/387)	0.30	6.1 % (7/114)	4.1 % (16/393)	0.35	3.7 % (20/544)	5.3 % (80/1496)	0.12
Killip class II–IV	27.3 % (9/33)	24.6 % (30/122)	0.75	10.0 % (2/20)	25.0 % (21/84)	0.15	26.7 % (32/120)	28.7 % (104/363)	0.68

AMI, acute myocardial infarction; STEMI, ST-segment elevation myocardial infarction.

study, the diagnosis of AMI was based on the Universal definition, including rise and/or fall of cardiac biomarker and ischemic sign or symptom [16], and acute treatments including reperfusion therapies were left to the discretion of individual cardiologists in charge, as previously reported [6,12–14].

2.2. Statistical analysis

In order to evaluate the treatment delay and outcomes of AMI patients during the COVID-19 pandemic, we compared AMI patients hospitalized in 2020 (pandemic period, $n = 1186$) with those in 2017–2019 (pre-pandemic period, $n = 4877$). To examine the impact of the first state of emergency (from April 7 to May 25) in particular, we set up six 49-day periods based on the duration of the national declaration of emergency as shown in Fig. 1. During each period, several indices associated with critical care for AMI in 2020 were compared to those in the previous three years. Moreover, we performed sub-group analysis for door-to-device time and in-hospital mortality according to ambulance use, presence of STEMI, or symptomatic heart failure with Killip class II–IV on arrival.

We applied Mann-Whitney test for continuous values and chi-square test for categorical variables. Continuous variables are expressed as median and inter quartile range (IQR). P-values of <0.05 were considered to be statistically significant. All statistical analyses were performed using the statistical software SPSS statistics 26 (IBM Corp, Armonk, NY, USA).

3. Results

Baseline characteristics of study population were summarized in

Supplementary Table 1. In 2020, 1186 patients with AMI were enrolled and their median age was 71 years, which was comparable with that of 4877 patients enrolled in 2017–2019. AMI patients in 2020 were characterized by the lower prevalence of male, hypertension, and dyslipidemia as compared with those in 2017–2019. In-hospital mortality remained constant for those 4 years. (10.2 % in 2017, 9.2 % in 2018, 11.0 % in 2019, 8.6 % in 2020, $P = 0.13$).

Under the state of emergency (from April 7 to May 25, 2020), the incidence of AMI, the prevalence of STEMI and Killip class \geq II on arrival, the use rate of ambulance, the performance rate of primary PCI were comparable with those during the same period of 2017–2019 (Fig. 1A–F). Moreover, the time elapsing from the symptom onset to hospital arrival did not change (125[74–325] min vs 140[62–350] min, $p = 0.95$), whereas the door to device time significantly increased during the emergent declaration compared with the previous three years (83 [65–111] min vs 74[54–108] min, $p = 0.04$) (Fig. 1G–H and Table 1). Importantly, the prolonged door to device time was noted among only the patients with Killip class I on arrival (83[64–116] min vs 72 [54–108] min, $p = 0.03$), but not those with Killip class \geq II (78[66–91] min vs 80[55–117] min, $p = 0.81$) (Table 1).

Meanwhile, in-hospital mortality including cardiac and non-cardiac death did not deteriorate during the state of emergency compared with those in 2017–2019 (6.7 vs 7.8 %, $P = 0.69$) (Fig. 1 and Supplementary Fig. S1), regardless of the ambulance use, type of MI, and presence or absence of symptomatic heart failure (Table 1).

4. Discussions

The present study demonstrated that, during the state of emergency for the COVID-19 pandemic in Japan compared to the same periods of

previous 3 years, the elapsing time from the symptom onset to hospital arrival, the performance rate of primary PCI, and in-hospital mortality were comparable, whereas the door-to-device time became longer. Furthermore, the prolonged door-to-device time was noted only in AMI patients with Killip class I, but not in those with Killip class \geq II on arrival.

Multicenter registry studies from Europe, Latin America, South-East Asia and North Africa demonstrated that the influence of the COVID-19 pandemic on the emergent care for STEMI could lead to a 16 % decrease in the number of primary PCI procedures, a significant delay in the reperfusion treatment, as well as increased in-hospital mortality [4,5]. In contrast, in Japan, although a single-center study from Osaka also reported a decrease (68.3 % from 82.5 %) in the performance rate of primary PCI for STEMI patients [17], most of the studies including a nationwide registry study demonstrated that the rate of primary PCI had remained high (87–92 %) in after COVID-19 pandemic [8–11], which was consistent with the present study. The high rate of primary PCI during the COVID-19 pandemic in Japan could be associated with a lower infection rate and case-fatality rate of COVID-19 (187.5 and 2.8 per 100,000 population as of December, 2020, respectively) relative to other countries [18]. Especially, in Miyagi prefecture, even during the state of emergency between April 7 and May 25, 2020, there were 62 people who tested positive for COVID-19 [19]. While, Japan which has proportionally narrow territory has an advantage in accessing to PCI capable hospitals, and the performance rate of primary PCI was relatively higher compared to other countries before this pandemic [6,7], which may have also led to the findings of the present study.

As shown in previous studies [4,10,11], the prolonged door-to-device time in the critical care for AMI patients during the COVID-19 pandemic was also noted in the present study. Treatment delays for AMI could be attributable to infection control and prevention of COVID-19 including recording a detailed medical history, wearing personal protective equipment (PPE) and doing polymerase chain reaction (PCR) testing. Importantly, longer door-to-device time was noted only in AMI patients with Killip class I on arrival, but not in those complicated with symptomatic heart failure or cardiogenic shock [20].

Since early revascularization is the only proven therapy to reduce high mortality levels in STEMI complicated by cardiogenic shock [21], the finding suggests that appropriate patient triage according to the severity of AMI appeared to be conducted even during the COVID-19 pandemic in Japan, resulting in the prevention of in-hospital mortality from worsening at least in part.

Some limitations should be mentioned for the present study. First, although almost all AMI patients were transferred to our participating hospitals in the Miyagi prefecture, not all patients might have been enrolled in this registry. Especially during the pandemic period, it was highly possible that many people were hesitated to visit hospitals, as previously reported, which could have affected the present results. Second, since this study is observational in nature, the precise mechanisms of the influence of the COVID-19 pandemic on the emergent care of AMI, especially the change in door-to-device time, remain to be fully elucidated. Moreover, we have no data whether patients were positive for COVID-19, which could affect the emergency care. Third, in this study, no data was available concerning cardiac function, procedural complication, in-hospital bleeding, or pharmacological therapy, which could have affected the results. Especially, in-hospital bleeding has been shown to have impacted the prognosis of patients with acute coronary syndrome even during the COVID-19 pandemic [22].

5. Conclusion

The COVID-19 pandemic seemed to affect the management of AMI, whereas critical care was maintained beyond the minimum needed in Japan.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcha.2022.101116>.

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