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ORIGINAL ARTICLE
Ischemic Heart Disease

Demographic Trends and Changes in the Pre- and In-Hospital Medical Management of Acute Myocardial Infarction During the First 12 Months of the COVID-19 Pandemic in Mie Prefecture

— Report From the Mie ACS Registry —

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Background: Even though hospital admissions for acute myocardial infarction (AMI) decreased globally during the COVID-19 pandemic in early 2020, limited information is available on subsequent demographic trends in the number of cases and management of AMI through the first 12 months of the COVID-19 pandemic.

Methods and Results: We assessed demographic trends, patient characteristics, and AMI outcomes (n=730) during the first 12 months of the COVID-19 pandemic and compared them with corresponding months during the control period (February 2016–January 2020; n=2,742) using data from the Mie ACS Registry. Although a 25.8% reduction in hospitalizations for AMI was observed in the 3 months following the declaration of a state of emergency (47.7 vs. 64.3/month; P=0.002), the total number of AMI patients was similar between the 12-month COVID-19 and control periods (60.8 vs. 57.2/month; P=0.58). The number of patients requiring direct ambulance transport was lower in the first half of the COVID-19 than control period (44.4% vs. 51.5; P=0.028). In-hospital mortality was higher in the second half of the COVID-19 than control period (8.9% vs. 5.8%; P=0.032).

Conclusions: Through the first 12 months of the COVID-19 pandemic, the number of AMI cases was similar to that in previous years. The COVID-19 pandemic changed the behavior of AMI patients and both pre- and in-hospital medical management, which significantly affected the severity and prognosis of AMI.

Key Words: Acute myocardial infarction; COVID-19 infection; Epidemiological study

Since late 2019, COVID-19 has spread worldwide.[1] The World Health Organization declared COVID-19 a pandemic on March 11, 2020 and lockdowns were implemented in several major cities around the world to control infection.

In Japan, the first case of COVID-19 was confirmed in the middle of January 2020. The first case of COVID-19 in Mie prefecture, the location of the Mie ACS Registry, was confirmed at the end of January 2020. A state of emergency was declared on April 7, 2020 in Tokyo, Osaka, Kanagawa, Saitama, Chiba, Hyogo, and Fukuoka prefectures, and was expanded to the entire nation, including Mie prefecture, on April 16, 2020. This led to behavioral changes in patients and affected access to medical facilities.[2,3]

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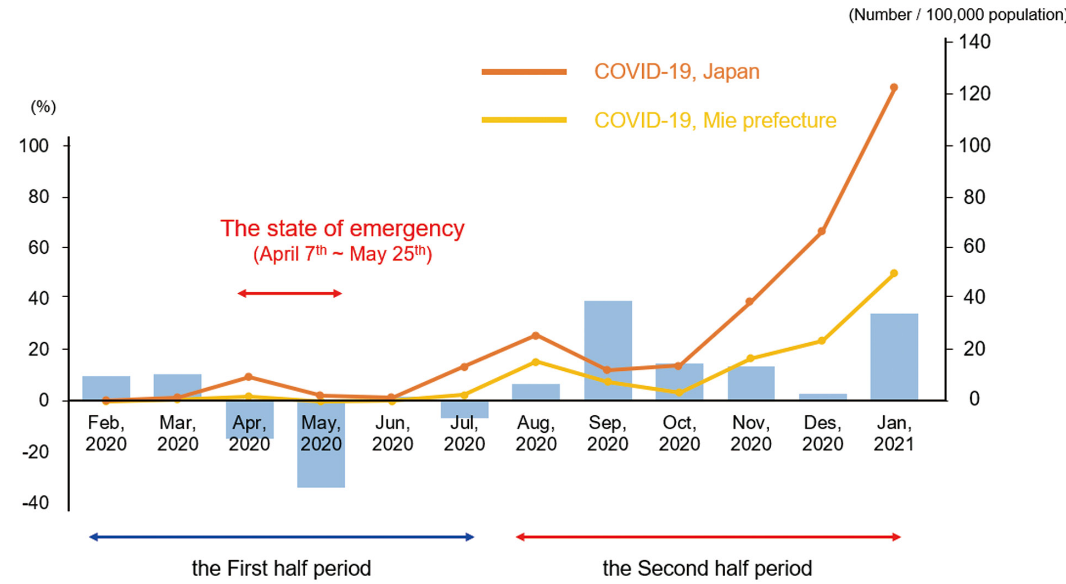

Figure 1. Monthly percentage changes in the incidence of acute myocardial infarction (AMI) during the COVID-19 pandemic from previous years (blue columns) and the number of COVID-19 cases per 100,000 population in Mie prefecture (yellow line) and Japan (orange line) during the COVID-19 pandemic.

The COVID-19 pandemic has increased the complexity of managing acute myocardial infarction (AMI). In several countries, the COVID-19 pandemic was associated with a reduction in the number of AMI patients in early 2020 because of fears surrounding seeing a doctor or visiting a hospital, or difficulties accessing medical facilities.[4–8] Significant increases in the rate of out-of-hospital cardiac arrests among AMI patients and in AMI severity and mortality were reported after the outbreak of COVID-19.[5,7,9–13]

The number of COVID-19 cases increased markedly in late 2020 and the pandemic has continued into 2022 in Japan. Limited information is currently available as to the effects of the COVID-19 pandemic on AMI through the first 12 months of the pandemic or on the pre- and in-hospital management of AMI patients in the COVID-19 era. Therefore, the present study investigated the frequency, patient characteristics, management, and clinical outcomes of AMI in the 12-month period after the start of the COVID-19 pandemic in Mie prefecture in Japan.

Methods

Study Population

This study enrolled 3,472 AMI patients registered with the Mie ACS Registry between February 2016 and January 2021, including 730 AMI patients registered during the COVID-19 period (between February 2020 and January 2021). The Mie ACS Registry is a prospective, ongoing, multicenter registry for acute coronary syndrome (ACS) that was started in 2013 in Mie prefecture, Japan.[14–16] We compared patient characteristics, pre- and in-hospital medical management, and clinical outcomes of AMI during the COVID-19 period with a control period (February 2016–January 2020). The first 12-months of the COVID-19 pandemic was divided into halves: February–July 2020 (first half) and August 2020–January 2021 (second half; **Supplementary Figure**). We compared the frequency of AMI and its characteristics in these 2 periods with those during the control period. We also investigated the frequency of screening tests for COVID-19 at the time of hospital admission and the use of full personal protective equipment (PPE) during percutaneous coronary intervention (PCI). The screening tests for COVID-19 were chest computed tomography (CT) to exclude COVID-19 pneumoniae, an antigen test, or a polymerase chain reaction (PCR) test.

The Mie ACS Registry was approved by the Institutional Review Board of the Mie University Graduate School of Medicine (Reference no. 2881) and the ethics committees of all participating institutions.[14–16] The Mie ACS Registry is registered with University Hospital Medical Information Network (UMIN) Clinical Trials Registry (ID: UMIN000036020).[14–16]

Definitions

All ACS patients who were admitted to each of the participating hospitals and diagnosed with ACS were eligible for inclusion in the Mie ACS Registry. The present study included all myocardial infarction (MI) patients, including those with recent MI, with and without PCI. The diagnosis of AMI was based on the Fourth Universal Definition of Myocardial Infarction.[17] Emergency PCI was defined as primary PCI performed within 6 h of hospital admission. Direct ambulance transport was defined as direct transport from the field to a PCI-capable institution by emergency medical services. Interfacility transport was defined as indirect transport via the office of a family physician or non-PCI-capable institutions to PCI-capable institutions.

Statistical Analysis

Normally distributed continuous variables are presented

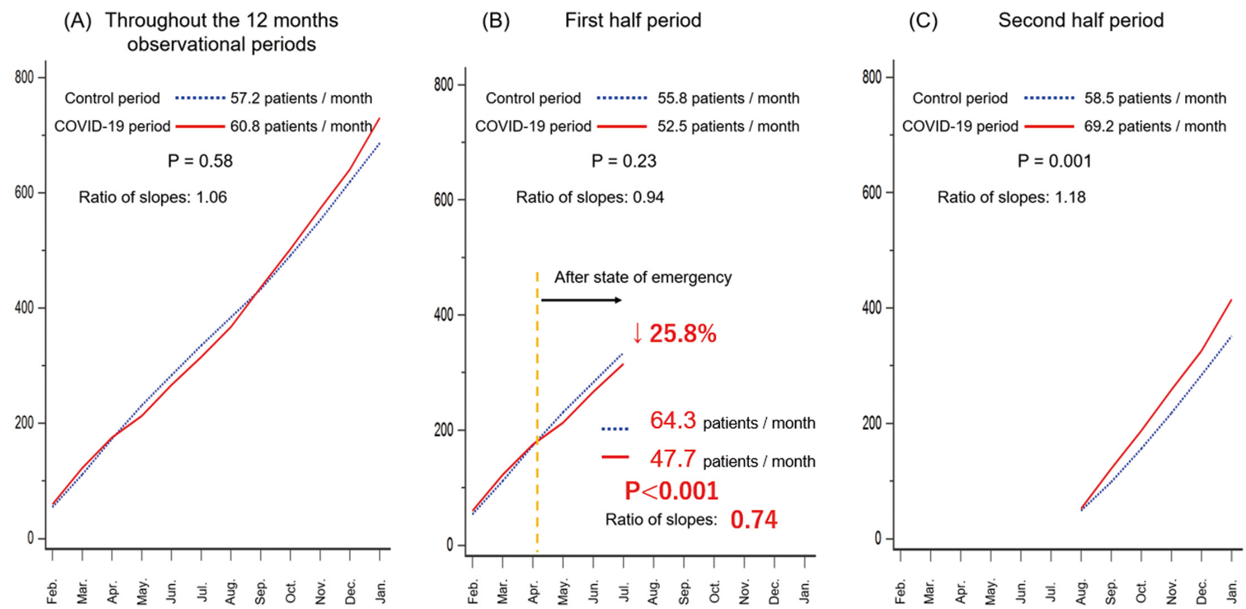

Figure 2. Linear regression trend lines for the cumulative number of cases of acute myocardial infarction (AMI) throughout the 12-month observation period during the COVID-19 pandemic (February 2020–January 2021) and the control period (February 2016–January 2020). (**A**) Cumulative number of AMI patients throughout the entire observational period. There was no significant difference in the slopes of the regression lines between the COVID-19 and control periods (60.8 vs. 57.2 patients/month; ratio of slopes: 1.06; P=0.58). (**B**,**C**) Cumulative number of AMI patients in the first (**B**) and second (**C**) halves of the COVID-19 period. During the first half of the COVID-19 period (**B**), the slopes of the regression lines between the COVID-19 and control periods did not differ before the declaration of a state of emergency (52.5 vs. 55.8 patients/month; ratio of slopes: 0.94; P=0.23), but did differ after the declaration (47.7 vs. 64.3 patients/month; ratio of slopes: 0.74; P=0.002). During the second half of the COVID-19 period (**C**), there was a significant difference in the slopes of the regression lines between the COVID-19 and control periods (69.2 vs. 58.5 patients/month; ratio of slopes: 1.18; P=0.001).

as the mean±SD, whereas those that were no normally distributed are presented as the median and interquartile range. Categorical variables are presented as numbers and percentages. The Chi-squared test or Mann-Whitney U test was used to compare categorical variables according to a nominal or ordinal scale. Student's t-test or the Wilcoxon rank-sum test was used for continuous variables, as appropriate. Linear regression analysis was performed on the cumulative number of AMI hospitalizations in the first 12 months of the COVID-19 pandemic and the control period, and analysis of covariance (ANCOVA) was used to compare the slopes of the 2 regression lines. Statistical analyses were conducted using SPSS Version 26.0 (IBM Corp., Armonk, NY, USA).

Results

Number of AMI Patients During the COVID-19 Period

Figure 1 shows monthly percentage changes in the incidence of AMI during the first 12 months of the COVID-19 pandemic compared with previous years, as well as the number of COVID-19 cases per 100,000 population in Mie prefecture and Japan. In response to the spread of COVID-19 infection, a state of emergency was declared in Japan from April 7 to May 25. The number of AMI patients decreased markedly from April to May 2020 compared with previous years. However, the number of AMI patients increased, despite the spread of COVID-19 infection, during the second half of the COVID period.

The cumulative incidence of AMI throughout the 12-month COVID-19 pandemic and control periods is shown by linear regression trend lines in **Figure 2**. There were no significant differences in the slopes of the regression lines between the COVID-19 and control periods (60.8 vs. 57.2 patients/month; ratio of slopes: 1.06; P=0.58). In the first half of the COVID-19 period, the slopes of the regression lines did not significantly differ between the COVID-19 and control periods (52.5 vs. 55.8 patients/month; ratio of slopes: 0.94; P=0.23). However, after a state of emergency was declared, there was a 25.8% reduction in the 3 months after the declaration in the number of cases of AMI (**Figure 2B**), with a significant difference in the slopes of the regression lines between the COVID-19 and control periods (47.7 vs. 64.3 patients/month; ratio of slopes: 0.74; P<0.001). In the second half of the COVID-19 period, despite an increase in the number of confirmed cases of COVID-19, the number of patients with AMI was higher than in the control period (69.2 vs. 58.5 patients/month; ratio of slopes 1.18; P=0.001; **Figure 2C**).

The number of patients ST-elevation MI (STEMI) was slightly lower in the COVID-19 than control period, with a marked reduction in STEMI patients noted in the first 3 months after the declaration of a state of emergency (31.3 vs. 41.5 patients/month; P=0.001; **Figure 3A**,**B**). However, in the second half of the COVID-19 period, even with a higher number of confirmed cases of COVID-19, the num-

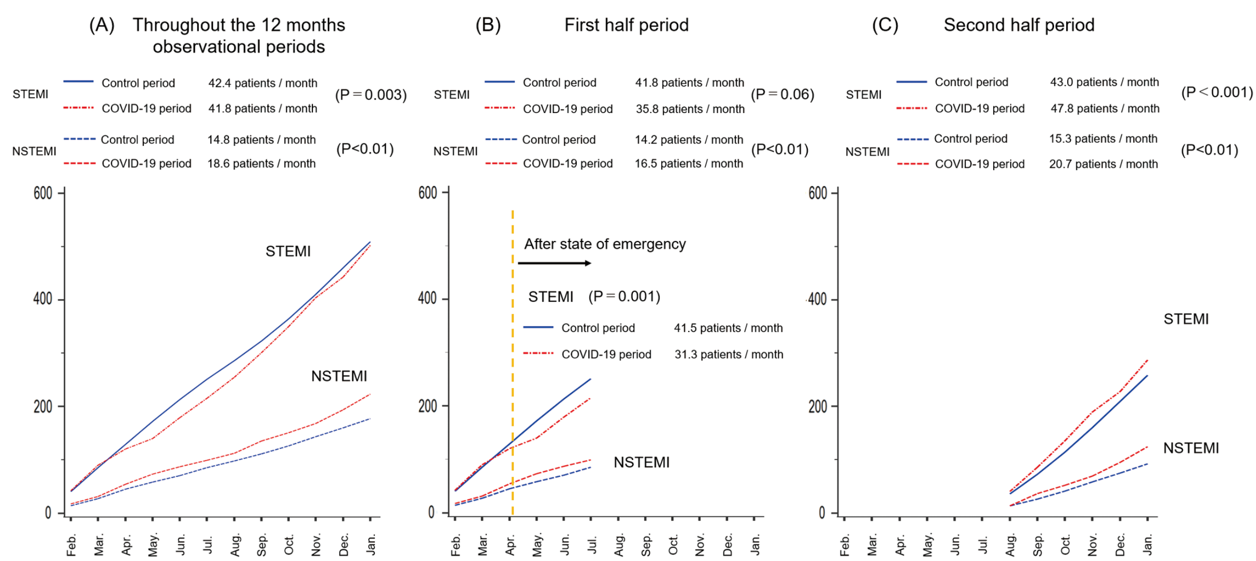

Figure 3. Linear regression trend lines for the cumulative number of cases of ST-elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI) throughout the 12-month observation period during the COVID-19 pandemic (February 2020–January 2021) and control period (February 2016–January 2020). (**A**) Cumulative number of STEMI and NSTEMI patients throughout the observation period. There were significant differences in the slopes of the regression lines between the COVID-19 and control periods for both STEMI (41.8 vs. 42.4 patients/month; ratio of slopes: 0.99; P=0.003) and NSTEMI (41.8 vs. 42.4 patients/month; ratio of slopes: 0.99; P=0.003). (**B**,**C**) Cumulative number of STEMI and NSTEMI patients in the first (**B**) and second (**C**) halves of the COVID-19 period. In the first half of the COVID-19 period (**B**), although there was no significant difference in the slopes of the regression lines for STEMI between the COVID-19 and control periods before the declaration of a state of emergency (35.8 vs. 41.8 patients/month; ratio of slopes: 0.86; P=0.06), after the declaration there was a significant difference in the slopes of the regression lines (31.3 vs. 41.5 patients/month; ratio of slopes: 0.69; P=0.001). For NSTEMI, there were significant differences in the slopes of the regression lines between the COVID-19 and control periods (16.5 vs. 14.2 patients/month; ratio of slopes: 1.17; P<0.01). In the second half of the COVID-19 period (**C**), there were significant differences in the slopes of the regression lines between the COVID-19 and control periods for both STEMI (47.8 vs. 43.0 patients/month; ratio of slopes: 1.12; P<0.001) and NSTEMI (20.7 vs. 15.3 patients/month; ratio of slopes: 1.27; P<0.01).

Table 1. Patient Characteristics in the Control and COVID-19 Periods

	12-month observation period (February–January)			First half (February–July)			Second half (August–January)		
	Control	COVID-19	P value	Control	COVID-19	P value	Control	COVID-19	P value
No. patients	2,742	730		1,340	315		1,402	415	
Age (years)	69.6±12.7	71.3±12.9	0.002	69.6±12.9	71.7±13.3	0.012	69.5±12.5	70.9±12.6	0.049
Male sex	2,109 (76.9)	546 (74.8)	0.239	1,014 (75.7)	224 (71.1)	0.097	1,095 (78.1)	322 (77.6)	0.840
BMI (kg/m^2)	23.2 [21.2–25.5]	23.5 [21.3–25.9]	0.219	23.2 [21.2–25.6]	23.4 [21.1–25.7]	0.992	23.2 [21.2–25.4]	23.6 [21.5–25.9]	0.120
Cardiovascular risk factors									
Hypertension	1,709 (62.3)	454 (62.2)	0.966	839 (62.6)	196 (62.2)	0.897	870 (62.1)	258 (62.2)	1
Diabetes	930 (33.9)	250 (34.2)	0.895	444 (33.1)	98 (31.1)	0.505	486 (34.7)	152 (36.6)	0.482
Dyslipidemia	1,257 (45.8)	353 (48.4)	0.226	616 (46.0)	157 (49.8)	0.233	641 (45.7)	196 (47.2)	0.614
Current smoker	707 (25.8)	196 (26.8)	0.569	335 (25.0)	75 (23.8)	0.717	372 (26.5)	121 (29.2)	0.315
Hemodialysis	50 (1.8)	18 (2.5)	0.292	29 (2.2)	8 (2.5)	0.673	21 (1.5)	10 (2.4)	0.201
Prior MI	218 (8.0)	70 (9.6)	0.152	108 (8.1)	23 (7.3)	0.728	110 (7.8)	47 (11.3)	0.029
Prior PCI	283 (10.3)	75 (10.3)	1	146 (10.9)	27 (8.6)	0.260	137 (9.8)	48 (11.6)	0.309
Prior CABG	21 (0.8)	6 (0.8)	0.815	8 (0.6)	3 (1.0)	0.448	13 (0.9)	3 (0.7)	1
Prior cerebral infarction	141 (5.1)	42 (5.8)	0.514	70 (5.2)	15 (4.8)	0.887	71 (5.1)	27 (6.5)	0.266

Unless indicated otherwise, data are given as the mean±SD, median [interquartile range], or n (%). The control period was from February 2016 to January 2019 and the COVID-19 period was from February 2020 to January 2021. BMI, body mass index; CABG, coronary artery bypass grafting; MI, myocardial infarction; PCI, percutaneous coronary intervention.

ber of STEMI patients increased and was higher than in the control period (47.8 vs. 43.0 patients/month; P<0.001; **Figure 3C**). Conversely, the number of non-STEMI (NSTEMI) patients increased throughout the year and was higher in the COVID-19 than in the control period (18.6 vs. 14.8 patients/month; P<0.01; **Figure 3A**). Unlike STEMI, the number of NSTEMI patients continued to increase, even after the declaration of a state of emergency (**Figure 3B**).

Clinical Characteristics and Pre- and In-Hospital Medical Management of AMI Patients During the COVID-19 and Control Periods

The clinical characteristics of AMI patients in the COVID-19 and control periods are summarized in **Tables 1** and **2**. The mean age of patients was higher during the COVID-19 than control period (71.3 vs. 69.6 years; P=0.002). The frequency of STEMI decreased significantly during the COVID-19 period (69.1% vs. 74.2%; P=0.007), particularly during the first half (68.3% vs. 74.7%; P=0.023). The proportion of AMI patients who were transported directly to hospital by ambulance was significantly lower in the first half of the COVID-19 period than in the control period (44.4% vs. 51.5%; P=0.028), and the onset-to-door time was significantly longer during the COVID-19 than control period (146.5 vs. 131.0 min; P=0.041). Conversely, the door-to-balloon (DTB) time was similar during the 12-month COVID-19 and control periods (82 vs. 78 min, respectively; P=0.121). However, the DTB time was significantly longer during the second half of the COVID-19 period than during the control period (85.5 vs. 77 min, respectively; P=0.032). The out-of-hospital cardiac arrest rate was higher during the COVID-19 than control period (6.4% vs. 4.5%; P=0.034). Furthermore, the prevalence of a more severe Killip class was significantly higher during

Table 2. Details of Acute Myocardial Infarction Patients During the Control and COVID-19 Periods

	12-month observation period (February–January)			First half (February–July)			Second half (August–January)		
	Control	COVID-19	P value	Control	COVID-19	P value	Control	COVID-19	P value
No. patients	2,742	730		1,340	315		1,402	415	
Diagnosis									
STEMI	2,035 (74.2)	502 (69.1)	0.007	1,001 (74.7)	215 (68.3)	0.023	1,034 (73.8)	287 (69.8)	0.130
Pathway for transport									
Direct ambulance	1,456 (53.1)	360 (49.3)	0.073	690 (51.5)	140 (44.4)	0.028	766 (54.6)	220 (53.0)	0.575
Interfacility transport	723 (26.4)	225 (30.8)	0.017	352 (26.3)	111 (35.2)	0.002	371 (26.5)	114 (27.5)	0.705
Walk in	502 (18.3)	132 (18.1)	0.914	263 (19.6)	57 (18.1)	0.579	239 (17.0)	75 (18.1)	0.657
In-hospital	61 (2.2)	13 (1.8)	0.564	35 (2.6)	7 (2.2)	0.843	26 (1.9)	6 (1.4)	0.676
Onset-to-door time (min)	131 [67–334.5]	146.5 [70.3–413.3]	0.041	134 [65–343]	144 [72–466]	0.076	128 [68–327.5]	147 [70–390]	0.250
STEMI setting	121 [64–287]	124 [63.8–333]	0.455	122 [61–294.5]	123 [61–330]	0.509	121 [67–281.3]	124 [65–338]	0.698
NSTEMI setting	180 [84–541]	249 [90–655.5]	0.068	176 [86.5–514.8]	293.5 [93.8–671.8]	0.047	181 [82.5–560]	208 [88–648]	0.476
DTB time (min)	78 [59–114]	82 [60–122]	0.121	78.5 [58–115]	79 [57–119]	0.907	77 [60–114]	85.5 [63–123.5]	0.032
STEMI setting	73 [56–97]	76 [56–103]	0.362	73 [55–100.8]	73 [52.3–102]	0.541	72 [57–93.5]	77 [59–103.5]	0.069
NSTEMI setting	121 [80–193.3]	119 [75–198]	0.887	116 [73.3–184.5]	108 [71.5–193.5]	0.644	128.5 [83–195.5]	128.5 [80.3–197.8]	0.915
Onset-to-door time <24 h	2,363 (86.2)	611 (83.8)	0.108	1,152 (86.0)	264 (83.8)	0.328	1,211 (86.4)	347 (83.8)	0.200
OOHCA	123 (4.5)	47 (6.4)	0.034	59 (4.4)	21 (6.7)	0.107	64 (4.6)	26 (6.3)	0.159
Emergency PCI	2,461 (89.8)	661 (90.5)	0.580	1,204 (89.9)	282 (89.5)	0.837	1,257 (89.7)	379 (91.3)	0.351
Hemodynamics									
Killip 1	2,113 (77.1)	520 (71.6)	0.001	1,021 (76.2)	2,225 (71.4)	0.256	1,092 (77.9)	295 (71.8)	0.001
Killip 2	251 (9.2)	73 (10.1)		1,021 (9.2)	33 (10.5)		128 (9.1)	40 (9.7)	
Killip 3	146 (5.3)	35 (4.8)		66 (4.9)	16 (5.1)		80 (5.7)	19 (4.6)	
Killip 4	232 (8.5)	98 (13.5)		130 (9.7)	41 (13.0)		102 (7.3)	57 (13.9)	
STEMI setting									
Killip 1	1,550 (76.2)	348 (69.3)	0.001	748 (74.7)	146 (67.9)	0.175	802 (77.6)	202 (70.4)	<0.001
Killip 2	198 (9.7)	55 (11.0)		96 (9.6)	27 (12.6)		102 (9.9)	28 (9.8)	
Killip 3	99 (4.9)	21 (4.2)		46 (4.6)	10 (4.7)		53 (5.1)	11 (3.8)	
Killip 4	188 (9.2)	78 (15.5)		111 (11.1)	32 (14.9)		77 (7.4)	46 (16.0)	

(**Table 2** continued the next page.)

	12-month observation period (February–January)			First half (February–July)			Second half (August–January)		
	Control	COVID-19	P value	Control	COVID-19	P value	Control	COVID-19	P value
NSTEMI setting									
Killip 1	563 (79.6)	172 (76.8)	0.541	273 (80.5)	79 (79.0)	0.604	290 (78.8)	93 (75.0)	0.617
Killip 2	53 (7.5)	18 (8.0)		27 (8.0)	6 (6.0)		26 (7.1)	12 (9.7)	
Killip 3	47 (6.6)	14 (6.2)		20 (5.9)	6 (6.0)		27 (7.3)	8 (6.5)	
Killip 4	44 (6.2)	20 (8.9)		19 (5.6)	9 (9.0)		25 (6.8)	11 (8.9)	
IABP use	355 (13.0)	111 (15.3)	0.112	176 (13.2)	52 (16.5)	0.123	179 (12.8)	59 (14.3)	0.408
VA-ECMO use	61 (2.2)	19 (2.6)	0.578	32 (2.4)	8 (2.5)	0.839	29 (2.1)	11 (2.7)	0.449
Ventilation use	185 (6.8)	69 (9.5)	0.016	96 (7.2)	31 (9.8)	0.126	89 (6.4)	38 (9.2)	0.048
Angiographic characteristics									
LAD culprit	1,208 (44.3)	347 (48.6)	0.043	593 (44.5)	144 (46.9)	0.446	615 (44.2)	203 (49.9)	0.048
LMT culprit	75 (2.8)	22 (3.1)	0.613	44 (3.3)	9 (2.9)	0.859	31 (2.2)	13 (3.2)	0.275
RCA culprit	986 (36.2)	234 (32.8)	0.095	481 (36.1)	102 (33.2)	0.356	505 (36.3)	132 (32.4)	0.158
LCX culprit	429 (15.7)	103 (14.4)	0.416	198 (14.8)	49 (16.0)	0.658	231 (16.6)	54 (13.3)	0.122
Other culprit	18 (0.7)	5 (0.7)	0.802	11 (0.8)	2 (0.7)	1.000	7 (0.5)	3 (0.7)	0.703
Multivessel disease	841 (30.9)	222 (31.0)	0.964	405 (30.4)	96 (31.2)	0.784	436 (31.3)	126 (30.8)	0.903
Strategy									
PCI	2,608 (95.1)	694 (95.1)	0.923	1,279 (95.4)	296 (94.0)	0.306	1,329 (94.8)	398 (95.9)	0.440
Aspiration	1,597 (63.2)	365 (55.3)	<0.001	794 (64.0)	157 (55.3)	0.008	803 (62.5)	208 (55.3)	0.014
Distal protection	219 (8.9)	35 (5.3)	0.003	115 (9.6)	13 (4.6)	0.006	104 (8.2)	22 (5.9)	0.151
Final TIMI 3 flow	2,266 (91.9)	579 (88.4)	0.006	1,098 (91.4)	248 (87.9)	0.086	1,168 (92.4)	331 (88.7)	0.033
CABG	69 (2.5)	16 (2.2)	0.688	32 (2.4)	14 (4.4)	0.056	37 (2.6)	2 (0.5)	0.006
Peak CPK (U/L)	1,474.0 [595.5–3,028.0]	1,288.0 [466.0–2,955.0]	0.012	1,557.5 [596.8–3,093.8]	1,299 [447–3,222]	0.069	1,432 [593.5–2,999]	1,260.5 [476–2,893.8]	0.090
STEMI setting	1,889 [870–3,576]	1,850.5 [682.5–3,610]	0.276	1,938 [869–3,616]	2,076.5 [659–3,760.5]	0.872	1,823 [877–3,535.8]	1,717 [676.8–1,514.3]	0.116
NSTEMI setting	633 [268.5–1,561.3]	556 [229.5–1,293.5]	0.191	693 [296–1,646.5]	532 [219.5–1,111]	0.043	547 [251.5–1,454.5]	595 [233.8–1,514.3]	0.925

Unless indicated otherwise, data are given as the median [interquartile range] or n (%). The control period was from February 2016 to January 2019 and the COVID-19 period was from February 2020 to January 2021. CABG, coronary artery bypass grafting; CPK, creatine phosphokinase; DTB, door-to-balloon; IABP, intra-aortic balloon pumping; LAD, left anterior descending coronary artery; LCX, left circumflex artery; LMT, left main trunk; NSTEMI, non-ST-elevation myocardial infarction; OOHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; RCA, right coronary artery; STEMI, ST-elevation myocardial infarction; TIMI, Thrombolysis in Myocardial Infarction; VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

Table 3. Patient Outcomes During the Control and COVID-19 Periods

	12-month observation period (February–January)			First half (February–July)			Second half (August–January)		
	Control	COVID-19	P value	Control	COVID-19	P value	Control	COVID-19	P value
No. patients	2,742	730		1,340	315		1,402	415	
In-hospital mortality	169 (6.2)	64 (8.8)	0.016	87 (6.5)	27 (8.6)	0.215	82 (5.8)	37 (8.9)	0.032
STEMI setting	121 (5.9)	47 (9.4)	0.009	67 (6.7)	20 (9.3)	0.189	54 (5.2)	27 (9.4)	0.012
NSTEMI setting	48 (6.8)	17 (7.6)	0.654	20 (5.9)	7 (7.0)	0.642	28 (7.6)	10 (8.1)	0.847
Mechanical complications	33 (1.2)	13 (1.8)	0.206	17 (1.3)	5 (1.6)	0.592	16 (1.1)	8 (2.0)	0.220
Free wall rupture	20 (0.7)	4 (0.6)	0.802	11 (0.8)	1 (0.3)	0.482	9 (0.6)	3 (0.7)	0.740
Ventricular septal rupture	9 (0.3)	8 (1.1)	0.014	5 (0.4)	3 (1.0)	0.182	4 (0.3)	5 (1.2)	0.032
Papillary muscle rupture	5 (0.2)	1 (0.1)	1	2 (0.2)	1 (0.3)	0.470	3 (0.2)	0 (0)	1

Unless indicated otherwise, data are given as n (%).The control period was from February 2016 to January 2019 and the COVID-19 period was from February 2020 to January 2021. NSTEM, non-ST segment elevation myocardial infarction; STEMI, ST-elevation myocardial infarction.

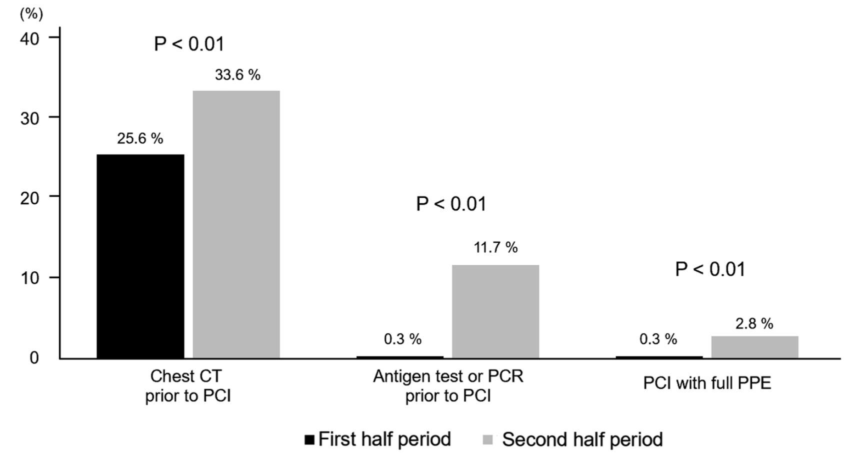

Figure 4. Comparison of the frequency of screening tests for COVID-19 and primary percutaneous coronary intervention (PCI) with full personal protective equipment (PPE) in acute myocardial infarction patients between the first and second halves of the COVID-19 period. CT, computed tomography; PCR, polymerase chain reaction.

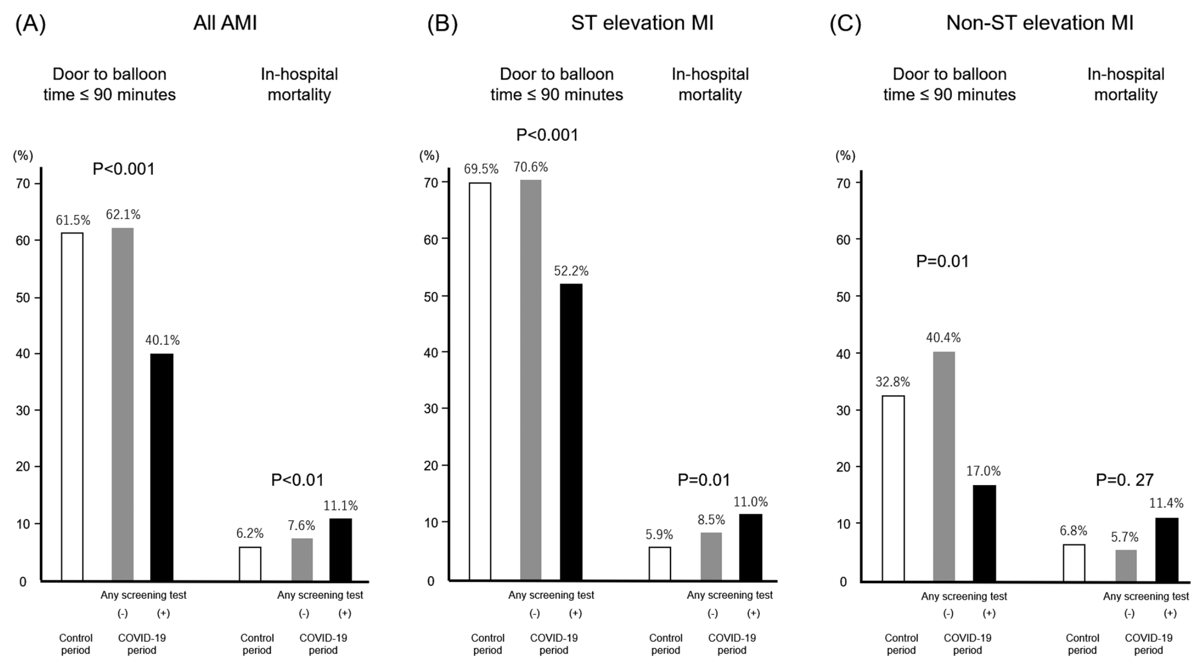

Figure 5. Association of COVID-19 screening tests before primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI) patients with door-to-balloon (DTB) time and in-hospital mortality. (**A**,**B**) Screening tests for COVID-19 and/or primary PCI with full personal protective equipment (PPE) reduced the rate of a DTB time ≤90 min and increased in-hospital mortality in AMI (**A**) and ST-elevation myocardial infarction (STEMI; **B**) patients. (**C**) Screening tests for COVID-19 reduced the rate of a DTB time ≤90 min, with a trend for increased in-hospital mortality in non-STEMI patients.

the COVID-19 period, particularly the second half (P<0.001), than during the control period.

Outcomes of AMI Patients During the COVID-19 and Control Periods

As indicated in **Table 3**, the in-hospital mortality rate of AMI was significantly higher during the COVID-19 than control period (8.8% vs. 6.2%; P=0.016), particularly during the second half (8.9% vs. 5.8%; P=0.032), and among STEMI patients (9.4% vs. 5.9%; P=0.009). The incidence of ventricular septal rupture was higher during the COVID-19 than control period (1.1% vs. 0.3%; P=0.014), whereas overall mechanical complication rates were similar (**Table 3**).

Screening Tests for COVID-19 and PCI Under Full PPE

The frequency of screening tests for COVID-19 increased with the spread of the pandemic (**Figure 4**). Antigen or PCR tests were performed on 11.7% of AMI patients prior to PCI and 2.8% of PCIs were performed under full PPE during the second half of the COVID-19 period, which was a significant increase from the first half. In the present study, all antigen and PCR tests were negative. In addition, AMI patients who underwent screening tests for COVID-19 and/or primary PCI under full PPE had a lower rate of achieving a DTB time of ≤90 min and higher in-hospital mortality (P<0.001; **Figure 5**).

Discussion

This is the first study to report demographic trends in the number of AMI patients in the first 12 months of the COVID-19 pandemic and the effects of COVID-19 on the pre- and in-hospital management of AMI throughout a whole prefectural medical area.

The significant findings in the present study are that: (1) the number of cases of AMI and the frequency of emergency PCI throughout the COVID-19 period were similar to those during the control period, although the number of AMI patients decreased in the first half of the COVID-19 period, particularly after the declaration of a state of emergency; (2) the proportion of AMI patients who were transported directly to hospital by ambulance was significantly lower in the first half of the COVID-19 period than in the control period; (3) there was a higher proportion of patients with more severe Killip class and higher rates out-of-hospital cardiac arrest and in-hospital mortality during the COVID-19 period; and (4) screening tests for COVID-19 and full PPE management were more often performed during the second half of the COVID-19 period.

In the present study, the number of AMI patients decreased markedly in the first half of the COVID-19 period, particularly after the declaration of a state of emergency, which is consistent with previous findings in Japan and worldwide.[4,7,11,18] A study conducted in England reported that the number of AMI cases decreased only in the first 2–3 months after the outbreak of the COVID-19 pandemic and then began to increase.[4] The decline started before the lockdown was imposed and increased thereafter.[4] In our analysis, the number of STEMI patients started to decrease after the declaration of a state of emergency, continued to decrease even after the state of emergency was lifted, and started to increase approximately 3 months later, which is consistent with the findings reported in England. These results suggest that a decrease in physical activity and mental stress due to social conditions, such as the declaration of a state of emergency, may have temporarily delayed the onset of STEMI for 2–3 months; however, no significant changes were observed in the number of cases throughout the year.[5,7] This result is reasonable because the development of STEMI is largely due to the formation of an intravascular plaque over many years and thrombus occlusion from plaque rupture. Even if the onset of STEMI is delayed for several months with rest, it will inevitably occur with resumption of physical activity and social stress.[19,20] In addition, AMI patients refrained from visiting hospitals and hesitated to call an ambulance because of the risk of COVID-19 infection and preferentially visited local clinics.[11] These factors may have contributed to the increased out-of-hospital cardiac arrest rate, prolonged onset-to-door time, and increase in both the number of patients with severe AMI and the in-hospital mortality rate in the present study, which are consistent with the findings of previous studies.[12,21,22]

Patients' behavioral changes also affected the transport pathway in the first half of the COVID-19 period with the spread of infection. During the 12-month observational periods, in-hospital mortality rates for AMI patients increased due to a prolonged onset-to-balloon time resulting from a decrease in direct ambulance transfers. Direct transfers decreased in the first half of the COVID-19 period; however, a reduction was also observed in the frequency of STEMI, which is considered to have a high mortality rate. Therefore, despite the increase in the onset-to-balloon time, the overall mortality rate for AMI was only slightly higher in the COVID-19 than control period. In contrast, there were no significant differences in the rates of STEMI or direct ambulance transport between the second half of the COVID-19 period and the control period, whereas there were significant increases in the chest CTs, PCR tests before PCI, and the use of full PPE, which predominantly accounted for the prolonged DTB time. This may have contributed to the significantly higher in-hospital mortality rate observed during the COVID-19 period. Preventing delays in the DTB time is one of the pressing issues that needs to be addressed during the COVID-19 period.

The number of patients with the left anterior descending artery (LAD) as the culprit artery was higher during the COVID-19 than control period, especially during the second half of the COVID-19 period. Although there is no clear reason for this phenomenon based on the data available in the Mie ACS Registry, similar findings have been reported from a national registry in Japan, in which there were significantly more AMI patients with LAD and left main trunk culprits during the COVID-19 than control period.[23] This may contribute to the poor prognosis of AMI patients in later years.[23]

The recovery of hospital admission rates among AMI patients in England suggests that the British Heart Foundation and British Cardiovascular Society publicity campaign, in which individuals with symptoms of MI were encouraged to visit a hospital, may have allayed fears of infection. Similarly, in April 2020 in Japan, the Cardiovascular Intervention and Therapeutics (CVIT) and Japanese Circulation Society academic societies revealed a strategy for AMI during the COVID-19 pandemic and primary PCI for STEMI was recommended under PPE. Moreover, the CVIT encouraged all individuals with symptoms of AMI to immediately go to a hospital instead of "staying at home". In Mie prefecture, primary PCI for AMI patients was not restricted during the COVID-19 period, which may be reflected by the similar total number of primary PCIs between the COVID-19 and control periods. Conversely, elective PCI was not performed as frequently after the declaration of the state of emergency in Japan.[24] Presumably a certain number of angina patients who did not undergo PCI became unstable and developed NSTEMI, leading to an increase in the number of NSTEMI patients during the COVID-19 period. Japanese national registry data confirmed an increase in the number of NSTEMI patients in 2020 during COVID-19 compared with 2019.[23] This increase is not only an increase in the percentage of NSTEMI patients, but also an increase in their absolute number. In the present study, as well as in the Japanese national registry data,[23] the number of NSTEMI patients during COVID-19 increased compared with the period of interest. The reason for this is assumed to be that, during the COVID-19 period, patients with unstable or stable angina who were prevented from accessing hospitals due to emergency declarations or other reasons developed NSTEMI due to a worsening of their medical condition.[23]

In contrast with our data from Japan, Lavie et al reported that, in Israel, the number of AMI patients during the first 12 months of the pandemic was lower than the average of the previous 3 years.[25] The variability in the rates of decline in the number of AMI patients across countries during the pandemic is evidence of the multiplicity of underlying factors, like the non-uniform intensity of the pandemic, variations in the stringency of lockdowns, and public health-related factors.

This study has some strengths. Although there have been a few papers reporting on the 12-month follow-up of the number of AMI patients after the COVID-19 pandemic, the analyses used national databases and did not present detailed patient data.[25] The data in this study provide detailed patient information over a 12-month period for AMI patients in an entire prefectural medical area.

Study Limitations

In this study we collected data in a relatively rural area, which was a non-epidemic area. Studies on urban areas that include epidemic areas will provide more detailed information on AMI during the COVID-19 pandemic. Further studies are warranted to examine changes in AMI during the COVID-19 pandemic. In addition, the main reason for the decline in the direct transfer rate is unknown and detailed information of indirect transfers is not available from the current registration data.

Conclusions

The number of AMI cases during the COVID-19 pandemic period was similar to that in previous years. The COVID-19 pandemic induced behavioral changes in AMI patients and altered pre- and in-hospital medical management, significantly affecting severity and prognosis of AMI patients.

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IRB Information

The Mie ACS Registry was approved by the Institutional Review Board of the Mie University Graduate School of Medicine (Reference no. 2881) and the ethics committees of all participating institutions. It has been registered with the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (ID: UMIN000036020).

Data Availability

Individual deidentified participant data (including data dictionaries), the Excel data used for analysis, and the study protocol will be shared upon request to the corresponding author. The data will be available for 1 year after publication.

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Supplementary Files

Please find supplementary file(s);
http://dx.doi.org/10.1253/circrep.CR-22-0050