



Incidence and Demographic Trends for Acute Coronary Syndrome in a Non-Epidemic Area During the Coronavirus Disease Pandemic in Japan

— A 2-Institutional Observational Study —

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Background: We investigated the incidence of acute coronary syndrome (ACS) in a non-epidemic area of coronavirus disease-2019 (COVID-19) in Japan.

Methods and Results: This observational study included consecutive patients admitted for ACS at 2 tertiary hospitals in Izumo City during the pandemic in Japan (n=42, March–July 2020). Although the monthly ACS incidence was comparable, the proportions of delayed admissions and high Killip class (III/IV) were significantly higher in this population than in historical cohorts (n=197, 2015–2019).

Conclusions: Our findings stress the importance of encouraging patients with ACS-related symptoms to visit medical services promptly, especially in non-epidemic areas.

Key Words: Acute coronary syndrome; Coronavirus disease 2019; Pandemics

Coronavirus disease-2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2), is an ongoing worldwide pandemic.¹ The widespread nature of the COVID-19 pandemic has incurred a huge healthcare burden and resulted in collapse of medical systems.² Studies in Western countries have reported that the incidence of acute myocardial infarction (AMI) dramatically decreased in the era of the COVID-19 pandemic compared with previous years,^{3–5} postulated to be a result of patients with AMI avoiding visits to hospitals. Furthermore, delay in arriving at a medical institution after symptom onset occurred.^{4,6,7} Even in Taiwan, where COVID-19 was non-epidemic, delays in admission of patients with AMI were observed; however, the incidence of AMI in Taiwan in 2020 was comparable to that reported in previous years.⁸ In Japan, although a nationwide survey showed that performance of primary percutaneous coronary intervention (PCI) for ST-elevation

myocardial infarction (STEMI) was preserved in most institutions during the pandemic,⁹ data regarding the incidence and demographics of acute coronary syndrome (ACS) are very scant. We investigated the incidence of ACS in Izumo City (rural Japan) where COVID-19 was non-epidemic during the pandemic (January–July 2020) and compared it with the incidence in the past 5 years (2015–2019). Furthermore, we investigated if the delay in admission of patients with ACS occurred during the pandemic in Japan (March–July 2020).

Methods

Study Design and Data Collection

This retrospective observational study was conducted at 2 tertiary hospitals in which a cardiac care unit was available (Shimane Prefectural Central Hospital [Institution A] and Shimane University Hospital [Institution B]) in Izumo

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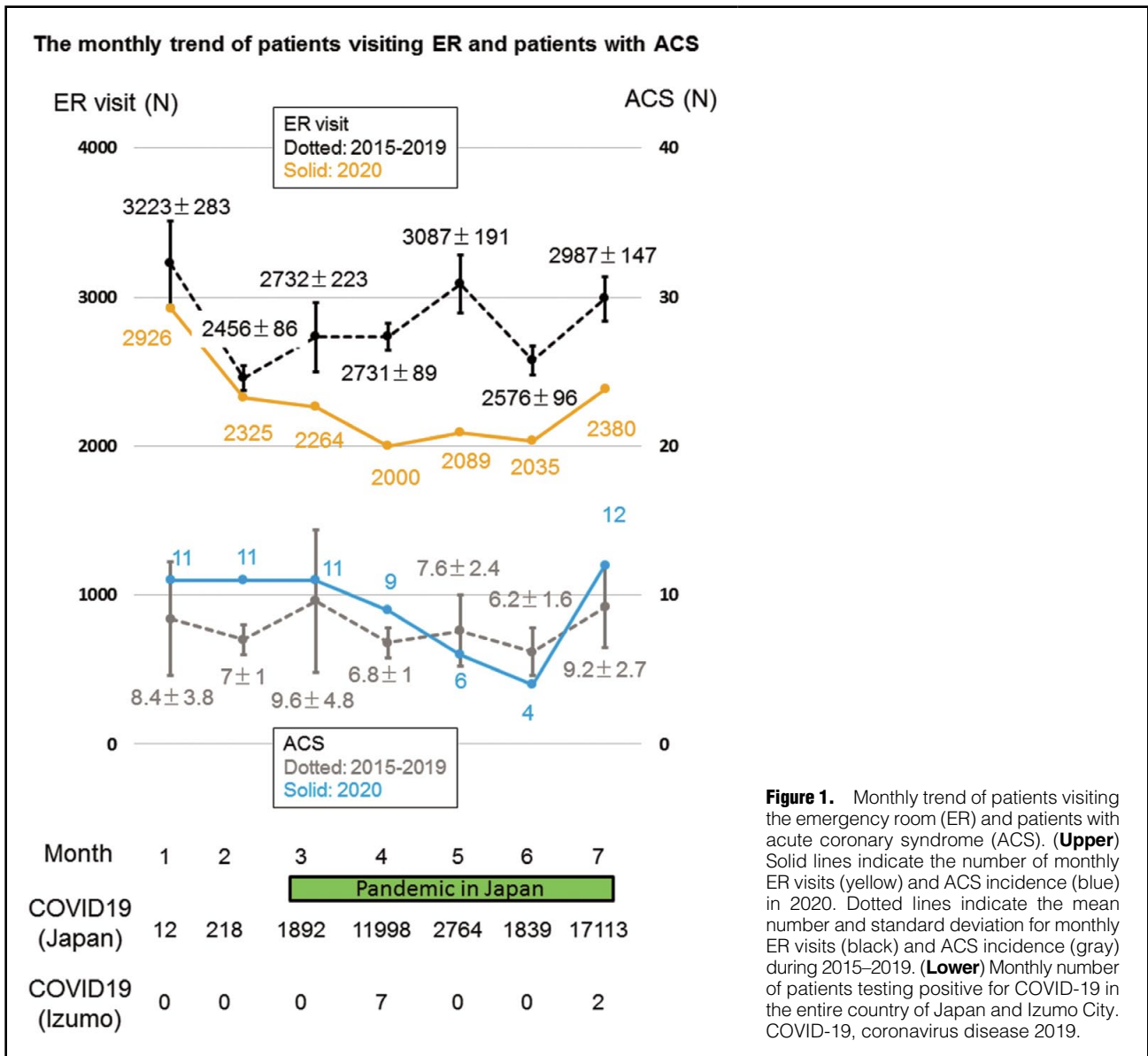


Figure 1. Monthly trend of patients visiting the emergency room (ER) and patients with acute coronary syndrome (ACS). (Upper) Solid lines indicate the number of monthly ER visits (yellow) and ACS incidence (blue) in 2020. Dotted lines indicate the mean number and standard deviation for monthly ER visits (black) and ACS incidence (gray) during 2015–2019. (Lower) Monthly number of patients testing positive for COVID-19 in the entire country of Japan and Izumo City. COVID-19, coronavirus disease 2019.

City. Izumo City is a medium-sized city (population in 2020: 174,686) in Shimane prefecture, a rural area in southwest Japan. No other institution in the city has the equipment to perform cardiac catheterization.¹⁰

With regard to the study period, the period of the COVID-19 pandemic overall was regarded as January–July 2020 and that of the pandemic in Japan was considered to be March–July 2020 because the number of patients who tested positive for COVID-19 in Japan has exceeded 1,000 since March. For evaluating if patients really avoided visiting hospital, the number of patients who visited the emergency room (ER) at the 2 institutions during the entire study period was also calculated. Consecutive patients who developed ACS, which constituted STEMI, non-STEMI (NSTEMI), and unstable angina pectoris (UAP), and who were admitted to hospital within 48 h after symptom onset were enrolled in the study. Patients who developed ACS as inpatients were excluded. Data were collected by reviewing electronic medical records at each institution, as previously

described.¹⁰ Patient demographics were then compared with a historical cohort (data of ACS patients in corresponding months from 2015 to 2019). A diagnosis of AMI was made as per the universal definition.¹¹ Elevation of cardiac enzymes was defined as a level above the 99th percentile of the high-sensitivity cardiac troponin assay. STEMI/NSTEMI was characterized as a diagnosis of AMI with/without an elevation of the ST-T segment in at least 2 contiguous ECG leads or development of left bundle branch block. Patients without elevation of cardiac enzymes were diagnosed as UAP. The requirement for informed consent was waived owing to the retrospective design of the study. Accordingly, an opt-out system design was selected for the present study, and all study-related information was disclosed on the website of each institution.

Statistical Analysis

Normally distributed variables are expressed as mean ± standard deviation, and non-normally distributed variables

	Overall COVID-19 pandemic (n=64, January–July, 2020)	Historical cohort (n=274, January–July, 2015–2019)	P value
Age (years), mean±SD	73±13	72±12	0.59
Male, n (%)	44 (69)	199 (73)	0.53
STEMI, n (%)	45 (70)	179 (65)	0.44
Peak CK (IU/L), median (IQR)	1,125 (413, 3,879)	1,083 (308, 2,524)	0.22
Time from symptom onset to arrival (h), median (IQR)	4 (1, 18)	2.5 (1, 8)	0.08
Killip class, mean±SD*	1.9±1.2	1.5±1	0.003
CPA at presentation, n (%)	6 (9)	23 (8)	0.81
Emergency CAG	52 (81)	218 (80)	0.76
PCI, n (%)	55 (86)	235 (86)	0.97
CABG, n (%)	3 (5)	20 (7)	0.45
Hospital stay (days), mean±SD	13 (7.5, 19)	13 (8, 19)	0.78
In-hospital deaths, n (%)	8 (12)	24 (9)	0.35

Numerical data are expressed as the mean±SD or as the median (interquartile range (IQR); 1st–3rd quartile). Categorical data are expressed as the percentage (%) and number. *Statistical significance (P<0.05). CABG, coronary artery bypass grafting; CAG, coronary angiography; CK, creatinine kinase; CPA, cardiopulmonary arrest; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

	Pandemic in Japan (n=42, March–July, 2020)	Historical cohort (n=197, March–July, 2015–2019)	P value
Age (years), mean±SD	74±12	72±12	0.63
Male, n (%)	31 (74)	141 (72)	0.77
STEMI, n (%)	35 (83)	136 (69)	0.06
Peak CK (IU/L), median (IQR)*	1,703 (793, 4,663)	1,132 (316, 2,402)	0.01
Time from symptom onset to arrival (h), median (IQR)	4.3 (1, 18)	2.5 (1, 7)	0.08
Killip class, mean±SD*	1.9±1.2	1.5±1	0.006
CPA at presentation, n (%)	4 (9)	16 (8)	0.77
Emergency CAG	34 (81)	159 (81)	0.97
PCI, n (%)	36 (86)	166 (84)	0.81
CABG, n (%)	2 (5)	16 (8)	0.45
Hospital stay (days), mean±SD	14 (9, 20)	13 (8, 20)	0.59
In-hospital mortality, n (%)	6 (14)	17 (9)	0.25

Numerical data are expressed as the mean±SD or as the median (interquartile range (IQR); 1st–3rd quartile). Categorical data are expressed as the percentage (%) and number. *Statistical significance (P<0.05). Abbreviations as in Table 1.

are presented as median and interquartile (1st and 3rd) range. Differences in continuous variables between groups were compared using the Mann-Whitney U test. Categorical variables are presented as frequency and proportion (%), and were compared using the chi-square (χ^2) test. All analyses were performed using JMP version 13.2 (SAS Institute Inc., Cary, NC, USA), with a P<0.05 considered statistically significant.

Results

Incidence of COVID-19-Positive Patients in Izumo City During the Pandemic

In Izumo City, 9 patients were diagnosed as COVID-19-positive during the period of the pandemic, and all were admitted to Institution A. No patient required the use of a ventilator or died of COVID-19. The number of patients testing positive for COVID-19 in 1 month was significantly lower in Izumo City than in Japan overall (0 [0, 1.5] vs. 1892 [623, 9689], P<0.0001).

ER Visits During the Pandemic

In contrast, the number of patients visiting the ER decreased during the study period. In particular, this number drastically decreased during the pandemic in Japan (**Figure 1**).

Incidence of ACS During the Pandemic

During the entire study period, 64 patients presented with ACS. The incidence of ACS per month during the pandemic and that in previous years was comparable (9.1±3 vs. 7.8±1.3, P=0.31, **Figure 1**). The patient demographics during the entire study period are shown in **Table 1**. Furthermore, the demographics during the pandemic in Japan were also compared (**Table 2**). The Killip class was significantly higher in 2020 than in previous years (1.9±1.2 vs. 1.5±1, P=0.003). The Killip class and peak creatinine kinase (CK) levels were significantly higher during the pandemic in Japan. Furthermore, the proportion of patients with symptom onset ≥24 h before admission and a Killip class of III/IV was significantly higher during this period (**Figure 2**).

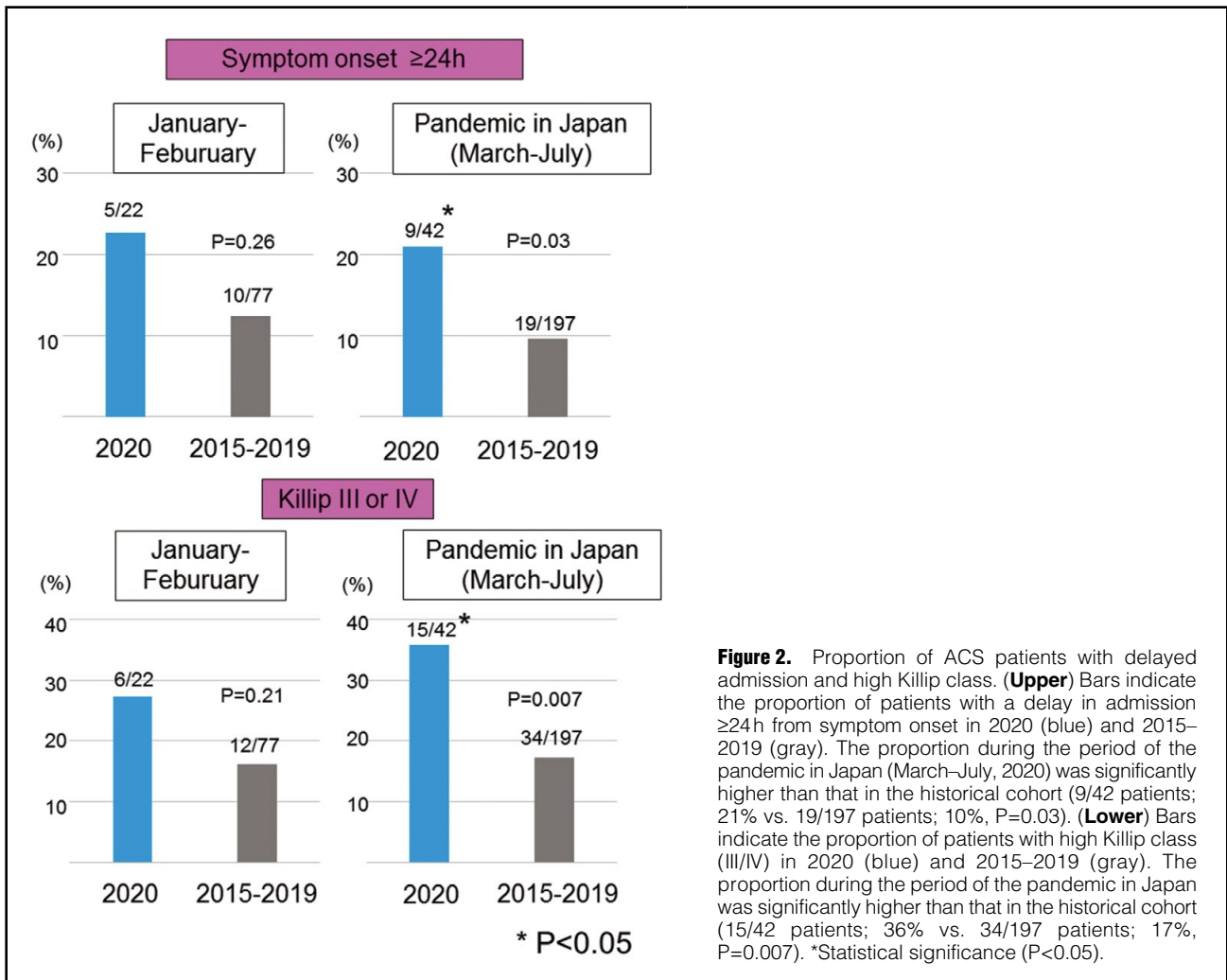


Figure 2. Proportion of ACS patients with delayed admission and high Killip class. (**Upper**) Bars indicate the proportion of patients with a delay in admission ≥ 24 h from symptom onset in 2020 (blue) and 2015–2019 (gray). The proportion during the period of the pandemic in Japan (March–July, 2020) was significantly higher than that in the historical cohort (9/42 patients; 21% vs. 19/197 patients; 10%, $P=0.03$). (**Lower**) Bars indicate the proportion of patients with high Killip class (III/IV) in 2020 (blue) and 2015–2019 (gray). The proportion during the period of the pandemic in Japan was significantly higher than that in the historical cohort (15/42 patients; 36% vs. 34/197 patients; 17%, $P=0.007$). *Statistical significance ($P<0.05$).

Discussion

To the best of our knowledge, this is the first study demonstrating the incidence of ACS in an area of Japan where COVID-19 was non-epidemic during the COVID-19 pandemic. Our findings were as follows. First, although the number of patients with COVID-19 was limited during the entire study period, the number of patients visiting the ER dramatically decreased during the pandemic in Japan (March–July 2020). Second, the incidence of ACS in an area where COVID-19 was non-epidemic in Japan was comparable with that reported in previous years. Third, in contrast, the proportion of patients with delayed admission for ACS after symptom onset significantly increased during the pandemic in Japan compared with that observed during previous years. Furthermore, an increase in the severity of patients with ACS was also observed, because they had significantly higher Killip class and peak CK levels than those reported in previous years.

In Japan, although a national lockdown strictly restricting personal movement was not enforced, the government requested nationwide closure of schools since March 1, 2020.^{12,13} In addition, a national state of emergency was declared on April 7, 2020 in areas with widespread COVID-19; this nationwide emergency state was extended

on April 16 and lifted in May 25.⁹ As a response, academic societies associated with cardiac catheterization declared postponement of non-urgent planned procedures to preserve medical resources.^{14,15} Life-saving procedures (i.e., primary PCI for STEMI patients) were not encouraged to be postponed, excluding cases of patients already diagnosed to have very severe SAR-Cov-2 infection.¹⁴ Indeed, a nationwide survey showed that $>90\%$ of institutions performed primary PCI for patients with STEMI as usual, even in areas where COVID-19 was epidemic.⁹ Our results also showed that procedures associated with ACS such as emergency coronary angiography, PCI, and coronary artery bypass grafting were maintained during the entire period. In contrast, studies in Western countries have shown that the incidence of AMI drastically decreased by 30–40% compared with prepandemic periods.^{3–5,7} As well as this decrease, the number of patients undergoing primary PCI for STEMI also dropped by nearly 13–40%.^{4,5,7,16} The reduction in the incidence of AMI reflected the reluctance of patients requiring emergency care to contact medical services, fearing exposure to COVID-19.^{3–5} Although a decreasing trend in the incidence of STEMI was observed in non-epidemic areas in Western countries,^{4,7} a study from a non-epidemic area in Asia showed that there was no reduction in the incidence of STEMI.⁸ The previous studies

have also shown that delays in contacting medical services after symptom onset were commonly observed in areas where COVID-19 was epidemic and non-epidemic.^{4,7,8} With regard to our data, there was no reduction in the incidence of ACS in the non-epidemic area in Japan. However, we also showed the proportion of patients with delayed hospitalization (≥ 24 h delay after symptom onset) was significantly increased during the pandemic in Japan compared with prepandemic times. These data was in line with previous studies.^{4,6-8} Furthermore, we added the information that the proportion of patients with severe ACSs (Killip class: III/IV, high peak CK levels) also increased during the pandemic. However, our data also showed that the short-term effects were limited because the in-hospital mortality was comparable; nonetheless, the delay may affect long-term adverse effects such as development of heart failure. Our results stress that it may be required to encourage patients experiencing symptoms to promptly contact medical services in non-epidemic areas.

Study Limitations

There were several limitations to note. First, data in this study were collected in the early phase of the pandemic (January–July 2020). The clinical situation may vary dynamically, given that the COVID-19 pandemic is still ongoing with the emergence of second and third waves. Hence, it is unknown if the trend we observed is applicable to current clinical settings. Further studies with a more long-term study period are warranted. Second, we collected data in a non-epidemic rural area. Studies in other areas (e.g., urban areas, epidemic areas) might help elucidate the trends in ACS incidence during the COVID-19 pandemic in Japan. Third, the present study was a 2-institutional retrospective observational study. Accordingly, our study may have missed patients who completed treatment for ACS at other institutions. However, this proportion would be limited because the number of cardiologists in other institutions is small.¹⁰

Conclusions

Our findings suggested that the ACS incidence during the COVID-19 pandemic in a non-epidemic area in Japan was comparable with that in previous years, although the number of patients visiting ER dramatically decreased. However, the proportion of patients with delayed admission and high severity significantly increased during the pandemic in Japan (March–July 2020). Our data also suggest the importance of encouraging patients with ACS-related symptoms to visit medical services promptly, especially in non-epidemic areas.

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Data Availability

The deidentified participant data will not be shared.

Disclosures

The authors declare no conflicts of interest. This research received no

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IRB Information

This study followed the Declaration of Helsinki and ethical standards of the responsible committee on human experimentation. The Institutional Review Boards of Shimane Prefectural Central Hospital (Churin R20-34) and Shimane University Hospital (20201031-1-5151) approved this study.

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