Editors' Choice

ORIGINAL PAPER

Nagoya J. Med. Sci. **83**. 697–703, 2021
doi:10.18999/nagjms.83.4.697

Prevalence of acute coronary syndrome during the pandemic of COVID-19 in the Tokai Region of Japan

Nobutaka Kudo[1,2], Akihito Tanaka[1], Hideki Ishii[1,2], Yusuke Uemura[3], Kensuke Takagi[4], Makoto Iwama[5], Ruka Yoshida[6], Taiki Ohashi[7], Hideki Kawai[8], Yosuke Negishi[9], Norio Umemoto[10], Miho Tanaka[11], Masato Watarai[3], Naoki Yoshioka[1,4], Itsuro Morishima[4], Toshiyuki Noda[5], Yukihiko Yoshida[6], Yosuke Tatami[7], Takashi Muramatsu[8], Toshikazu Tanaka[9], Hiroshi Tashiro[10], Yasunobu Takada[11], Hideo Izawa[8], Eiichi Watanabe[2] and Toyoaki Murohara[1]

[1]*Department of Cardiology, Nagoya University Graduate School of Medicine, Nagoya, Japan*
[2]*Department of Cardiology, Fujita Health University Bantane Hospital, Nagoya, Japan*
[3]*Cardiovascular Center, Anjo Kosei Hospital, Anjo, Japan*
[4]*Department of Cardiology, Ogaki Municipal Hospital, Ogaki, Japan*
[5]*Department of Cardiology, Gifu Prefectural General Medical Center, Gifu, Japan*
[6]*Department of Cardiology, Japanese Red Cross Society, Nagoya Daini Hospital, Nagoya, Japan*
[7]*Department of Cardiology, Toyota Kosei Hospital, Toyota, Japan*
[8]*Department of Cardiology, Fujita Health University School of Medicine, Toyoake, Japan*
[9]*Department of Cardiology, Okazaki Municipal Hospital, Okazaki, Japan*
[10]*Department of Cardiology, Ichinomiya Municipal Hospital, Ichinomiya, Japan*
[11]*Department of Cardiology, Konan Kosei Hospital, Konan, Japan*

ABSTRACT

The outbreak of coronavirus disease 19 (COVID-19) has had a great impact on medical care. During the COVID-19 pandemic, the rate of hospital admissions has been lower and the rate of in-hospital mortality has been higher in patients with acute coronary syndrome (ACS) in Western countries. However, in Japan, it is unknown whether the COVID-19 pandemic has affected the incidence of ACS. In the study, eleven hospitals in the Tokai region participated. Among enrolled hospital, we compared the incidence of ACS during the COVID-19 pandemic (April and May, 2020) with that in equivalent months in the preceding year as the control. During the study period; April and May 2020, 248 patients with ACS were admitted. Compared to April and May 2019, a decline of 8.1% [95% confidence interval (CI) 5.2–12.1; P = 0.33] in admissions for ACS was observed between April and May 2020. There was no significant difference in the strategy for revascularization and in-hospital deaths between 2019 and 2020. In conclusion, the rate of admission for ACS slightly decreased during the COVID-19 pandemic, compared to the same months in the preceding year. Moreover, degeneration of therapeutic procedures for ACS did not occur.

Keywords: COVID-19, acute coronary syndrome

Abbreviations:
ACS: acute coronary syndrome

Received: September 9, 2020; accepted: February 16, 2021

Corresponding author; Hideki Ishii, MD, PhD

Department of Cardiology, Fujita Health University Bantane Hospital, 3-6-10 Otobashi, Nakagawa-ku, Nagoya 454-8509, Japan

Tel: +81-52-323-5656, Fax: +81-52-323-6399, E-mail: hkishii@med.nagoya-u.ac.jp

COVID-19: coronavirus disease 2019
PCI: percutaneous coronary intervention
STEMI: ST elevation myocardial infarction

INTRODUCTION

Since the initial detection of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus in 2019, the number of coronavirus disease 19 (COVID-19) cases have been increasing and more than 6,416,000 cases including approximately 383,000 deaths have been reported worldwide as of June 4, 2020.[1]

A report has suggested relationships between COVID-19 and cardiac disease.[2] The cytokine storm due to inflammatory respiratory disease may induce coronary plaque rupture, resulting in onset of acute coronary syndrome (ACS).[3,4] In contrast, reports have suggested a decreased in the incidence of acute myocardial infarction (AMI) during the COVID-19 outbreak in Western countries.[5-8] However, limited data are available on the incidence of ACS during the COVID-19 pandemic in Japan.

Moreover, the COVID-19 pandemic might prompt hospitals to suspend or delay medical services. Because specific factors may greatly affect the clinical outcomes in patients with ACS, it is important to evaluate how the pandemic situation has affected the rate of in-hospital mortality in patients with ACS.

The aim of the present study was to evaluate the influence of the COVID-19 pandemic on the incidence of ACS in Japan.

METHODS

We performed a retrospective observational study in 11 hospitals in the Tokai area of Japan. There was at least one board-certified interventionist of the Japanese Association of Cardiovascular Intervention and Therapeutics in every participating hospital that had high performance for emergency percutaneous coronary intervention (PCI). We evaluated patients with ACS who were admitted to each hospital from April 1 to May 31, 2020.

Some variables were compared between the study period (April 1 to May 31, 2020) and the control: the inter-year period (April 1 to May 31, 2019). ST elevation myocardial infarction (STEMI), non-STEMI, and unstable angina were defined as previously reported.[9] Treatment strategies including revascularization and medical treatment were left to the discretion of the individual cardiologists in charge. The study protocol and use of registry data were approved by the institutional ethics committee at each hospital in accordance with the Declaration of Helsinki.

We obtained data on coronary risk factors such as hypertension, diabetes, dyslipidemia and renal function. In addition, coronary angiographical findings and methods of coronary revascularization were collected. As the in-hospital outcomes, data on door-to-balloon time in STEMI cases and in-hospital death were also analyzed.

STATISTICAL ANALYSIS

Continuous variables are presented as mean (± standard deviation) or median with the

interquartile range. Categorical variables are presented as percentages. As to continuous variables, differences between the study and the control periods were analyzed by a Student unpaired t-test or Mann-Whitney *U* test. As to categorical variables, comparisons across the 2 periods were performed by a chi-square test. Point differences with 95% confidence intervals are presented for incidence of ACS.

Statistical analysis was performed using SPSS Version 22 (IBM Corp., Armonk, NY, USA). Differences were considered significant at $P < 0.05$.

RESULTS

The study included consecutive 248 patients with ACS who were admitted between April 1 and May 31, 2020. We compared them to 270 subjects in the preceding year. Compared to April 1 to May 31, 2019, there was a 8.1% [95% confidence interval (CI) 5.2–12.1; P = 0.33] reduction of ACS cases between April 1 and May 31, 2020. Except for 2 cases, we performed coronary angiography (CAG) and decided strategies for coronary revascularization. One in 2019 was a 96 year-old female who presented with typical STEMI. Because of very high age as well as frailty, we did not perform CAG. One in 2020 who was admitted due to anterior-septal STEMI suffered from cardiac rupture, resulting in death before CAG.

Table 1 Clinical characteristics of enrolled patients

	2019 n=270	2020 n=248	p-value
Age, y	70.9±11.5	68.5±12.0	0.02
Male	212 (78.5%)	198 (79.8%)	0.71
Body mass index	23.7±3.4	23.9±4.1	0.69
Hypertension	205 (75.9%)	171 (69.0%)	0.08
Diabetes	99 (36.7%)	90 (36.3%)	0.93
Dyslipidemia	205 (75.9%)	186 (75.0%)	0.81
Current smoking	68 (25.2%)	71 (28.6%)	0.38
estimated glomerular filtration rate <60 mL/min/1.73m^2	118 (43.7%)	119 (48.0%)	0.33
Hemodialysis	12 (4.4%)	14 (5.6%)	0.53
Prior myocardial infarction	32 (11.9%)	35 (14.1%)	0.44
Prior PCI	63 (23.3%)	59 (23.8%)	0.90
Prior CABG	16 (5.9%)	7 (2.8%)	0.09
Types of ACS			0.38
STEMI	147 (54.4%)	120 (48.4%)	
Non-STEMI	47 (17.4%)	47 (19.0%)	
Unstable angina	76 (28.1%)	81 (32.7%)	

Target vessel			0.60
LMT	10 (3.7%)	10 (4.0%)	
LAD	106 (39.3%)	111 (44.8%)	
LCX	41 (15.2%)	38 (15.3%)	
RCA	91 (33.7%)	76 (30.6%)	
Graft	4 (1.5%)	1 (0.4%)	
Multivessel/ unclear	18 (6.7%)	12 (4.8%)	
Treatment for Revascularization			0.19
PCI	242 (89.6%)	233 (94.0%)	
CABG	17 (6.3%)	8 (3.2%)	
Medication	11 (4.1%)	7 (2.8%)	
Mechanical Support			
Impella®	2 (0.7%)	1 (0.4%)	1.00
IABP	39 (14.4%)	36 (14.5%)	0.98
PCPS	7 (2.6%)	8 (3.2%)	0.67

ACS: acute coronary syndrome
CABG: coronary artery bypass graft
IABP: intra-aortic balloon pumping
LAD: left anterior descending artery
LCX: left circumflex artery
LMT: left main trunk
PCI: percutaneous coronary intervention
PCPS: percutaneous cardiopulmonary support
RCA: right coronary artery
STEMI: ST elevation myocardial infarction

Table 1 shows clinical characteristics in both periods. There was no significant difference in baseline characteristics including various coronary risk factors, except for age. Types of ACS was also comparable (Figure 1). Notable, methods of revascularization and mechanical supports were performed in usual manner. We collected door-to-balloon time in STEMI cases and in-hospital death as in-hospital outcomes (Table 2). Direct PCI was performed in 141 and 118 STEMI patients in 2019 and 2020, respectively. Door-to-balloon time was similar [78.5 (62.0–119.8) in 2019 vs. 81.0 (60.0–102.0) min in 2020, P = 0.54]. Rate of in-hospital death was 5.6% of cases in 2019 and in 5.2% in 2020. No significant difference was seen between two periods (p = 0.84).

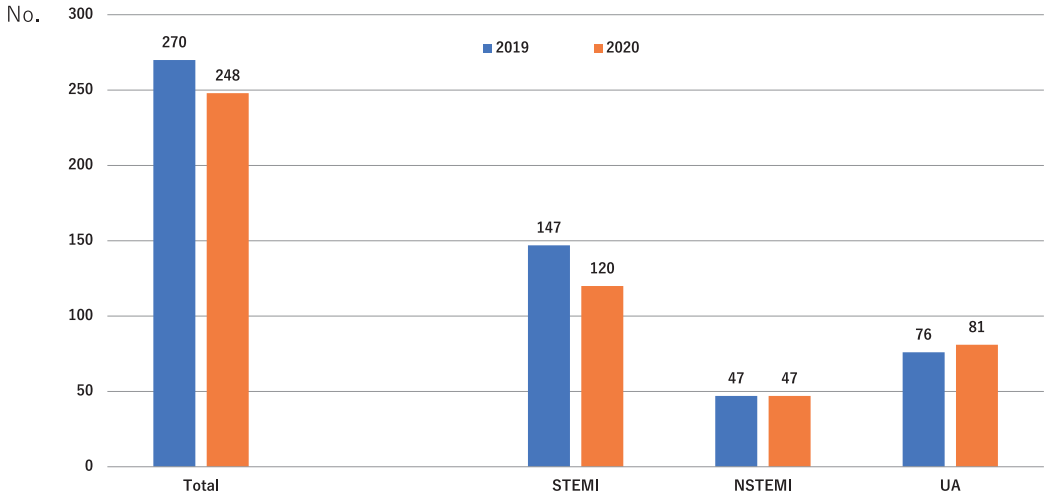

Fig. 1 Comparison of the absolute numbers of acute coronary syndrome in 2019 and 2020
Comparison of the absolute numbers of admissions for all acute coronary syndrome, ST elevation myocardial infarction (STEMI), non-STEMI and unstable angina (UA) between April and May 2019 (blue bars) and April and May 2020 (orange bars).

Table 2 Clinical outcomes

	2019	2020	p-value
In-hospital mortality	15 (5.6%) (n=270)	13 (5.2%) (n=248)	0.84
Door-to-balloon time in STEMI cases undergoing direct PCI	78.5 (62.0–119.8) (n=141)	81.0 (60.0–102.0) (n=118)	0.54

PCI: percutaneous coronary intervention
STEMI: ST elevation myocardial infarction

DISCUSSION

The first cases of COVID-19 was reported in Japan on January 17, 2020. Since then, the COVID-19 has been widely spread throughout Japan, and the Japanese government declared a state of emergency nationwide on April 16, 2020. In such situations, one of exploring points was to understand how the pandemic was impacting hospital admissions and the care of patients with ACS. During the COVID-19 pandemic, to protect the medical care system, the governments in many countries have given the alarm that people should have social distances as well as refrain from going outside as much as possible. Unfortunately, the degeneration of medical performance, for example, such as the postponement or cancelling of many elective procedures, might have a significant negative impact on society. As of mid-April 2020, some parts of scheduled PCIs were postponed according to a statement from academic societies such as the Japanese Circula-

tion Society. On the other hand, a recent study suggests that most of the Japanese institutions normally continued to perform primary PCI for STEMI cases even in the COVID-19 pandemic.[10] Our study showed that the incidence of ACS during the COVID-19 pandemic (April and May 2020) was similar to that in the equivalent months in 2019. In addition, emergency care for patients with ACS was performed as usual in the participant hospitals in the Tokai area, central Japan, during the COVID-19 pandemic. To the best our knowledge, our paper was the first report of ACS description in Japan during COVID-19 pandemic. From this point, our findings are of significance.

A report has suggested that COVID-19 is related to ischemic events such as stroke.[11] However, a significant decrease in ACS-related hospitalization rates (approximately 30%) was seen in northern Italy between February 20, 2020 and March 31, 2020, compared to the same period in the previous year.[5] A similar tendency was also seen in the US and Austria.[7,8] There may be a close association between COVID-19 and out-of-hospital cardiac mortality in Italy.[12] Thus, there is a possibility that many patients with ACS could not reach the hospital, resulting in an increase of sudden deaths. With regard to in-hospital mortality of the STEMI cases, the fatality rate was 13.7% during the pandemic in Italy, while that in the equivalent period in 2019 was 4.1% ($P < 0.001$).[6] On the contrast, the medical system in Japan was functioning well even during the pandemic, despite the fact that there are a limited number of critical care beds per 100,000 people in Japan, compared to Western countries.[13] It is noteworthy that the door-to-balloon-time in STEM and in-hospital mortality were similar between the pandemic and control periods in our study. However, we had no data on out-of-hospital cardiac mortality around catchment-areas.

Under the state of emergency declared on April 16, the Japanese government requested that people to refrain from going outside unless there was an urgent needed. As time passed, suppression of consultations, which might be associated with the loss of regular medications, raises a social problem. Poor adherence to medications may exacerbate lifestyle diseases such as hypertension, dyslipidemia and diabetes and may induce thrombotic events.[14] In addition, chronic emotional stress induces cardiovascular events.[15] During an emergency period, low physical activity raises a social problem. Such influences may greatly affect the onset of cardiovascular diseases over a long period. From this point of view, there are possible increased risks of cardiovascular disease. Therefore, data on the incidence of cardiovascular events, particularly ACS, during the chronic phases after the COVID-19 pandemic should be collected. In addition, it is unclear whether patients with ACS during the COVID-19 pandemic would have similar prognoses to those in the control period.

The study has some limitations. First, the number of participating hospitals was 11 and all hospitals were located in the Tokai region. Hence, the results could not be generalized to entire Japan and it is unknown if it represents a representative result of Japan. Second, as mentioned above, pre-hospital death due to ACS was not evaluated in the study. Therefore, it was possible that onset of ACS was underestimated. Third, we did not evaluate important data such as the onset-to-balloon time, which may affect patients' prognosis. The parameters might affect clinical outcomes in enrolled patients.

In conclusion, compared to the equivalent period in 2019, the rate of admission for ACS slightly decreased during the COVID-19 pandemic (April and May 2020) in the Tokai Region of Japan. The in-hospital mortality rate and strategies for ACS did not significantly differ between the study and control periods. Finally, we must do our best to prevent the degeneration of medical care in future outbreaks.

ACKNOWLEDGEMENT

We would like to thank all the participating hospitals for their efforts. We thank Hiroshi Takahashi, BSc for excellent assistance with the manuscript. This work was supported by the grants-in-aid of the 24th General Assembly of the Japanese Association of Medical Sciences.

CONFLICT OF INTEREST

There is no conflict of interest regarding the manuscript.

REFERENCE

1 World Health Organization. https://www.who.int/emergencies/diseases/novel-coronavirus-2019. Accessed December 20, 2020.
2 Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol*. 2020;5(7):802–810. doi:10.1001/jamacardio.2020.0950.
3 Corrales-Medina VF, Musher DM, Shachkina S, Chirinos JA. Acute pneumonia and the cardiovascular system. *Lancet*. 2013;381(9865):496–505. doi:10.1016/S0140-6736(12)61266-5.
4 Guzik TJ, Mohiddin SA, Dimarco A, et al COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. *Cardiovasc Res*. 2020;116(10):1666–1687. doi:10.1093/cvr/cvaa106.
5 De Filippo O, D'Ascenzo F, Angelini F, et al. Reduced rate of hospital admissions for ACS during Covid-19 outbreak in northern Italy. *N Engl J Med*. 2020;383(1):88–89. doi:10.1056/NEJMc2009166.
6 De Rosa S, Spaccarotella C, Basso C, et al. Reduction of hospitalizations for myocardial infarction in Italy in the COVID-19 era. *Eur Heart J*. 2020;41(22):2083–2088. doi:10.1093/eurheartj/ehaa409
7 Metzler B, Siostrzonek P, Binder RK, Bauer A, Reinstadler SJ. Decline of acute coronary syndrome admissions in Austria since the outbreak of COVID-19: the pandemic response causes cardiac collateral damage. *Eur Heart J*. 2020;41(19):1852–1853. doi:10.1093/eurheartj/ehaa314.
8 Garcia S, Albaghdadi MS, Meraj PM, et al. Reduction in STsegment elevation cardiac catheterization laboratory activations in the United States during COVID-19 pandemic. *J Am Coll Cardiol*. 2020;75(22):2871–2872. doi:10.1016/j.jacc.2020.04.011.
9 Kimura K, Kimura T, Ishihara M, et al. JCS 2018 guideline on diagnosis and treatment of acute coronary syndrome. *Circ J*. 2019;83(5):1085–1196. doi:10.1253/circj.CJ-19-0133.
10 Ishii H, Amano T, Yamaji K, et al. Implementation of percutaneous coronary intervention during the COVID-19 pandemic in Japan - nationwide survey report of the Japanese association of cardiovascular intervention and therapeutics for cardiovascular disease. *Circ J*. 2020;84(12):2185–2189. doi:10.1253/circj.CJ-20-0708.
11 Oxley TJ, Mocco J, Majidi S, et al. Large-vessel stroke as a presenting feature of Covid-19 in the young. *N Engl J Med*. 2020. doi:10.1056/NEJMc2009787.
12 Baldi E, Sechi GM, Mare C, et al. Out-of-hospital cardiac arrest during the Covid-19 outbreak in Italy. *N Engl J Med*. 2020;382(20):e60. doi:10.1056/NEJMc2009787.
13 Data from Statista. URL: https://www.statista.com/chart/21105/number-of-critical-care-beds-per-100000-inhabitants/. Accessed on December 20, 2020.
14 Allonen J, Nieminen MS, Sinisalo J. Poor adherence to beta-blockers is associated with increased long-term mortality even beyond the first year after an acute coronary syndrome event. *Ann Med*. 2020;52(3–4):74–84. doi:10.1080/07853890.2020.1740938.
15 Kario K, Matsuo T, Kobayashi H, Yamamoto K, Shimada K. Earthquake-induced potentiation of acute risk factors in hypertensive elderly patients: possible triggering of cardiovascular events after a major earthquake. *J Am Coll Cardiol*. 1997;29(5):926–33. doi:10.1016/s0735-1097(97)00002-8.