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CITATION:

Watanabe, Shusuke ...[et al]. Medium-Term Impact of the Coronavirus Disease 2019
Pandemic on the Practice of Percutaneous Coronary Interventions in Japan. *Journal of
Atherosclerosis and Thrombosis* 2022, 29(11): 1571-1587

ISSUE DATE:

2022-11-01

URL:

<http://hdl.handle.net/2433/277765>

RIGHT:

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Medium-Term Impact of the Coronavirus Disease 2019 Pandemic on the Practice of Percutaneous Coronary Interventions in Japan

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Aims: Declines in cardiovascular diseases during the first surge of coronavirus disease 2019 (COVID-19) have been reported. With the repeating surges of COVID-19, we aim to investigate the medium-term impact of the COVID-19 pandemic on the practice of percutaneous coronary interventions (PCIs).

Methods: We performed a descriptive analysis of rates of PCIs, utilizing administrative data in Japan. Changes in the proportion of severe cases and in-hospital mortality since the start of the COVID-19 pandemic were investigated using interrupted time series (ITS) analyses.

Results: From April 2018 to February 2021, 38,696 and 28,585 cases of elective and emergency PCIs, respectively, were identified. The rates of PCIs decreased during the first and third COVID-19 surges. The ratios of monthly rates of elective PCIs to that in the corresponding months during the previous 2 years were 50.3% in May 2020 and 76.1% in January 2021. The decrease in rates of emergency PCIs was smaller than that of elective PCIs. The ITS analyses did not identify any significant changes in the proportion of severe cases and in-hospital mortality.

Conclusions: We found that the impacts of COVID-19 on PCIs were larger in the first surge than in the subsequent and larger in the elective than in the emergency; this continued over the medium-term. During the COVID-19 pandemic, in-hospital mortality of cases undertaking emergency PCIs did not change.

See editorial vol. 29: 1563-1564

Key words: Percutaneous coronary intervention, Acute myocardial infarction, Stable angina, COVID-19, Mortality rate

Introduction

A large number of excess deaths due to coronavirus disease 2019 (COVID-19) has been reported globally¹⁾, which forced many countries to implement wide-ranging nonpharmaceutical interventions²⁾. As is normal during the courses of an infectious disease outbreak, many countries have experienced repeating surges of COVID-19³⁾.

Besides the direct impact of COVID-19, indirect impacts on other aspects of health have been reported. Focusing on cardiovascular diseases, significant decreases in the volume of various diseases, such as acute coronary syndrome (ACS)⁴⁻⁶⁾, heart failure⁷⁾, and arrhythmia⁸⁾, have been reported. Nevertheless,

the impact on other conditions in subsequent surges is not in agreement. A report from the United Kingdom showed a significant decrease in acute myocardial infarction (AMI) during that country's second lockdown period⁹⁾. Conversely, a report from the United States revealed no significant decrease in AMI during subsequent surges of COVID-19¹⁰⁾.

Many countries applied policies to postpone elective surgeries to ensure capacity to hospitalize patients with COVID-19¹¹⁾. Nevertheless, the impact of the policies on the quality of treatment of other areas of diseases, including cardiovascular diseases, has not been made distinct.

We analyzed time trends in the practice of percutaneous coronary interventions (PCIs) over an

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Received: July 27, 2021 Accepted for publication: November 3, 2021

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approximately 1 year period following the start of the COVID-19 pandemic in Japan. To elucidate the changes in the practice of PCIs carried out over the medium-term, we focused on the following four points:

- The impact of COVID-19 on the rates of PCIs conducted during each surge
- Whether there is a difference between the time trends in the rates of elective versus emergency PCIs
- Whether there is an impact on the rates of PCIs over the longer term
- Whether there is an impact on the outcome of PCIs

Aim

To elucidate the medium-term impact of the COVID-19 pandemic on the practice of PCIs.

Methods

Setting of the Time Period Based on the COVID-19 Pandemic in Japan

Japan has experienced repeating surges of COVID-19. **Supplementary Fig. 1** shows the trends in the number of new cases that tested positive for COVID-19 and in the number of severe cases, on the basis of official data published on the homepage of the Japanese government's Ministry of Health, Labour, and Welfare¹². **Supplementary Fig. 1** shows three surges: the first with a peak in May 2020, the second with a peak in August 2020, and the third with a peak in January 2021. In terms of nonpharmaceutical interventions, the Japanese government has twice declared an emergency from April 2020 to February 2021. An emergency declaration enables specified prefectural governors to undertake proactive nonpharmaceutical interventions¹³, including the requests for residents to prevent from going outdoors for nonemergency reasons¹⁴. Unlike other countries, such as the United States, United Kingdom, and France, interventions undertaken in Japan lacked legal enforcement and relied on voluntary efforts by residents¹⁵. The first period covered by an emergency declaration was from April 7, 2020, to May 25, 2020¹³, whereas the second period was from January 8, 2021, to March 21, 2021¹³. In this study, we set the period since April 2020 as the period covered by the COVID-19 pandemic, because during this period repeated surges of COVID-19 infections and nonpharmaceutical interventions were experienced, resulting in COVID-19 having a major impact on Japanese society.

Data Source

The data source for this study was Diagnosis Procedure Combination (DPC) data attained from the Quality Indicator/Improvement Project (QIP) database^{4, 16, 17}. The QIP database is managed by the Department of Healthcare Economics and Quality Management, Kyoto University School of Public Health. DPC data are collected from participating hospitals, which comprise acute care hospitals; these include hospitals of various sizes and that cover various geographical areas over Japan and include both public and private hospitals. The names of the QIP participating hospitals that have agreed to be made public in advance are listed on the QIP website (http://med-econ.umin.ac.jp/QIP/sanka_byouin.html). DPC data have been shown to be valid, compared with data attained from medical records^{18, 19} and include clinical data, having been utilized to show the impact of COVID-19 on clinical practice in Japan^{4, 16, 17}.

This study was conducted according to the principles of the Declaration of Helsinki and was approved by the Ethics Committee, Kyoto University Graduate School, and Faculty of Medicine (approval number: R0135) with a waiver of informed consent prior to data collection.

Study Population

The study population included patients hospitalized in hospitals that continuously provide data to the QIP from April 2018 to March 2021, admitted from April 2018 to February 2021, who aged 18 years or older and were treated with PCIs. PCIs were identified using PCI codes recorded in the E and F files of DPC data.

Among patients who received PCIs, patients undergoing elective PCIs and patients undergoing emergency PCIs were defined on the basis of their treatment procedure and diagnosis. For diagnoses, the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) was applied.

The criteria for patients with elective PCIs were as follows:

- With a diagnosis of angina, except for unstable angina (I20.x except for I20.0 and I25.x), as the most medical-resource-intensive disease and as the disease of trigger for admission.
- Recorded as a planned hospitalization.

The criteria for patients with emergency PCIs were as follows:

- With a diagnosis of ACS (I20.0, I21.x, I22.x, I23.x, or I24.x) as the most medical-resource-intensive disease and as the disease of trigger for admission.

- PCIs were performed on the admission date or on the day following admission.
- Recorded as emergency hospitalization.

Descriptive Analysis of the Rates of PCI

Our primary outcome of interest was the change of rates of elective and emergency PCIs during the COVID-19 pandemic. The rates during each COVID-19 surge were analyzed. As rates of PCIs exhibit seasonality, rates in each month were compared with rates in the corresponding month during the previous 2 years. The descriptive analyses were performed for the rates of cases undergoing elective PCIs, of cases undergoing emergency PCIs, and of all cases undergoing PCIs (including the cases which were excluded due to being unable to classify).

A descriptive analysis of rates was also undertaken in limited areas with proactive nonpharmaceutical intervention policies to tackle COVID-19. The areas include Hokkaido, Tochigi, Saitama, Chiba, Tokyo, Kanagawa, Gifu, Aichi, Osaka, Kyoto, Hyogo, and Fukuoka, where the first or the second emergency declaration was implemented for a longer period than in other areas of Japan¹³.

Interrupted Time Series Analysis for Changes in the Proportion of Severe Cases

Interrupted time series (ITS) analysis was applied to assess the impact of the COVID-19 pandemic on the proportion of severe cases of patients undergoing elective and emergency PCIs. For patients undergoing elective PCIs, the Canadian Cardiovascular function (CCS) classification was used, whereas for patients undergoing emergency PCIs, the Killip classification was used. Changes in the proportion of severe patients were evaluated, i.e., a CCS classification of 3 or more for cases undergoing elective PCIs²⁰ and a Killip classification of 3 or more for cases undergoing emergency PCIs^{21, 22}.

Additionally, for cases undergoing emergency PCIs, the change in the proportion of cases initially undertaking mechanical or pharmaceutical circulatory support, i.e., cases undertaking mechanical ventilation (MV) or circulation support, or cases administered vasopressors in the same day or the next day of admission, was also investigated. Venoarterial extracorporeal membrane oxygenation, intra-aortic balloon pumping, or artificial heart are defined as circulation support.

Interrupted Time Series Analysis for Changes in in-Hospital Mortality

ITS analysis was applied to investigate the changes in in-hospital mortality of cases undergoing

emergency PCIs at the start of the COVID-19 pandemic. Besides the analysis of mortality for all cases undergoing emergency PCIs, an analysis that was limited to severe cases (Killip classification of 3 or more) was performed to control for severity.

Statistical Analysis

In the descriptive analyses, 95% confidence intervals of the ratio of rates were calculated under the assumption that the number of events per day follows a Poisson distribution.

For the ITS analyses, segmented regression analysis was performed to identify the level change of the proportion of severe patients over the change point. The time unit applied was 1 week, and the seasonality was adjusted using harmonic terms (sines and cosines). As the first surge of COVID-19 began around April 2020 and the first emergency declaration was introduced on April 7, 2020, the week beginning from April 5, 2020, was set as the change point.

Statistical analyses were carried out using R version 4.0.5 (R Foundation for Statistical Computing, Vienna, Austria) and the R package “*tsModel*.”

Results

Patient Characteristics

From April 2018 to March 2021, 242 hospitals continuously provided data to the QIP. Of the patients admitted to these hospitals, 86,196 cases were identified as having undergone PCI during their hospitalization. Of these cases, 38,696 and 28,585 cases were classified as undergoing elective and emergency PCIs, respectively (**Supplementary Fig. 2**). **Table 1** shows a comparison of patients' characteristics between the periods before and after April 2020. The patients' characteristics are fairly persistent over the start of the COVID-19 pandemic. For demographics, cases undergoing elective and emergency cases were old (median age was 72 and 71 years, respectively) and included more males than females (the proportion of males was 78.4% and 75.6%). For comorbidities, cases undergoing elective PCIs and emergency PCIs include the intermediate degree of diabetes-mellitus patients (45.3% and 33.1%, respectively) and patients with heart failure (25.3% and 31.0%, respectively).

Trend of PCI Rates

Table 2 and Fig. 1 (a and b) show the trend of the ratio of rates of cases undergoing elective and emergency PCIs in each month to that in corresponding months in the previous 2 years.

For elective PCI rates, two periods saw major

Table 1. Patient characteristics

	Elective PCI cases			Emergency PCI cases		
	All (<i>n</i> =38,696)	April 2018– April 2020 (24 months) (<i>n</i> =28,055)	April 2020– February 2021 (11 months) (<i>n</i> =10,641)	All (<i>n</i> =28,585)	April 2018– April 2020 (24 months) (<i>n</i> =20,086)	April 2020– February 2021 (11 months) (<i>n</i> =8,499)
Demographics						
Age, years*	72 [65, 78]	72 [65, 78]	72 [65, 78]	71 [61, 80]	71 [61, 79]	72 [62, 80]
Sex (male), <i>n</i> (%)	30,329 (78.4)	21,945 (78.2)	8,384 (78.8)	21,611 (75.6)	15,202 (75.7)	6,409 (75.4)
Comorbidities						
Hypertension, <i>n</i> (%)	26,838 (69.4)	19,627 (70.0)	7,211 (67.8)	19,801 (69.3)	14,008 (69.7)	5,793 (68.2)
DM, <i>n</i> (%)	17,530 (45.3)	12,552 (44.7)	4,978 (46.8)	9,456 (33.1)	6,638 (33.0)	2,818 (33.2)
Dyslipidaemia, <i>n</i> (%)	26,313 (68.0)	18,930 (67.5)	7,383 (69.4)	20,051 (70.1)	14,077 (70.1)	5,974 (70.3)
History of smoking, <i>n</i> (%)	19,325 (49.9)	13,975 (49.8)	5,350 (50.3)	13,811 (48.3)	9,679 (48.2)	4,132 (48.6)
Prior MI, <i>n</i> (%)	4,159 (10.7)	3,106 (11.1)	1,053 (9.9)	1,043 (3.6)	756 (3.8)	287 (3.4)
Stroke, <i>n</i> (%)	428 (1.1)	307 (1.1)	121 (1.1)	243 (0.9)	165 (0.8)	78 (0.9)
PAD, <i>n</i> (%)	206 (0.5)	147 (0.5)	59 (0.6)	222 (0.8)	165 (0.8)	57 (0.7)
Heart failure, <i>n</i> (%)	9,772 (25.3)	6,946 (24.8)	2,826 (26.6)	8,866 (31.0)	6,335 (31.5)	2,531 (29.8)
Elixhauser Comorbidity Index*	2 [0, 7]	2 [0, 7]	3 [0, 7]	3 [0, 7]	3 [0, 7]	3 [0, 7]
CCS classification						
I, <i>n</i> (%)	13,748 (35.5)	9,914 (35.3)	3,834 (36.0)	-	-	-
II, <i>n</i> (%)	11,661 (30.1)	8,336 (29.7)	3,325 (31.2)	-	-	-
III, <i>n</i> (%)	3,928 (10.2)	2,822 (10.1)	1,106 (10.4)	-	-	-
IV, <i>n</i> (%)	430 (1.1)	288 (1.0)	142 (1.3)	-	-	-
II–IV, <i>n</i> (%)	16,019 (41.4)	11,446 (40.8)	4,573 (43.0)	-	-	-
Killip classification						
I, <i>n</i> (%)	-	-	-	11,875 (41.5)	8,325 (41.4)	3,550 (41.8)
II, <i>n</i> (%)	-	-	-	6,011 (21.0)	4,236 (21.1)	1,775 (20.9)
III, <i>n</i> (%)	-	-	-	1,807 (6.3)	1,318 (6.6)	489 (5.8)
IV, <i>n</i> (%)	-	-	-	2,805 (9.8)	1,916 (9.5)	889 (10.5)
II–IV, <i>n</i> (%)	-	-	-	10,623 (37.2)	7,470 (37.2)	3,153 (37.1)
Most resource-intensive diagnosis						
I20.X (Angina pectoris) except of I20.0 (Unstable angina)	27,765 (71.8)	20,147 (71.8)	7,618 (71.6)	-	-	-
I20.0 (Unstable angina)	-	-	-	4,870 (17.0)	3,440 (17.1)	1,430 (16.8)
I21.X (Acute myocardial infarction)	-	-	-	23,293 (81.5)	16,344 (81.4)	6,949 (81.8)
I22.X (Subsequent myocardial infarction)	-	-	-	10 (0.0)	9 (0.0)	1 (0.0)
I23.X (Certain current complications following acute myocardial infarction)	-	-	-	61 (0.2)	38 (0.2)	23 (0.3)
I24.X (Other acute ischaemic heart diseases)	-	-	-	351 (1.2)	255 (1.3)	96 (1.1)
I25.X (Chronic ischaemic heart disease)	10,931 (28.2)	7,908 (28.2)	3,023 (28.4)	-	-	-

PCI, percutaneous coronary intervention; DM, diabetes mellitus; HF, hart failure; MI, myocardial infarction; PAD, peripheral artery disease; CCS, Canadian Cardiovascular Society

*Indicates median values [1st quartile, 3rd quartile].

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Table 2. Ratio of incident rate of cases undergoing elective and emergency PCIs in each month to that in corresponding months in the previous 2 years

	Rate ratio for cases undergoing elective PCIs (95%CI)	Rate ratio for cases undergoing emergency PCIs (95%CI)
Apr 2020	75.0% (69.3-81.1)	83.8% (76.6-91.6)
May 2020	50.3% (45.9-55.0)	88.3% (80.6-96.6)
Jun 2020	76.6% (71.0-82.6)	98.0% (89.9-106.8)
Jul 2020	85.9% (79.9-92.3)	102.9% (94.5-111.9)
Aug 2020	95.7% (88.7-103.2)	92.7% (84.8-101.2)
Sep 2020	98.1% (90.9-105.9)	89.8% (82.1-98.3)
Oct 2020	91.4% (85.0-98.2)	102.0% (93.8-110.7)
Nov 2020	90.1% (83.8-96.8)	91.9% (84.3-100.1)
Dec 2020	93.9% (87.4-100.8)	93.0% (85.7-100.9)
Jan 2021	76.1% (70.3-82.4)	93.6% (86.2-101.6)
Feb 2021	82.8% (76.8-89.3)	84.8% (77.4-92.8)
total (Apr 2020 - Feb 2021)	83.0% (81.1-84.9)	92.8% (90.5-95.3)

PCI; percutaneous coronary intervention
CI; confidence interval

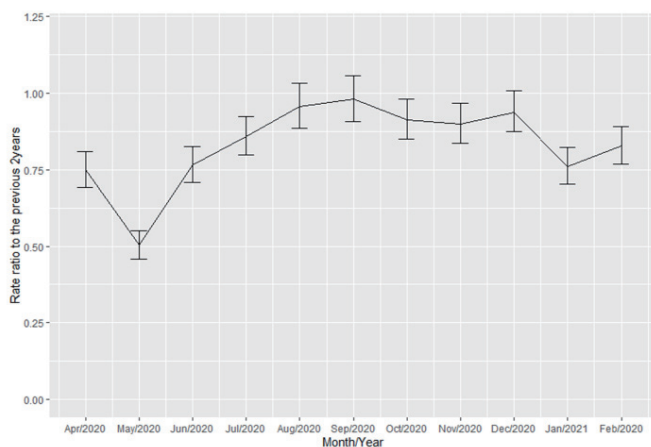


Fig. 1a. Trend of the ratio of rates of cases undergoing elective PCIs in each month to that in corresponding months in previous 2 years

The error bars indicate the confidence intervals.

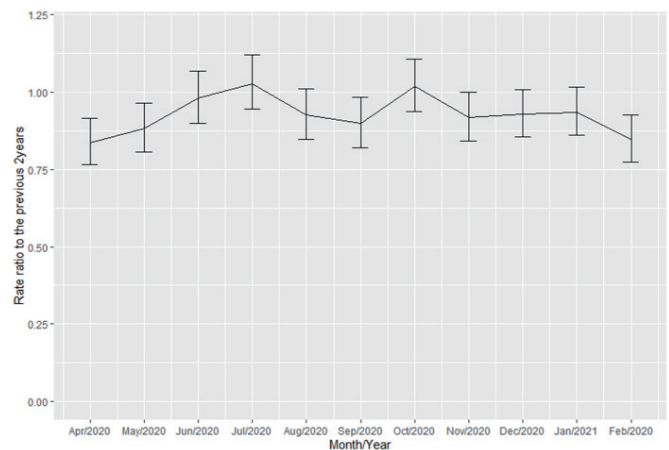


Fig. 1b. Trend of the ratio of rates of cases undergoing emergency PCIs in each month to that in corresponding months in previous 2 years

The error bars indicate the confidence intervals.

reductions. The first reduction showed a peak in May 2020 (the rate ratio to that in the corresponding months during the previous 2 years was 50.3%; hereafter, the ratio calculated in the same way will be indicated as the rate ratio), and the second reduction period showed a peak in January 2021 (the rate ratio was 76.1%). In the months between these two periods of rate reduction, the reduction was small compared with the remaining months, but the rates did not exceed the previous 2 years. From April 2020 to February 2021, the rate reduction was continuously accumulated, and the accumulated rate ratio was 83.0%.

For rates of emergency PCIs, two major periods of reduction occurred. One showed a peak in April 2020 and the other showed a peak in February 2021. The rate ratios in April 2020 and February 2021 were 83.8% and 84.8%, respectively, and the accumulated rate ratio from April 2020 to February 2021 was 92.8%.

Supplementary Table 1 and Supplementary Fig. 3a, and Supplementary Fig. 3b show the same data for the prefectures that implemented proactive COVID-19 policies. The period during which the rates was reduced was not notably different from the nationwide analysis, but the size of the reduction was

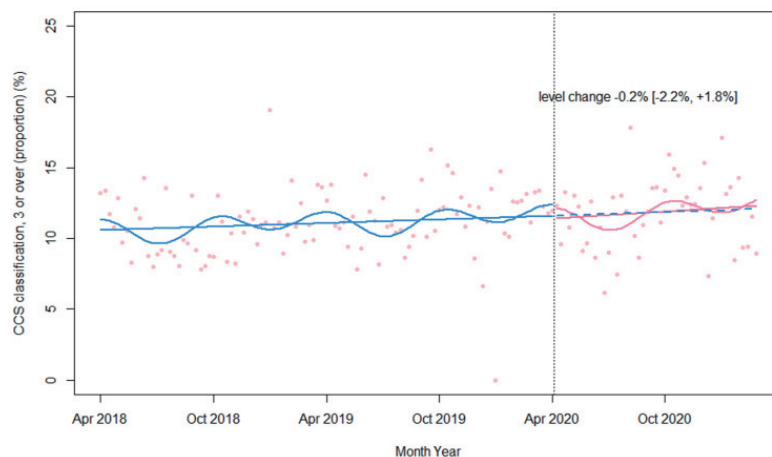


Fig. 2a. Interrupted time series analysis for changes in the proportion of severe cases in cases undergoing elective PCIs

The proportion of severe cases in cases undergoing elective PCIs is plotted on the vertical axis and year and month on the horizontal axis. Blue curved line: predicted value of the proportion of severe cases based on the seasonally adjusted regression model before the change point (the week beginning from April 5, 2020).

Blue straight line: linear predicted value of the proportion of severe cases before the change point.

Pink curved line: predicted value of the proportion of severe cases based on the seasonally adjusted regression model after the change point.

Pink straight line: linear predicted value of the proportion of severe cases after the change point.

Blue dotted straight line: predicted value of the proportion of severe cases after the change point based on the observations before the change point.

Vertical dotted line indicates the change point (the week beginning from April 5, 2020).

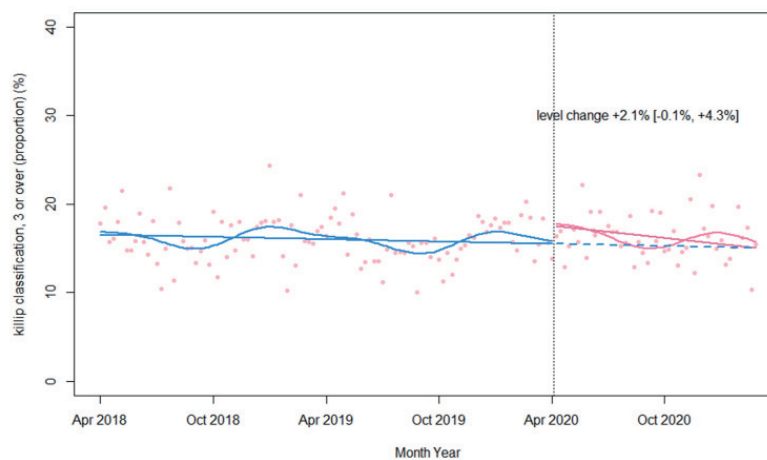


Fig. 2b. Interrupted time series analysis for changes in the proportion of severe cases in cases undergoing emergency PCIs

The proportion of severe cases in cases undergoing emergency PCIs is plotted on the vertical axis and year and month on the horizontal axis. Blue curved line: predicted value of the proportion of severe cases based on the seasonally adjusted regression model before the change point (the week beginning from April 5, 2020).

Blue straight line: linear predicted value of the proportion of severe cases before the change point.

Pink curved line: predicted value of the proportion of severe cases based on the seasonally adjusted regression model after the change point.

Pink straight line: linear predicted value of the proportion of severe cases after the change point.

Blue dotted straight line: predicted value of the proportion of severe cases after the change point based on the observations before the change point.

Vertical dotted line indicates the change point (the week beginning from April 5, 2020).

larger. The accumulated rate ratio from April 2020 to February 2021 for elective and emergency PCIs were 77.5% and 88.0%, respectively.

Supplementary Table 2, Supplementary Table 3, Supplementary Fig. 4, and Supplementary Fig. 3c showed the results of the analyses for all cases undergoing PCIs. The change of rates was milder than

that for cases undergoing elective PCIs and greater than that for cases undergoing emergency PCIs.

Interrupted Time Series Analysis for Changes in the Proportion of Severe Cases

Figs. 2a and 2b show the trends in the proportions of severe cases in cases with elective and

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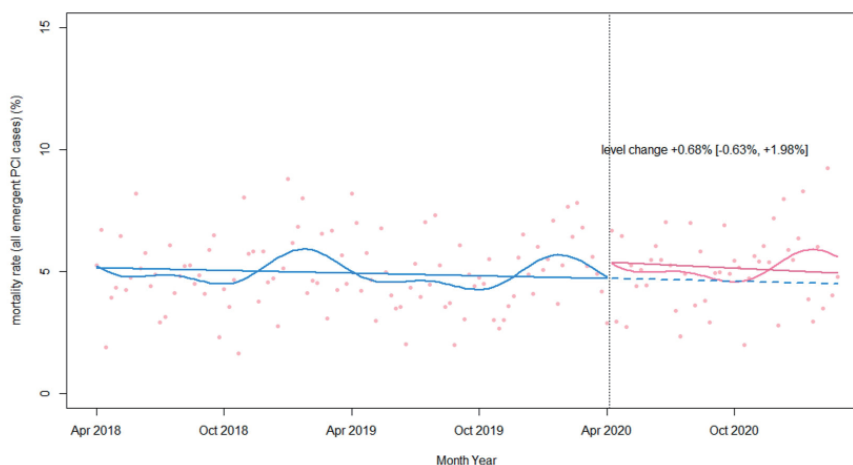


Fig. 3. Interrupted time series analysis for the in-hospital mortality of all cases undergoing emergency PCIs

The in-hospital mortality in all cases undergoing emergency PCIs is plotted on the vertical axis and year and month on the horizontal axis. Blue curved line: predicted value of the in-hospital mortality based on the seasonally adjusted regression model before the change point (the week beginning from April 5, 2020). Blue straight line: linear predicted value of the in-hospital mortality before the change point. Pink curved line: predicted value of the in-hospital mortality based on the seasonally adjusted regression model after the change point. Pink straight line: linear predicted value of the in-hospital mortality after the change point. Blue dotted straight line: predicted value of the in-hospital mortality after the change point based on the observations before the change point. Vertical dotted line indicates the change point (the week beginning from April 5, 2020).

emergency PCIs, respectively. We found no significant changes in the proportions of severe cases at the change point for elective PCIs (estimated level change -0.2% ; 95% CI, -2.2% to $+1.8\%$) or for emergency PCIs (estimated level change $+2.1\%$; 95% CI, -0.1% to $+4.3\%$). **Supplementary Fig. 5** shows the trends in the proportion of cases initially undertaking mechanical or pharmaceutical circulatory support in cases undergoing emergency PCIs, and we found no significant changes in neither of the analyses.

Interrupted Time Series Analysis for in-Hospital Mortality of Cases Undergoing Emergency PCIs

There were 1,453 in-hospital deaths in patients undergoing PCIs; 1,423 of these deaths were in patients undergoing emergency PCIs. **Figs. 3** shows the trends of in-hospital mortality rates for all cases undergoing emergency PCIs. **Supplementary Fig. 6** shows the trends of in-hospital mortality limited to severe cases undergoing emergency PCIs. We found no significant level changes in either of the analyses. The estimated level change for all cases undergoing emergency PCIs was $+0.68\%$ (95% CI, -6.3% to $+1.98\%$), and that for severe cases undergoing emergency PCIs was $+0.69\%$ (95% CI, -5.99% to $+7.37\%$).

Discussion

We analyzed the trend in PCIs during the COVID-19 pandemic using data from a large DPC database. Our main findings clarified the medium-term impact of the surges of COVID-19 on the practice of PCIs as described in the following sections.

The first and third surges of COVID-19 had a clear impact on the rates of PCIs, but it was difficult to identify any impact from the second surge. The first period that showed a reduction in PCI rates occurred around May 2020, which corresponded with the first surge of the COVID-19 pandemic, whereas the second period during which a reduction was observed was around January 2021, which corresponded with the third surge. Clearly, the second reduction in rates was smaller than the first. This reduction in the rates is consistent with prior reports^{4-9, 23, 24}. However, our findings of a difference in the impact of each surge could not be explained simply by the influence of the surge in COVID-19. Although the volume of patients with COVID-19 was the smallest during the first surge, the impact on the rates of PCIs was largest during the first surge.

To disentangle these complex situations, an adjustment process based on the guidelines should be considered. **Supplementary Table 4** summarizes the process of the emergency declarations and the relevant guidelines. As in several countries¹¹), academic bodies

in Japan have released several sets of guidelines with recommendations for the adjustment of treatments performed during the COVID-19 pandemic. On June 10, 2020, the JCS released the revised version of JCS Recommendations²⁵⁾, which recommended that cardiovascular disease professionals should monitor the COVID-19 situation around them and postpone nonemergency treatments and tests if medical resources are about to be occupied by patients with COVID-19. The guidelines for cardiovascular diseases were established in practice following the first surge.

The process of establishment of the guideline can partly explain the potential mechanism of the degree of the decrease in rates of elective PCIs during each surge. During the second and third surges of COVID-19, the guideline for PCIs had already been established, so adjustments in medical treatments were expected to have been undertaken in a unified manner, instead of a confused manner which possibly results in excessive shrink of health services. The guideline is considered to have encouraged health professionals to prepare for coming surges in an organized manner, resulting in a small impact of the surges on the rates of PCIs. Additionally, other various factors, including shortage of medical resources during the COVID-19 pandemic^{26, 27)}, was considered to influence the case volumes of PCIs.

There was a clear difference between the changes in the rate of elective and emergency PCIs during the surges of COVID-19. Although cases that underwent both types of PCIs were reduced, the degree of reduction was greater for elective than for emergency PCIs. This is consistent with the guidelines, which recommended professionals postpone nonemergency treatments during surges of COVID-19. However, although the change is small, cases that underwent emergency PCIs were also reduced during the surges of COVID-19. This reduction cannot be explained by the guidelines, but this finding is consistent with a previous survey, which revealed that a certain number of PCI centers (22.8%–20.4%, depending on the survey time) shrunk PCIs for high-risk non-ST elevation ACS patients during the first surge of COVID-19²⁸⁾. The reduction in emergency PCIs might reflect the tendency that patients are less likely to visit hospitals to avoid exposure to COVID-19, as previous studies⁴⁻⁶⁾ suggested. Since DPC data does not include data of patients who did not visit the hospital, it is difficult to confirm whether patients' hesitancy existed or not from DPC data. Change of social environment due to the epidemic of the COVID-19, including change in working pattern, may influence the incident rate of cardiovascular diseases.

It was made clear that the impact of COVID-19 on PCIs continued over the medium-term. If a certain amount of postponed elective PCIs were implemented in the periods between the surges, then this excess of cases of elective PCIs during these periods should be observed; however, such an excess was not observed. For 11 months, from April 2020, the reductions in the rates of elective and emergency PCIs were approximately 20% and 10%, respectively.

The ITS analysis showed no change in the proportion of severe cases in cases undergoing elective PCIs. Patients' severity may not be considered as an important factor in the postponement process. From patients' perspectives, severity may not be an important factor in their hesitancy to visit hospitals.

The ITS analyses showed no major change in the proportion of severe cases or in-hospital mortality for cases undergoing emergency PCIs. No major change in the proportion of severe cases suggests that the standard to undertake emergency PCIs did not change under the pressure of COVID-19. Additionally, no significant change in in-hospital mortality suggested the quality of emergency PCIs was maintained despite the COVID-19 pandemic, which were persistent with previous reports^{29, 30)}.

The result of our study highlights the difference between the situation of Japan and those of other countries. In other countries, a significant impact on volumes and processes of PCIs has been reported. Approximately 50% reduction in case volume of PCIs after the first lockdown period has been reported³¹⁾, and patients with indications for coronary artery bypass grafting were treated with PCIs from the United Kingdom³²⁾, a significant increase in door to balloon time and mortality has been reported from Europe³³⁾, and delay of treatment for MI has been reported from Turkey³⁴⁾. Compared with these countries, the impact observed in this study was minimal. The reduction of rates in the first surge was approximately 50% for elective PCIs and 20% for emergency PCIs, and a significant change in the proportion of severe cases complicated with cardiac arrest or cardiogenic shock and an increase in in-hospital mortality was not observed. Our result showing no significant change in the treatment process is consistent with other prior studies in Japan^{4, 28)}. One possible explanation is the relatively low impact of COVID-19 in Japan. In fact, the rate of deaths due to COVID-19 in Japan was lower than that reported in other high-income countries³⁵⁾. Nevertheless, a report from Sweden³⁶⁾, where the impact of COVID-19 is relatively large³⁵⁾, showed a small impact on case volumes and process of PCIs. The degree of impact of COVID-19 can be influenced by various factors,

including resilience or the potential capacity of health systems.

Our study has several limitations. First, our data only comprise administrative DPC data from QIP participating hospitals. The study does not include all DPC data in Japan and is reliant on the voluntary provision of data. Hence, selection bias could not be avoided. Second, because of the dependence on administrative data, the classification into elective PCIs and emergency PCIs was not comprehensive. Out of 86,196 cases undergoing PCIs, 18,915 cases (21.9%) could not be classified into either of these two types of PCIs. These unclassified PCIs included cases that underwent PCI, but the most resource-intensive diagnosis was an unrelated disease, such as renal failure, as well cases whose recorded diagnosis and hospitalization process did not match, such as planned hospitalization with a diagnosis of AMI. Although most cases with PCIs were included in the analysis and the classification definition was consistent over the study period, drop-outs due to the limits of classification may have resulted in selection bias. Third, since procedural mortality rates should be infinitesimally small in cases undergoing elective PCIs, using mortality rates to estimate quality in elective PCI procedures is thought to be flagrant. Further research is warranted to elucidate the influences on long-term outcomes.

Conclusion

In conclusion, our study revealed that the impacts of COVID-19 on PCIs were larger in the first surge than the subsequent, larger in the elective than in the emergent, and continued over the medium-term. During the COVID-19 pandemic, in-hospital mortality of cases undertaking emergency PCIs did not change.

Acknowledgements

We thank all the participating hospitals and all the staff members.

Source of Funding

This study was supported by JSPS KAKENHI [Grant Number JP19H01075] from the Japan Society for the Promotion of Science, by the GAP Fund Program of Kyoto University type B, by Humanities, Social/Behavioral Sciences, and Natural Sciences Interdisciplinary Research Project of Kokoro Research Center, Kyoto University, and by Health Labour Sciences Research Grant from the Ministry of Health,

Labour and Welfare, Japan [20HA2003] to Yuichi Imanaka. The funders played no role in the study design, data collection and analysis, decision to publish or preparation of the manuscript.

Conflicts of Interest

There is no conflict of interest to be declared.

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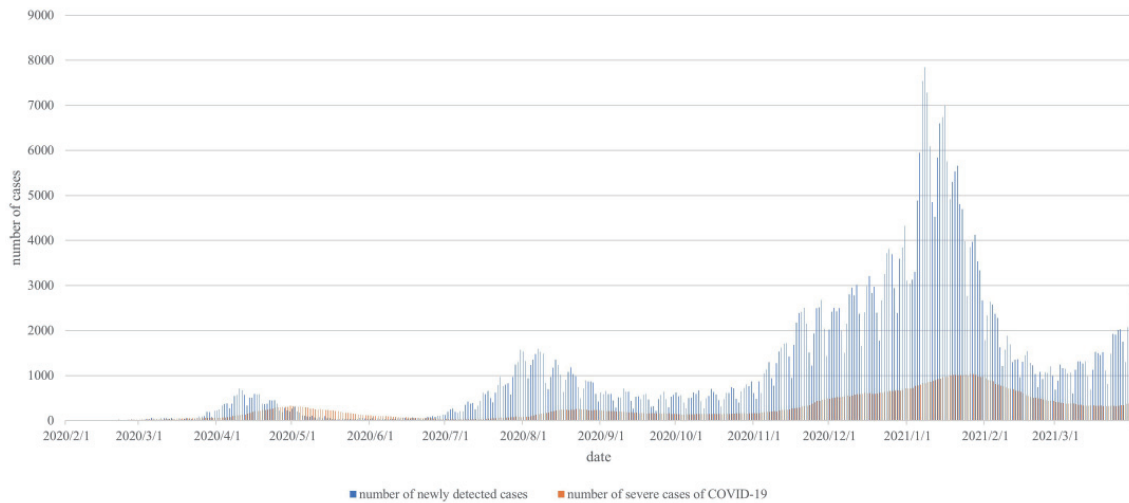
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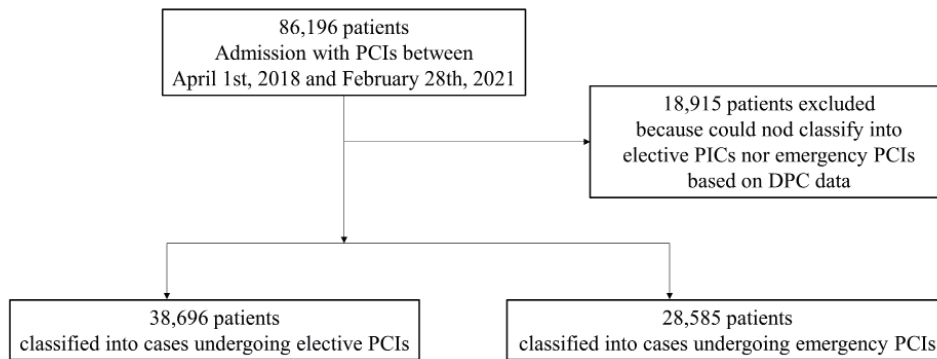
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Supplementary Fig. 1. Trend of case numbers of COVID-19 in Japan
COVID-19: coronavirus disease 2019



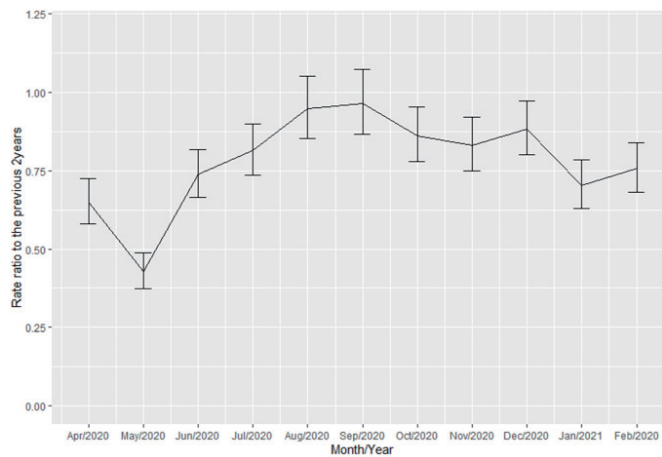
Supplementary Fig. 2. Flowchart of the patients' selection and classification process

Supplementary Table 1. Ratio of incident rate of cases undergoing elective and emergency PCIs in each month to that in corresponding months in previous 2 years, limited to the areas with proactive COVID-19 policies

	Rate ratio for cases undergoing elective PCIs (95%CI)	Rate ratio for cases undergoing emergency PCIs (95%CI)
Apr 2020	64.9% (58.0-72.5)	84.1% (73.9-95.4)
May 2020	42.7% (37.4-48.7)	80.1% (70.6-90.9)
Jun 2020	73.8% (66.4-81.9)	99.4% (87.9-112.2)
Jul 2020	81.5% (73.7-90.1)	95.5% (84.7-107.5)
Aug 2020	94.9% (85.3-105.3)	83.0% (73.2-94.1)
Sep 2020	96.6% (86.8-107.4)	88.8% (78.1-100.7)
Oct 2020	86.2% (77.8-95.4)	90.2% (80.1-101.3)
Nov 2020	83.2% (75.1-92.1)	87.7% (77.6-98.8)
Dec 2020	88.4% (80.1-97.4)	88.1% (78.6-98.5)
Jan 2021	70.4% (62.9-78.6)	93.6% (83.5-104.9)
Feb 2021	75.7% (68.1-84.0)	77.4% (68.1-87.8)
total (Apr 2020 - Feb 2021)	77.5% (75.1-80.0)	88.0% (84.9-91.2)

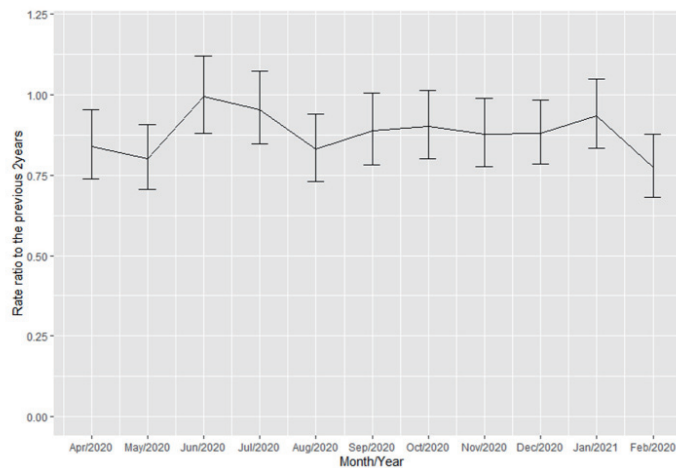
COVID-19; Coronavirus disease 2019 PCI; percutaneous coronary intervention CI; confidence interval

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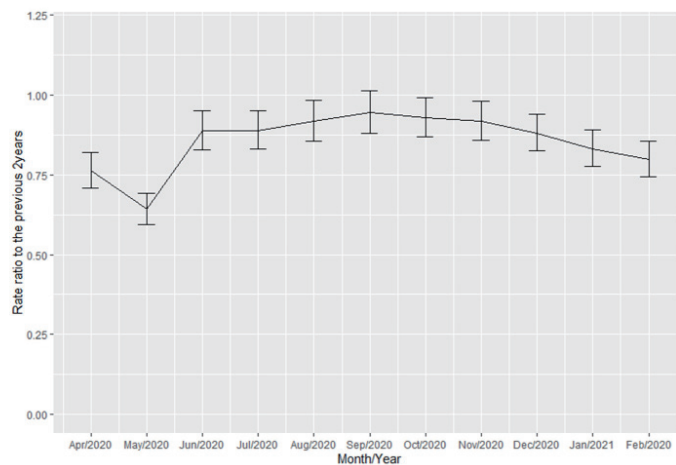
Supplementary Fig. 3a. Trend of the ratio of rates of cases undergoing elective PCIs in each month to that in corresponding months in previous 2 years, limited to the areas with proactive COVID-19 policies

The error bars indicate the confidence intervals.



Supplementary Fig. 3b. Trend of the ratio of rates of cases undergoing emergency PCIs in each month to that in corresponding months in previous 2 years, limited to the areas with proactive COVID-19 policies

The error bars indicate the confidence intervals.



Supplementary Fig. 3c. Trend of the ratio of rates of all cases undergoing PCIs in each month to that in corresponding months in previous 2 years, limited to the areas with proactive COVID-19 policies

The error bars indicate the confidence intervals.

Supplementary Table 2. Ratio of incident rates of all cases undergoing PCIs in each month to that in corresponding months in previous 2 years

	Rate ratio for cases undergoing PCIs (95%CI)
Apr 2020	79.9% (75.9-84.1)
May 2020	69.9% (66.2-73.8)
Jun 2020	88.2% (83.9-92.7)
Jul 2020	93.9% (89.4-98.5)
Aug 2020	94.3% (89.6-99.2)
Sep 2020	97.5% (92.6-102.7)
Oct 2020	97.7% (93.1-102.5)
Nov 2020	94.1% (89.7-98.8)
Dec 2020	93.2% (88.8-97.7)
Jan 2021	85.3% (81.2-89.7)
Feb 2021	85.2% (80.9-89.6)
total (Apr 2020 - Feb 2021)	88.9% (87.6-90.3)

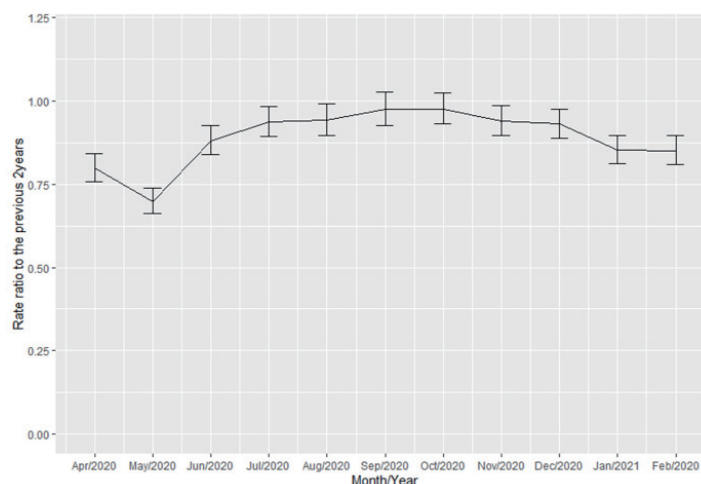
PCI; percutaneous coronary intervention
CI; confidence interval

Supplementary Table 3. Ratio of incident rate of all cases undergoing PCIs in each month to that in corresponding months in previous 2 years, limited to the areas with proactive COVID-19 policies

	Rate ratio for cases undergoing PCIs (95%CI)
Apr 2020	76.3% (71.0-82.0)
May 2020	64.3% (59.6-69.4)
Jun 2020	88.8% (82.9-95.0)
Jul 2020	88.9% (83.1-95.1)
Aug 2020	91.9% (85.6-98.5)
Sep 2020	94.5% (87.9-101.4)
Oct 2020	92.9% (86.9-99.3)
Nov 2020	91.9% (85.9-98.2)
Dec 2020	88.2% (82.6-94.0)
Jan 2021	83.3% (77.8-89.1)
Feb 2021	79.8% (74.4-85.6)
total (Apr 2020 - Feb 2021)	85.4% (83.6-87.1)

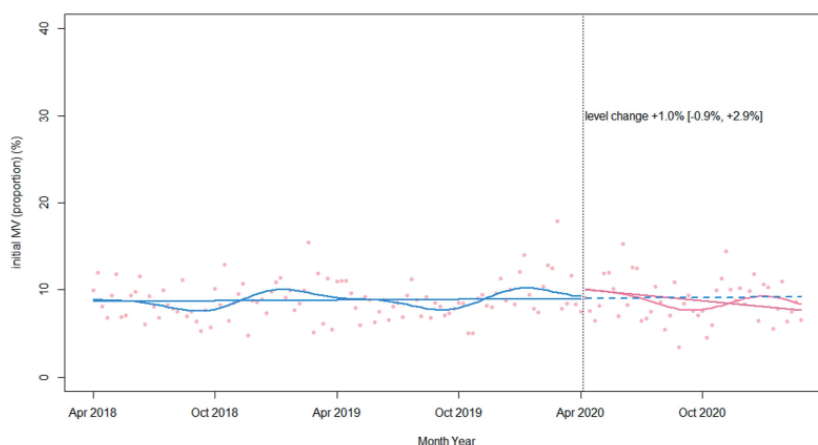
COVID-19; Coronavirus disease 2019
PCI; percutaneous coronary intervention
CI; confidence interval

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Supplementary Fig. 4. Trend of the ratio of rates of all cases undergoing PCIs in each month to that in corresponding months in previous 2 years

The error bars indicate the confidence intervals.



Supplementary Fig. 5a. Interrupted time series analysis for changes in the proportion of cases initially undertaking MV in cases undergoing emergency PCIs

The proportion of cases initially undertaking MV is plotted on the vertical axis and year and month on the horizontal axis.

Blue curved line: predicted value of the proportion of cases initially undertaking MV based on the seasonally adjusted regression model before the change point (the week beginning from April 5, 2020).

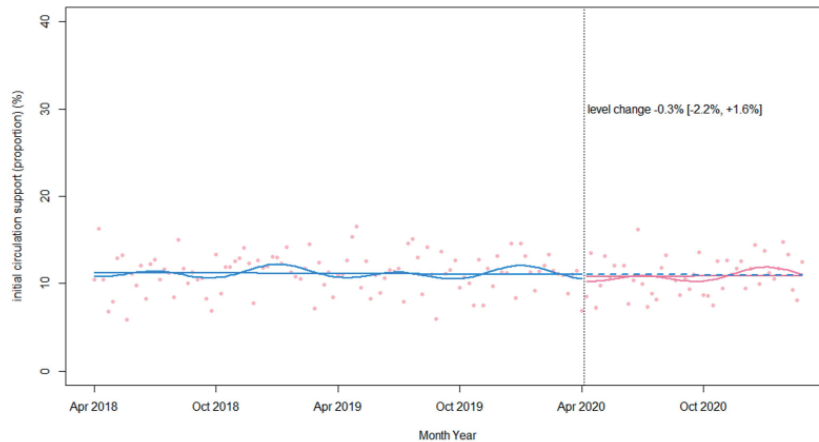
Blue straight line: linear predicted value of the proportion of cases initially undertaking MV before the change point.

Pink curved line: predicted value of the proportion of cases initially undertaking MV based on the seasonally adjusted regression model after the change point.

Pink straight line: linear predicted value of the proportion of cases initially undertaking MV after the change point.

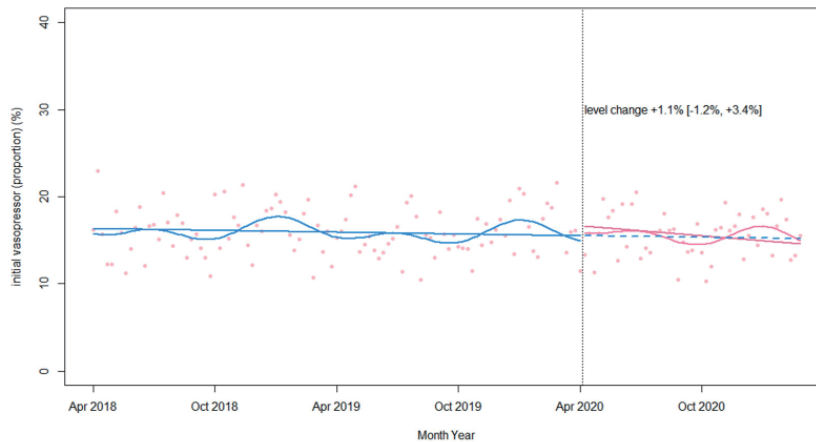
Blue dotted straight line: predicted value of the proportion of cases initially undertaking MV after the change point based on the observations before the change point.

Vertical dotted line indicates the change point (the week beginning from April 5, 2020).



Supplementary Fig. 5b. Interrupted time series analysis for changes in the proportion of cases initially undertaking circulation support in cases undergoing emergency PCIs

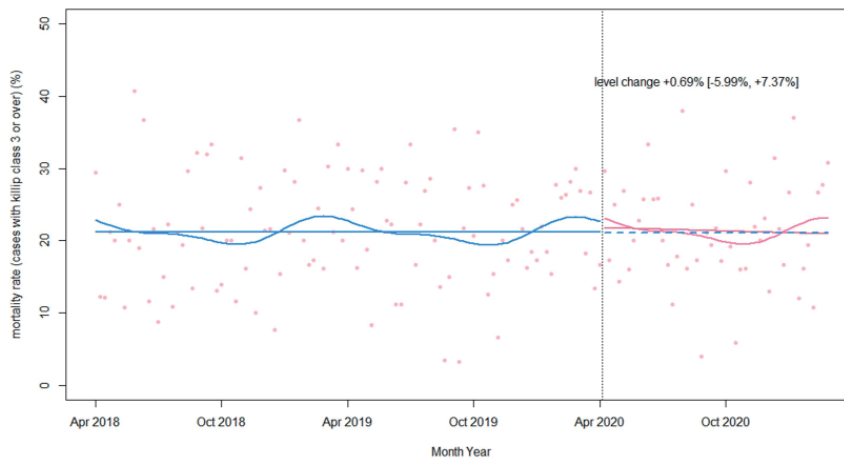
The proportion of cases initially undertaking circulation support is plotted on the vertical axis and year and month on the horizontal axis. Blue curved line: predicted value of the proportion of cases initially undertaking circulation support based on the seasonally adjusted regression model before the change point (the week beginning from April 5, 2020). Blue straight line: linear predicted value of the proportion of cases initially undertaking circulation support before the change point. Pink curved line: predicted value of the proportion of cases initially undertaking circulation support based on the seasonally adjusted regression model after the change point. Pink straight line: linear predicted value of the proportion of cases initially undertaking circulation support after the change point. Blue dotted straight line: predicted value of the proportion of cases initially undertaking circulation support after the change point based on the observations before the change point. Vertical dotted line indicates the change point (the week beginning from April 5, 2020).



Supplementary Fig. 5c. Interrupted time series analysis for changes in the proportion of cases initially administered vasopressors in cases undergoing emergency PCIs

The proportion of cases initially administered vasopressors is plotted on the vertical axis and year and month on the horizontal axis. Blue curved line: predicted value of the proportion of cases initially administered vasopressors based on the seasonally adjusted regression model before the change point (the week beginning from April 5, 2020). Blue straight line: linear predicted value of the proportion of cases initially administered vasopressors before the change point. Pink curved line: predicted value of the proportion of cases initially administered vasopressors based on the seasonally adjusted regression model after the change point. Pink straight line: linear predicted value of the proportion of cases initially administered vasopressors after the change point. Blue dotted straight line: predicted value of the proportion of cases initially administered vasopressors after the change point based on the observations before the change point. Vertical dotted line indicates the change point (the week beginning from April 5, 2020).

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Supplementary Fig. 6. Interrupted time series analysis for the in-hospital mortality of severe cases undergoing emergency PCIs

The in-hospital mortality in severe cases undergoing emergency PCIs is plotted on the vertical axis and year and month on the horizontal axis. Blue curved line: predicted value of the in-hospital mortality based on the seasonally adjusted regression model before the change point (the week beginning from April 5, 2020).

Blue straight line: linear predicted value of the in-hospital mortality before the change point.

Pink curved line: predicted value of the in-hospital mortality based on the seasonally adjusted regression model after the change point.

Pink straight line: linear predicted value of the in-hospital mortality after the change point.

Blue dotted straight line: predicted value of the in-hospital mortality after the change point based on the observations before the change point.

Vertical dotted line indicates the change point (the week beginning from April 5, 2020).

Supplementary Table 4. Emergency declarations and guidelines for cardiovascular diseases

Date	Event
April 7 2020	Start of the first emergency declaration.
April 9 2020	'Joint statement for COVID-19 by the Japanese Circulation Society and the Japan Stroke Society'. This did not include clear guidelines for medical practice.
April 26 2020	'Recommendation to maintain healthcare system for circulation diseases during the COVID-19 epidemic'. No postponement of emergency treatments or tests is recommended.
May 25 2020	End of the first emergency declaration.
June 10 2020	'Recommendation to maintain healthcare system for circulation diseases during the COVID-19 epidemic (revised)'. Recommended that professionals involved in the treatment and care of cardiovascular diseases monitor the COVID-19 situation around them and to postpone no emergency treatments and tests when medical resources are about to be occupied by COVID-19 patients.
January 8 2021	Start of the second emergency declaration.
March 21 2021	End of the second emergency declaration.