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Impact of the COVID-19 pandemic on time to treatment, treatment patterns and outcomes among patients with acute coronary syndrome in Yogyakarta, Indonesia: a retrospective cohort study

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ABSTRACT

Objective This study aimed to evaluate the impact of the COVID-19 pandemic on the management of acute coronary syndrome (ACS) in Yogyakarta, Indonesia with respect to time to treatment, treatment pattern and treatment outcome.

Design This is a retrospective cohort study in which medical records of hospitalised patients with ACS were reviewed.

Setting Three hospitals in Yogyakarta, Indonesia.

Participants Patients hospitalised with ACS during two pandemic periods (first pandemic period: March–August 2020; second pandemic period: March–August 2021) and prepandemic period (March–August 2019).

Outcome measures Time to treatment, treatment pattern and treatment outcome.

Results A total of 598 patients with ST-elevation myocardial infarction (STEMI) and 615 with non-ST-elevation ACS were identified. Of these, 313, 484 and 416 were identified during the prepandemic period, first pandemic period and second pandemic period, respectively. For STEMI, the proportion of patients with a delay from symptom onset to first medical contact (FMC) was significantly higher during the second pandemic period as compared with the prepandemic period (47.7% vs 32.0%, OR=1.84, 95% CI 1.18, 2.85). The proportion of patients with STEMI with delayed door-to-balloon (D2B) time was significantly higher during the second pandemic period as compared with the prepandemic period (99.4% vs 92.9%, OR=13.08, 95% CI 1.57, 108.73). Significantly longer mean total ischaemic time (45.85 hours vs 30.29 hours, mean difference=14.56, 95% CI 1.85, 27.28) was observed among patients with STEMI during the second year of the pandemic as compared with the prepandemic period. No significant differences between the prepandemic period and the first pandemic period were found in terms of proportion of patients with STEMI with a delay in time from symptom onset to FMC, delayed D2B time and total ischaemic time. Only Global Registry of Acute Coronary Events risk score (OR=1.04, 95% CI 1.03, 1.05) was a significant predictor of in-hospital mortality in the multivariate analysis.

Conclusions This study suggests a significant impact of the COVID-19 pandemic on time to treatment among patients with ACS. Health systems need to be well prepared to support effective and timely treatment of patients with ACS during future crisis.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study examined the impact of the COVID-19 pandemic on comprehensive aspects of management of patients with acute coronary syndrome (i.e., time to treatment, treatment patterns, and outcomes) and covered two pandemic periods compared with a prepandemic baseline.
⇒ This study was conducted in a middle-income country, where delay in for acute coronary syndrome treatment during the pre-COVID-19 period was considered a significant problem.
⇒ Limitations of using data obtained from a retrospective review of medical records include incomplete data and difficulty in verifying the information.
⇒ The association between in-hospital mortality cases and COVID-19 infection was not explored.
⇒ The impact of the COVID-19 pandemic on out-of-hospital mortality was not examined.

INTRODUCTION

Since 2019, COVID-19, an infectious disease caused by SARS-CoV-2, has devastatingly impacted public health and health systems worldwide. As of December 2022, there had been 632 million cases of COVID-19 infection, with 6.6 million deaths reported globally.[1] Furthermore, this pandemic led to a significant disruption in health service delivery. Many routine services were postponed by healthcare facilities to efficiently allocate resources to COVID-19 care. Many patients also avoided going to healthcare facilities due to fear of contracting COVID-19.[2] In addition, extensive campaigns aimed

at limiting disease transmission were launched, ranging from voluntary stay-at-home measures to strict lockdowns, to restrict travel and interactions within the population.[3] Consequently, a significant decline in service utilisation was observed during the pandemic, particularly among individuals with less severe illness.[2 4]

Acute coronary syndrome (ACS) is a time-critical condition where effective and timely treatment is necessary to reduce mortality and complications.[5–7] Nevertheless, a reduction in ACS-related hospital admissions was consistently observed during the COVID-19 pandemic.[8 9] Furthermore, delays in ACS treatment, especially increased time from symptom onset to the first medical contact (FMC), were identified in many countries during the pandemic.[9 10] In several countries, reduction in the number of reperfusion procedures and shortening of length of stay at the hospital were also reported during the pandemic.[9]

Before the COVID-19 pandemic, inadequate and delayed treatment among patients with ACS has been a worldwide significant problem,[11] including in Indonesia.[12–15] A previous study reported that only 4.7% of patients with ST-elevation myocardial infarction (STEMI) in Indonesia received primary percutaneous coronary intervention (PPCI).[13] The median (IQR) time from symptom onset to FMC of patients with STEMI ranged from approximately 24 (7–48) hours to 26.8 (10–48) hours,[13 14] while the time from symptom onset to FMC was longer than 12 hours in almost 80% of ACS cases.[12] The mean referral time of patients with ACS from non-percutaneous coronary intervention (PCI) hospitals to PCI centres was more than 3 hours,[15] which far exceeded the recommended target of no more than 30 min.[5 6] An unacceptably high mortality rate among patients with ACS was also observed in the country.[13 14]

At the end of 2022, 6.51 million total cases of COVID-19 infections with 159 000 total deaths were reported in Indonesia.[1] Like other countries, the healthcare system in Indonesia was overwhelmed during the pandemic. Limited capacity of the healthcare system in terms of human resources, medical supplies, structure and systems (eg, hospital beds, referral system) to deliver essential health services under the pandemic crisis was reported.[16] The balance between restricting health service utilisation to limit viral transmission and providing optimal ACS treatments posed a significant challenge to the health system in Indonesia. To date, evidence of the impact of the COVID-19 pandemic on ACS management in Indonesia has been scarce. A previous study conducted in one tertiary hospital in Jakarta, Indonesia reported longer door-to-device and total ischaemic time among patients with STEMI during the COVID-19 period (March–May 2020) as compared with the pre-COVID-19 period (March–May 2019).[17] Another study, conducted in five tertiary hospitals in Indonesia, reported significant decrease in STEMI admissions, longer door-to-balloon time (D2B) and longer total ischaemic time during the COVID-19 pandemic (February–June 2020) as compared with the prepandemic period.[18] It should be noted that both studies could not identify the significant impact of the COVID-19 pandemic on time from symptom onset to FMC among patients with STEMI.[17 18] Nevertheless, it should be noted that the first case of COVID-19 in Indonesia was identified in March 2020.[19] On 21 May 2020, there were 773 new cases, while the highest peak of new cases was observed in July 2021 and February 2022.[19] Therefore, the impact of the pandemic might not be fully captured in the previous studies.[17 18] This study aims to evaluate the impact of the COVID-19 pandemic on ACS management in Yogyakarta, Indonesia in terms of (1) time to treatment and (2) treatment pattern. In addition, the impact of the COVID-19 pandemic on in-hospital mortality of patients with ACS was also examined. Our hypothesis was that the pandemic led to delay in treatment, reduction in the proportion of patients undergoing PCI and an increase in in-hospital mortality. The results of this study can serve as an important lesson for the health system to maintain optimal ACS care during any emergency crisis in the future.

METHODS

Study design

A retrospective cohort study was conducted. All consecutive adult patients (≥18 years) hospitalised with ACS (The International Classification of Diseases, Tenth Revision (ICD-10) codes: I20.0, I21.0–I21.4, I21.9, I22.0–I22.2, I22.8–9) at three selected hospitals in Yogyakarta, Indonesia during three specified periods (ie, pre-COVID-19 period, first year of the COVID-19 pandemic and second year of the COVID-19 pandemic) were identified from hospitals' databases. The periods of March–August 2020 (first year of the COVID-19 pandemic) and March–August 2021 (second year of the COVID-19 pandemic) were categorised as the COVID-19 period, while the period of March–August 2019 was classified as the pre-COVID-19 period. Patients' medical records during hospitalisation with ACS were retrospectively reviewed and extracted by trained nurses under the supervision of cardiologists.

Setting

Yogyakarta, the capital city of the Special Region of Yogyakarta, is an important economic hub of Indonesia, located in the south-central part of the island of Java, Indonesia. The city is home to a population of approximately 460 000, with a population density of 13 007 people per square kilometre. Yogyakarta has 1 tertiary hospital and 54 secondary hospitals. Among these hospitals, seven are capable of performing PCI. For this study, three hospitals were chosen as the study sites that reflected the referral system of the city.

The first hospital is a 235-bed secondary district public hospital with two cardiologists. The second hospital is a 186-bed secondary private hospital with six cardiologists, including two non-full-time interventional cardiologists. The third hospital is a 762-bed tertiary hospital with 22

cardiologists, including 5 full-time interventional cardiologists. Notably, all except the first one are PCI-capable centres, whereas the third hospital is the largest PCI-capable centre in Yogyakarta. The hospitals are approximately 10–35 km away from each other.

Data collection

The following patient characteristics were collected from the medical record review: sex, age, type of ACS, body mass index, Killip class, smoking status, event of cardiac arrest during admission and the Global Registry of Acute Coronary Events (GRACE) risk score. A GRACE risk score of >140 points indicated a high probability of in-hospital death.[5 20] A higher Killip class (>II) indicated a higher risk of heart failure and future major adverse cardiac events, including long-term mortality.[21 22] For patients with STEMI, time from ACS symptom onset to FMC and time the patient received fibrinolytic and/or PCI from FMC were extracted. On the other hand, time from symptom onset to FMC and time the patient received anticoagulant injection and PCI (if necessary) from FMC were extracted among those with non-ST-elevation acute coronary syndrome (NSTEACS). Time from symptom onset to FMC was defined as the duration since patients had ACS symptoms until they arrived at the hospital. Door-to-needle (DTN) time was defined as the duration since patients with STEMI presented to the hospital until they received fibrinolytic injection. D2B time was the period between the arrival of patients with STEMI at the hospital and PCI implementation. Total ischaemic time was the period from symptom onset to patients with STEMI receiving reperfusion therapy or patients with NSTEACS receiving anticoagulant. For treatment pattern, the reperfusion therapy (ie, fibrinolytic and/or PCI) that each patient received was extracted. Concerning treatment outcome, in-hospital mortality was extracted. Data collection was performed between February and August 2022.

Data analysis

Patients with ACS were classified into STEMI and NSTEACS; NSTEACS consisted of non-ST-elevation myocardial infarction (NSTEMI) and unstable angina (UA).[20] This study used the updated guideline recommendation to define delayed time from symptom onset to FMC (ie, >12 hours), delayed DTN time (ie, >30 min) and delayed D2B time (ie, >90 min).[5 6 20] For patients with STEMI, the proportions of those with delayed time from onset to FMC, delayed DTN time and delayed D2B time were calculated. On the other hand, only delayed time from symptom onset to FMC was calculated for patients with NSTEACS. Categorical variables were described as absolute numbers and percentages. For continuous variables, normally distributed variables were described as mean and SD, while non-normally distributed variables were described as median with IQR. To compare the general characteristics of patients, time to treatment, treatment patterns and treatment outcome (ie, in-hospital mortality) across three periods (ie, two pandemic periods and the prepandemic period), generalised linear mixed model (GLMM) with the hospital as random effect was adopted to account for multilevel data as our patients were nested within the hospitals. GLMM was

Table 1 Characteristics of patients with ACS across three pandemic periods

	Prepandemic (2019)	First year of pandemic (2020)	Second year of pandemic (2021)	P value*
Male, n (%)	227 (72.5)	345 (71.3)	306 (73.6)	0.766
Type of ACS, n (%)				0.400
STEMI	147 (47)	228 (47.1)	223 (53.6)	
NSTEACS	166 (53)	256 (52.9)	193 (46.4)	
Age, median (IQR), n	60 (17), 313	61 (16), 484	61 (15), 416	0.651
Obesity, n (%)	64 (22.9)	151 (33.1)	122 (31.5)	0.027
Killip class, n (%)				0.023
I	148 (47.9)	277 (57.2)	195 (46.9)	
II	103 (33.3)	125 (25.8)	138 (33.2)	
III	43 (13.9)	42 (8.7)	50 (12.0)	
IV	15 (4.9)	40 (8.3)	33 (7.9)	
Smoker, n (%)	161 (52.3)	261 (54.1)	265 (63.7)	0.005
Cardiac arrest, n (%)	18 (5.8)	19 (3.9)	10 (2.4)	0.062
GRACE risk score, median (IQR), n	139 (52), 266	133.5 (59), 412	139 (51), 365	0.151
Infected with COVID-19, n (%)	0 (0)	4 (0.8)	23 (5.5)	<0.001

*Generalised linear mixed model.
ACS, acute coronary syndrome; GRACE, Global Registry of Acute Coronary Events; NSTEACS, non-ST-elevation acute coronary syndrome; STEMI, ST-elevation myocardial infarction.

Table 2 Time to treatment profiles by COVID-19 pandemic period

	n	Median (IQR)	Mean (SD)	Mean difference* (95% CI)
STEMI				
Time from symptom onset to FMC (hours)				
Prepandemic (2019)	147	7.00 (17.00)	22.09 (47.25)	Ref
During first year of pandemic (2020)	226	9.00 (18.05)	25.89 (57.29)	3.81 (–7.85, 15.46)
During second year of pandemic (2021)	222	11.36 (29.13)	34.65 (60.49)	12.56 (0.87, 24.26)
Door-to-balloon time (hours)				
Prepandemic (2019)	98	10.01 (29.76)	22.26 (25.99)	Ref
During first year of pandemic (2020)	163	6.48 (19.42)	17.94 (29.25)	–2.29 (–8.23, 3.64)
During second year of pandemic (2021)	169	6.25 (14.22)	14.76 (19.62)	–5.36 (–11.26, 0.54)
Door-to-needle time (hours)				
Prepandemic (2019)	85	1.67 (2.75)	3.67 (6.63)	Ref
During first year of pandemic (2020)	96	1.62 (2.66)	5.53 (16.19)	0.18 (–4.49, 4.48)
During second year of pandemic (2021)	82	1.42 (2.43)	8.26 (23.92)	3.91 (–0.93, 8.71)
Total ischaemic time (hours)				
Prepandemic (2019)	147	10.68 (27.25)	30.29 (50.55)	Ref
During first year of pandemic (2020)	226	15.62 (38.31)	37.29 (62.19)	6.41 (–6.42, 18.85)
During second year of pandemic (2021)	220	20.00 (48.75)	45.85 (65.85)	14.56 (1.85, 27.28)
NSTEACS				
Time from symptom onset to FMC (hours)				
Prepandemic (2019)	160	10.12 (38.79)	33.16 (56.52)	Ref
During first year of pandemic (2020)	254	7.93 (22.86)	30.28 (52.40)	–3.99 (–15.27, 7.28)
During second year of pandemic (2021)	192	11.44 (38.63)	38.64 (63.85)	3.44 (–8.57, 15.45)
Total ischaemic time (hours)				
Prepandemic (2019)	146	26.20 (44.05)	50.37 (65.63)	Ref
During first year of pandemic (2020)	238	20.71 (46.52)	46.87 (60.59)	–6.63 (–20.07, 6.80)
During second year of pandemic (2021)	187	30.75 (59.54)	60.81 (76.19)	4.99 (–9.19, 19.18)

*Generalised linear mixed model.
FMC, first medical contact; NSTEACS, non-ST-elevation acute coronary syndrome; Ref, reference; STEMI, ST-elevation myocardial infarction.

also employed to examine the effect of the COVID-19 pandemic on in-hospital mortality after adjusting for covariates. A p value <0.05 was used to indicate statistical significance, except for bivariate analysis in which a p value <0.2 was used to determine candidate factors for multivariate analysis. SPSS Statistics Software V.23.0 and STATA V.17.0 were used to analyse the data.

Patient and public involvement

None.

RESULTS

Of the total 1213 patients with ACS identified, 598, 340 and 275 were patients with STEMI, NSTEMI and UA, respectively. 313 patients were hospitalised in 2019, while 484 and 416 patients were hospitalised in 2020 and 2021, respectively (online supplemental figure 1). The characteristics of patients with ACS for each of the COVID-19 periods are reported in table 1. The median (IQR) length of stay of the patients was 4 (3) days. Overall, patients with ACS from the three studied periods were generally similar except for significant differences in obesity, smoking status, Killip class and prevalence of COVID-19 infection.

Time to treatment

The time to ACS treatment during each of the COVID-19 periods is presented in table 2. For patients with STEMI, a longer mean time from symptom onset to FMC was reported during the second year of the pandemic as compared with the prepandemic period (34.65 hours vs 22.09 hours). According to the results of the GLMM, the mean time from symptom onset to FMC among patients with STEMI during the second year of the pandemic was 12.59 hours significantly longer than that of the prepandemic period (mean difference=12.56, 95% CI 0.87, 24.26). Furthermore, the mean total ischaemic time among patients with STEMI was longer during the second year of the COVID-19 pandemic as

Table 3 Delayed time to treatment by COVID-19 pandemic period

	n	%	OR (95% CI)*
STEMI			
Delayed time from symptom onset to FMC (n=595)			
Prepandemic (2019)	47	32.0	
During first year of pandemic (2020)	84	37.2	1.19 (0.76, 1.85)
During second year of pandemic (2021)	106	47.7	1.84 (1.18, 2.85)
Delayed door-to-needle time (n=263)			
Prepandemic (2019)	74	87.1	
During first year of pandemic (2020)	81	84.4	0.77 (0.33, 1.81)
During second year of pandemic (2021)	72	87.8	1.05 (0.42, 2.64)
Delayed door-to-balloon time (n=430)			
Prepandemic (2019)	91	92.9	
During first year of pandemic (2020)	146	89.6	0.67 (0.26, 1.69)
During second year of pandemic (2021)	168	99.4	13.08 (1.57, 108.73)
NSTEACS			
Delayed time from symptom onset to FMC (n=606)			
Prepandemic (2019)	73	45.6	
During first year of pandemic (2020)	107	42.1	0.84 (0.56, 1.25)
During second year of pandemic (2021)	92	47.9	1.02 (0.67, 1.57)

*Generalised linear mixed model.
FMC, first medical contact; NSTEACS, non-ST-elevation acute coronary syndrome; STEMI, ST-elevation myocardial infarction.

compared with the prepandemic period (45.85 hours vs 30.29 hours). According to the results of the GLMM, the mean total ischaemic time among patients with STEMI during the second year of the pandemic was 14.56 hours significantly longer than that of the prepandemic period (mean difference=14.56, 95% CI 1.85, 27.28). No significant difference in terms of time from symptom onset to FMC, DTB, DTN and total ischaemic time between the prepandemic period and the first year of the pandemic was observed among patients with STEMI. For patients with NSTEACS, no significant difference in terms of time from symptom onset to FMC and total ischaemic time was identified between the prepandemic period and during the pandemic period.

Table 3 compares the proportion of patients with delayed treatment between the prepandemic period and the two pandemic periods. For patients with STEMI, the proportion of patients with a delayed time from onset to FMC during the second year of the pandemic was found to be significantly higher than that of the prepandemic period (47.7% vs 32.0%, OR=1.84, 95% CI 1.18, 2.85). Also, the proportion of patients with STEMI with delayed D2B time was significantly higher during the second year of the pandemic as compared with the prepandemic period (99.4% vs 92.9%, OR=13.08, 95% CI 1.57, 108.73). On the other hand, no significant difference in terms of proportion of patients with delayed time from onset to FMC, delayed DTB time and delayed DTN time between the prepandemic period and the first year of the pandemic was observed among patients with STEMI.

Treatment pattern

Table 4 presents ACS treatment patterns by COVID-19 pandemic period. For patients with STEMI, no significant difference between the two pandemic periods and the prepandemic period was found in terms of the proportion of patients who underwent PCI. However, a lower proportion of patients with STEMI who underwent PPCI during the second year of the pandemic as compared with the prepandemic period was identified (18.3% vs 31.6%, OR=0.43, 95% CI 0.24, 0.79). For patients with NSTEACS, the proportion of patients who underwent PCI during the two pandemic periods and the prepandemic period was similar.

Treatment outcomes

As shown in table 4, no significant difference in terms of in-hospital mortality was found among patients with STEMI between the two pandemic periods and the prepandemic period. On the other hand, significantly lower mortality among patients with NSTEACS was found during the second year of the pandemic as compared with the prepandemic period (7.3% vs 13.9%, OR=0.48, 95% CI 0.24, 0.98). The effect of the COVID-19 pandemic on in-hospital mortality was further examined using multivariate analysis, as shown in table 5. According to the bivariate analysis, age, gender, type of ACS, cardiac

Table 4 Treatment pattern and outcome by COVID-19 pandemic period

	n	%	OR (95% CI)*
STEMI			
Underwent PCI (n=598)			
Prepandemic (2019)	98	66.7	
During first year of pandemic (2020)	163	71.5	0.97 (0.51, 1.86)
During second year of pandemic (2021)	169	75.8	1.24 (0.63, 2.42)
Underwent PPCI (n=430)			
Prepandemic (2019)	31	31.6	
During first year of pandemic (2020)	38	23.3	0.59 (0.34, 1.05)
During second year of pandemic (2021)	31	18.3	0.43 (0.24, 0.79)
In-hospital mortality (n=598)			
Prepandemic (2019)	21	14.3	
During first year of pandemic (2020)	51	22.4	1.63 (0.93, 2.86)
During second year of pandemic (2021)	31	13.9	0.91 (0.50, 1.67)
NSTEACS			
Underwent PCI (n=615)			
Prepandemic (2019)	63	38.0	
During first year of pandemic (2020)	109	42.6	1.53 (0.83, 2.84)
During second year of pandemic (2021)	85	44	1.15 (0.62, 2.15)
In-hospital mortality (n=615)			
Prepandemic (2019)	23	13.9	
During first year of pandemic (2020)	26	10.2	0.70 (0.38, 1.28)
During second year of pandemic (2021)	14	7.3	0.48 (0.24, 0.98)

*Generalised linear mixed model.
NSTEACS, non-ST-elevation acute coronary syndrome; PCI, percutaneous coronary intervention; PPCI, primary percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

arrest, smoking status, obesity, systolic blood pressure, Killip class, GRACE risk score, COVID-19 pandemic period, delayed onset to FMC and COVID-19 infection were found to be associated with in-hospital mortality. Nevertheless, only seven variables (ie, gender, COVID-19 pandemic period, smoking, obesity, GRACE risk score, delayed onset to FMC and COVID-19 infection) were entered into the model. Systolic blood pressure, age, Killip class, cardiac arrest and type of ACS were considered correlated with the GRACE risk score and were not included in the regression model. Our findings indicated that only GRACE risk score was a significant predictor of in-hospital mortality after adjusting for other variables in the model (OR=1.04, 95% CI 1.03, 1.05).

DISCUSSION

To the best of our knowledge, this is the first multicentre study to evaluate the quality of ACS care throughout the pandemic in Indonesia. Similar to previous studies,[9 10] we found that the time from symptom onset to FMC of patients with STEMI was significantly longer during the second year of the pandemic compared with the prepandemic period. As a result, the proportion of patients with STEMI with a delayed time from onset to FMC was significantly higher during the second year of the pandemic as compared with the prepandemic period. This may partly be attributed to the hesitancy to visit the hospital or the unintentional effect of lockdown policies during the pandemic. Fear of contracting COVID-19[23] and difficulty in finding transportation during the lockdown[24 25] may have also contributed to such delays. In addition, the role of media in providing daily reports on how hospitals prepared for and treated COVID-19 patients also contributed to patients' perception of the overwhelmed health services, leading to reduced access to medical services.[26] Notably, a previous study conducted in Jakarta, Indonesia[17] did not observe the impact of the COVID-19 pandemic on time from onset to FMC. This is most likely because the previous study was conducted very early in the pandemic (ie, 2020), when the number of COVID-19 cases was quite small and there were less limitations in movement.

Current guidelines recommend that all patients with ACS should undergo COVID-19 testing at the time of hospital arrival and that the D2B time should still be less than 120 min.[27] Such target is challenging, particularly

Table 5 Factors affecting in-hospital mortality

Variables	OR (95% CI)*
Constant	0.0003 (0.00008, 0.0015)
Gender (ref: female)	
Male	0.65 (0.33, 1.29)
COVID-19 period (ref: prepandemic, 2019)	
First year of pandemic (2020)	1.31 (0.72, 2.36)
Second year of pandemic (2021)	0.65 (0.34, 1.24)
Smoking status (ref: smoker)	
Smoker	1.11 (0.58, 2.13)
Obesity (ref: non-obese)	
Obese	0.59 (0.32, 1.09)
GRACE risk score	1.04 (1.03, 1.05)
COVID-19 infection (ref: not infected)	
Infected	1.87 (0.50, 6.95)
Delayed time from symptom onset to FMC (ref: not delayed)	
Delayed	0.86 (0.52, 1.39)

*Generalised linear mixed model.
FMC, first medical contact; GRACE, Global Registry of Acute Coronary Events; ref, reference.

among developing countries. Previous studies showed a significant increase in D2B time during the COVID-19 pandemic.[17 23] Although we did not observe a significant difference in the mean D2B time between the prepandemic period and during the pandemic periods in our study, it should be noted that the mean D2B among patients with STEMI far exceeded the generally recommended target of 90 min in all three pandemic periods (mean of 22.26 hours in 2019, 17.94 hours in 2020 and 14.76 hours in 2021). In addition, there was a significantly higher proportion of patients with STEMI experiencing delayed D2B time during the second year of the pandemic as compared with the prepandemic period. The most likely explanations for this delay were the additional procedures required to evaluate potential COVID-19 infection before the delivery of ACS care,[28] the limited number of health staff/cardiologists and the additional process of protection of healthcare personnel and hospital environment.[29] It is recommended that at least one cath lab and healthcare worker should be allocated for treatment of confirmed or suspected patients with ACS who are infected with COVID-19.[27] However, none of our study sites has a dedicated and isolated catheterisation laboratory for COVID-19 patients. This may also be one of the potential contributors to prolongation of D2B time.[17 18] Furthermore, the differential diagnosis between non-COVID-19 ACS and ACS-induced myocardial injuries might also contribute to the longer D2B time. Specifically, respiratory symptoms among patients with myocardial infarction at hospital presentation during the COVID-19 pandemic frequently led to presumption of COVID-19 infection than delay in receiving treatment to resolve the myocardial infarction.[30] In addition, ECG alterations and increased cardiac biomarkers from SARS-CoV-2 infection might mimic myocardial infarction (STEMI mimicry).[31 32]

While we did not observe a significant difference in the proportion of patients with STEMI and NSTEACS who underwent PCI across the three studied periods, there was significantly less PPCI performed in patients with STEMI during the pandemic period compared with the prepandemic period. This finding is consistent with previous studies in other countries[33 34] as well as previous studies in Indonesia.[17 18] This is most likely a result of the limited number of health staff/cardiologists and the very late presentation of patients with ACS during the pandemic period.

A recent systematic review[11] suggested that in-hospital mortality of patients with STEMI in low-income and middle-income countries significantly increased during the COVID-19 pandemic, while those of patients with STEMI in high-income countries were not different. Consistent with previous studies in Indonesia,[17 18] our study could not identify a significant difference between prepandemic and pandemic periods in terms of in-hospital mortality among patients with STEMI. Similar to previous studies, cardiac arrest,[35] male gender,[36 37] obesity,[38] smoking,[37 39] GRACE risk score,[40–43] COVID-19 pandemic period,[42 44] COVID-19 infection[42 44 45] and delayed time from symptom onset to FMC[41 46] were associated with in-hospital mortality in our bivariate analysis. Nevertheless, only GRACE risk score was found to be an independent predictor (OR=1.04, 95% CI 1.03, 1.04, p<0.001), after adjusting for other covariates. Notably, COVID-19 infection might not be a significant predictor of in-hospital mortality in our study possibly due to the low incidence of COVID-19 infection among our sample (<6%).

It should be noted that approximately 70% of our study sample were male. This is consistent with previous studies which reported that ≥70% of patients with ACS in Indonesia during the prepandemic period were male.[13–15] This could be partly due to the sex differences in symptoms of ACS so that women with chest pain were likely to be underdiagnosed and to have delayed treatment, as well as the disparity in access to treatment among women.[47 48] While previous studies suggested that there might be gender disparity in terms of outcomes of ACS,[47] our study could not identify the significant difference between men and women in terms of in-hospital mortality after adjusting for other covariates. Nevertheless, further studies examining the inequity of access for women as well as its relationship with ACS outcome are warranted.

This study has potential limitations. First, this study was conducted only in three hospitals in Yogyakarta. The findings from this study might not reflect the impact of the COVID-19 pandemic across all hospitals in Indonesia. Second, the challenges of obtaining data from the retrospective review of medical records involved incomplete data and difficulty in verifying the information.

While incomplete data were perhaps inevitable, several measures were performed to improve data accuracy in our study. For example, our medical record reviews were conducted by nurses who were familiar with the medical records of the settings under the supervision of cardiologists. In case of unclear or inconsistent information, data verification was performed by a discussion with the cardiologists. In addition, a structured and standardised data abstraction form with a clear operational definition of each variable was developed to ensure the quality of the collected data. Third, it should also be noted that the differences across COVID-19 pandemic periods identified in this study might be explained by inadequate control of confounders to some extent. To gain a better understanding of the impact of the COVID-19 pandemic on ACS care, the process of care-seeking during the pandemic and the barriers to seeking ACS care, qualitative studies are also warranted. In addition, the cause of in-hospital mortality was not comprehensively examined in terms of whether it was associated with COVID-19 infection or the ACS itself. However, due to a limited number of infected cases, we believe that this issue may unlikely interfere with our findings and interpretations. Lastly, the impact of the COVID-19 pandemic on out-of-hospital mortality from ACS was not explored in this study.

Based on the findings of our study, efforts should be made by health authorities to improve ACS management in Indonesia. Since prehospital delay is commonly reported, the first and foremost strategy should be about providing public health education to improve the early recognition of ACS symptoms and the need to seek timely medical treatment. Formation of a partnership between the healthcare system, patient organisations and the media to disseminate such information is warranted. In addition, health facilities should design effective care pathways for patients with ACS during times of crisis. A clear care process should be designed and communicated throughout hospital settings.

CONCLUSION

The COVID-19 pandemic significantly and adversely affects ACS management, leading to significant treatment delay. Efforts should be made to ensure that patients with ACS receive timely and effective treatments even during a pandemic. Campaigns and education media aimed at increasing awareness of ACS symptoms and the importance of seeking immediate medical care should be launched accordingly. National ACS care process during times of crisis should be developed and disseminated to ensure timely provision of ACS treatment.

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REFERENCES

1 World Health Organization. WHO Coronavirus (COVID-19) Dashboard, 2022. Available: https://covid19.who.int/
2 Grines CL. SCAI consumer survey comparing fear of COVID-19 versus heart attack or stroke. *Catheter Cardiovasc Interv* 2021;97:193–4.
3 Garcia S, Stanberry L, Schmidt C, *et al*. Impact of COVID-19 pandemic on STEMI care: An expanded analysis from the United States. *Cathet Cardio Intervent* 2021;98:217–22.
4 Moynihan R, Sanders S, Michaleff ZA, *et al*. Impact of COVID-19 pandemic on utilisation of healthcare services: a systematic review. *BMJ Open* 2021;11:e045343.

5 Ibanez B, James S, Agewall S, *et al*. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2017;39:119–77.
6 Jneid H, Addison D, Bhatt DL, *et al*. 2017 AHA/ACC Clinical Performance and Quality Measures for Adults With ST-Elevation and Non-ST-Elevation Myocardial Infarction: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. *J Am Coll Cardiol* 2017;70:2048–90.
7 Irawati S, Dharma S, Taxis K, *et al*. Association between Adherence to Guideline-Recommended Preventive Medications and In-Hospital Mortality among Non-Reperfused ST-Elevation Myocardial Infarction Patients Admitted to a Tertiary Care Academic Center in a Developing Country. *Glob Heart* 2020;15:8.
8 Helal A, Shahin L, Abdelsalam M, *et al*. Global effect of COVID-19 pandemic on the rate of acute coronary syndrome admissions: a comprehensive review of published literature. *Open Heart* 2021;8:e001645.
9 Kiss P, Carcel C, Hockham C, *et al*. The impact of the COVID-19 pandemic on the care and management of patients with acute cardiovascular disease: a systematic review. *Eur Heart J Qual Care Clin Outcomes* 2021;7:18–27.
10 Mogharab V, Ostovar M, Ruszkowski J, *et al*. Global burden of the COVID-19 associated patient-related delay in emergency healthcare: a panel of systematic review and meta-analyses. *Global Health* 2022;18:58.
11 Beza L, Leslie SL, Alemayehu B, *et al*. Acute coronary syndrome treatment delay in low to middle-income countries: A systematic review. *Int J Cardiol Heart Vasc* 2021;35:100823.
12 Dharma S, Juzar DA, Firdaus I, *et al*. Acute myocardial infarction system of care in the third world. *Neth Heart J* 2012;20:254–9.
13 Qanitha A, Uiterwaal CSPM, Henriques JPS, *et al*. Characteristics and the average 30-day and 6-month clinical outcomes of patients hospitalised with coronary artery disease in a poor South-East Asian setting: the first cohort from Makassar Cardiac Center, Indonesia. *BMJ Open* 2018;8:e021996.
14 Qanitha A, Uiterwaal CSPM, Henriques JPS, *et al*. Predictors of medium-term mortality in patients hospitalised with coronary artery disease in a resource-limited South-East Asian setting. *Open Heart* 2018;5:e000801.
15 Dharma S, Andriantoro H, Purnawan I, *et al*. Characteristics, treatment and in-hospital outcomes of patients with STEMI in a metropolitan area of a developing country: an initial report of the extended Jakarta Acute Coronary Syndrome registry. *BMJ Open* 2016;6:e012193.
16 Mahendradhata Y, Andayani NLPE, Hasri ET, *et al*. The Capacity of the Indonesian Healthcare System to Respond to COVID-19. *Front Public Health* 2021;9:649819.
17 Dharma S, Dakota I, Firdaus I, *et al*. Performance of Primary Angioplasty for STEMI during the COVID-19 Outbreak. *Int J Angiol* 2021;30:148–54.
18 Firman D, Mangkuanom AS, Iryuza N, *et al*. Decrease in the Number of Patients Presenting With ST-Segment Elevation Myocardial Infarction Across Catheterization Centers in Indonesia During the Coronavirus Disease 2019 Pandemic. *Front Cardiovasc Med* 2021;8:676592.
19 Edouard M, Hannah R, Lucas RG, *et al*. Coronavirus pandemic (covid-19). OurWorldinData.org; 2020. Available: https://ourworldindata.org/coronavirus
20 Collet J-P, Thiele H, Barbato E, *et al*. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J* 2020;42:1289–367.
21 Vicent L, Velásquez-Rodríguez J, Valero-Masa MJ, *et al*. Predictors of high Killip class after ST segment elevation myocardial infarction in the era of primary reperfusion. *Int J Cardiol* 2017;248:46–50.
22 Parakh K, Thombs BD, Bhat U, *et al*. Long-term significance of Killip class and left ventricular systolic dysfunction. *Am J Med* 2008;121:1015–8.
23 Chew NWS, Ow ZGW, Teo VXY, *et al*. The Global Effect of the COVID-19 Pandemic on STEMI Care: A Systematic Review and Meta-analysis. *Can J Cardiol* 2021;37:1450–9.
24 Braiteh N, Rehman WU, Alom M, *et al*. Decrease in acute coronary syndrome presentations during the COVID-19 pandemic in upstate New York. *Am Heart J* 2020;226:147–51.
25 Erol MK, Kayıkçıoğlu M, Kılıçkap M, *et al*. Treatment delays and in-hospital outcomes in acute myocardial infarction during the COVID-19 pandemic: A nationwide study. *Anatol J Cardiol* 2020;24:334–42.
26 Lidin M, Lyngå P, Kinch-Westerdahl A, *et al*. Patient delay prior to care-seeking in acute myocardial infarction during the outbreak of the coronavirus SARS-CoV2 pandemic. *Eur J Cardiovasc Nurs* 2021;20:752–9.
27 Chieffo A, Stefanini GG, Price S, *et al*. EAPCI Position Statement on Invasive Management of Acute Coronary Syndromes during the COVID-19 pandemic. *Eur Heart J* 2020;41:1839–51.
28 Bahuva R, Aoun J, Goel SS. Management of Acute Coronary Syndrome in the COVID Era. *Methodist Debakey Cardiovasc J* 2021;17:16–21.
29 Cameli M, Pastore MC, Mandoli GE, *et al*. COVID-19 and Acute Coronary Syndromes. *Curr Data Future Front Cardiovasc Med* 2021;7.
30 Henein MY, Bytyçi I, Nicoll R, *et al*. Obesity Strongly Predicts COVID-19-Related Major Clinical Adverse Events in Coptic Clergy. *J Clin Med* 2021;10:2752.
31 Ng S, Juzar DA. Challenges in STEMI Management during COVID-19 Pandemic. *Indones J Cardiol* 2020;41.
32 Esteves V, Zukowski CN, FAd L, *et al*. The Association between Covid-19 and ST Elevation Myocardial Infarction: Variable Clinical Presentations on a Case Report Series. *Int J Cardiovasc Sci* 2020;33:429–35.
33 Daoulah A, Hersi AS, Al-Faifi SM, *et al*. STEMI and COVID-19 Pandemic in Saudi Arabia. *Curr Probl Cardiol* 2021;46:100656.
34 Araiza-Garaygordobil D, Montalto C, Martinez-Amezcua P, *et al*. Impact of the COVID-19 pandemic on hospitalizations for acute coronary syndromes: a multinational study. *QJM* 2021;114:642–7.
35 Pramudyo M, Yahya Af Fau - Martanto E, Martanto E Fau - Tiksnadi BB, *et al*. Predictors of In-Hospital Mortality in Patients with Acute Coronary Syndrome in Hasan Sadikin Hospital. *Acta Med Indones* 2022;54:379–88.
36 Fernández-Martínez NF, Ortiz-González-Serna R, Serrano-Ortiz Á, *et al*. Sex Differences and Predictors of In-Hospital Mortality among Patients with COVID-19: Results from the ANCOHVID Multicentre Study. *Int J Environ Res Public Health* 2021;18:9018.
37 Ali SF, Smith EE, Bhatt DL, *et al*. Paradoxical association of smoking with in-hospital mortality among patients admitted with acute ischemic stroke. *J Am Heart Assoc* 2013;2:e000171.
38 Williams MJA, Lee M, Alfadhel M, *et al*. Obesity and All Cause Mortality Following Acute Coronary Syndrome (ANZACS-QI 53). *Heart Lung Circ* 2021;30:1854–62.
39 Gupta T, Kolte D, Khera S, *et al*. Smoker's Paradox in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention. *J Am Heart Assoc* 2016;5:e003370.
40 Chotechuang Y, Phrommintikul A, Muenpa R, *et al*. The prognostic utility of GRACE risk score in predictive cardiovascular event rate in STEMI patients with successful fibrinolysis and delay intervention in non PCI-capable hospital: a retrospective cohort study. *BMC Cardiovasc Disord* 2016;16:212.
41 Sofidis G, Otountzidis N, Stalikas N, *et al*. Association of GRACE Risk Score with Coronary Artery Disease Complexity in Patients with Acute Coronary Syndrome. *J Clin Med* 2021;10:2210.
42 Solano-López J, Zamorano JL, Pardo Sanz A, *et al*. Risk factors for in-hospital mortality in patients with acute myocardial infarction during the COVID-19 outbreak. *Rev Esp Cardiol* 2020;73:985–93.
43 Wójcik M, Karpiak J, Zarębа L, *et al*. The GRACE risk score in patients with ST-segment elevation myocardial infarction and concomitant COVID-19. *Arch Med Sci Atheroscler Dis* 2022;7:e116–23.
44 Saad M, Kennedy KF, Imran H, *et al*. Association Between COVID-19 Diagnosis and In-Hospital Mortality in Patients Hospitalized With ST-Segment Elevation Myocardial Infarction. *JAMA* 2021;326:1940–52.
45 Primessnig U, Pieske BM, Sherif M. Increased mortality and worse cardiac outcome of acute myocardial infarction during the early COVID-19 pandemic. *ESC Heart Fail* 2021;8:333–43.
46 Grech N, Xuereb R, England K, *et al*. When the patients stayed home: the impact of the COVID-19 pandemic on acute cardiac admissions and cardiac mortality in Malta. *Z Gesundh Wiss* 2022;30:1725–31.
47 Cader FA, Banerjee S, Gulati M. Sex Differences in Acute Coronary Syndromes: A Global Perspective. *J Cardiovasc Dev Dis* 2022;9:239.
48 Sella YO, Manistamara H, Apriliawan S, *et al*. Characteristic differences of chest pain in male and female patients with acute coronary syndrome: A pilot study. *J Public Health Res* 2021;10:2242.