In-Hospital Major Adverse Cardiovascular Events in Patients with STEMI during COVID-19 Pandemic

by Sefri Noventi Sofia

Original Article

In-Hospital Major Adverse Cardiovascular Events in Patients with STEMI during COVID-19 Pandemic

Arjatya Pramadita Mangkoesoebroto, Yan Herry, Sefri Noventi Sofia, Udin Bahrudin

Departement of Cardiology and Vascular Medicine Dr. Kariadi Hospital/
Faculty of Medicine Diponegoro University Semarang, Indonesia

Abstract

Author Affiliation:
Departement of Cardiology and Vascular Medicine
Dr. Kariadi Hospital/Faculty of Medicine
Diponegoro University Semarang,
Indonesia

Author Correspondence:
Udin Bahrudin
Dr. Sutomo Street No. 16 Semarang,
Central Java 50244,
Indonesia

E-mail:
bahrudin00@gmail.com;
bahrudin00@lecturer.undip.ac.id

Background : The Coronavirus Disease 2019 (COVID-19) pandemic has become a global burden, changing healthcare system and affecting patients with ST segment elevation myocardial infarction (STEMI). Several countries reported a decrease in hospital admission, changing management, increase total ischemic time, and major cardiovascular events (MACE) in the pandemic era. However, there is limited data especially in Indonesia. The objectives of this study was to know the differences in admissions, characteristics, management and in-hospital MACE in STEMI patients between pre and pandemic era.

Methods : Comparative observational analytical study was done on 169 patients in the pre-pandemic (12 March 2019–11 March 2020) compared to 163 patients in the pandemic era (12 March 2020–30 September 2021) with STEMI at Dr. Kariadi Semarang Hospital. Assessment of monthly admission rates, total ischaemic time, reperfusion management, COVID-19 status and MACE were carried out.

Results : During the COVID-19 pandemic, there was a decrease in the average admission of 14.1 to 8.6 patients per month (p<0.001), increase total ischaemic time of 8.78 (3.22-19.68) hours to 10.22 (3.20–20.43) hours (p<0.001), decreased use of primary PCI (97.0% vs. 83.4%, p<0.001), increased fibrinolytic (1.8% vs 8.6%, p=0.010) and no reperfusion (1.2% vs 8.0%, p=0.007). There was a significant increase in MACE in the era of the COVID-19 pandemic (10.7% vs 22.1%, p=0.008), with mortality (4.7% vs 11.7%, p=0.035), stroke (1.2% vs 1.8%, p=0.680), cardiogenic shock (4.1% vs 11.0%, p=0.030), and acute pulmonary edema (3.6% vs 10.4%, p=0.024).

Conclusion : There was a decrease in admissions and primary PCI procedure, increase use of fibrinolytics and without reperfusion, total ischemic time prolongation, and significant increase of in-hospital MACE in STEMI patients during the COVID-19 pandemic.

Keywords : ST-segment elevation myocardial infarction, COVID-19 pandemic, total ischaemic time, management, major adverse cardiac event

INTRODUCTION

Since the Coronavirus Disease 2019 (COVID-19) pandemic which began in Wuhan, China, in December 2019, there has been a sharp increase in confirmed patients, which has led to changes in health services and community restrictions. The phenomenon of the COVID-19 pandemic does not only affect patients with COVID-19 but has a wider impact. In fact, to date, there have been several studies reporting a reduction in hospital admission rates in STEMI patients.[1-7] In China, it was stated that there was a 51.4% decrease in STEMI patient admissions and an increase in patients who did not get reperfusion compared to 2018 and 2019.[1] There is a study in five hospitals in Indonesia that reports a significant reduction in STEMI patients from 338 to 190 patients in 2020, as well as a decrease in the use of primary PCI.[7] In addition to a decrease in admissions, there has also been an increase in delays, both delays for patients coming to health facilities (patient delay) and prolonged time in the health care system (hospital delay). Several studies found that the time from the onset of typical ischemia symptoms to first medical contact (FMC) and ischemic time increased significantly.[4,7-11] Meta-analysis study by Zhu et al. that compared the characteristics and outcomes of STEMI patients found that in six articles there were an increase in onset to FMC time (SMD 0.51, 95% CI, 0.24-0.78, p<0.001) in the COVID-19 pandemic era compared to before the COVID-19 pandemic.[12]

In addition, there were several studies that reported an increase in poor outcomes in STEMI patients during the pandemic era. The China Chest Pain Center's conducted a study on 28,189 STEMI patients from 2019-2020. Apart from finding a decrease in admissions to health services and a change in reperfusion strategy, there was also an increase in the incidence of death in hospital (OR 1.21; 95% CI: 1.07-1,37;p=0.003) and heart failure (OR 1.10;95% CI: 1.02-1.18; p=0.020).[13]

The differences in health services between developed and developing countries, such as hospital availability, early screening and rapid microbiological examination, availability of an isolation catheterization rooms, and geographical differences allow for differences in outcomes in this population. As a result, it is necessary at this time to investigate and analyze differences in admissions, characteristics, management, and in-hospital MACE in STEMI patients between the pandemic era and before the pandemic era.

METHODS

This was an observational study with a cross-sectional design. Total sampling was carried out on STEMI patients at Dr Kariadi General Hospital Semarang in the period March 12 2019 to March 11 2020 in the group before the COVID-19 pandemic era and March 12 2020 to September 30 2021 for the COVID-19 pandemic era group with STEMI diagnosis criteria based on symptoms (eg persistent chest pain) and signs (eg 12-lead ECG) consistent with myocardial ischemia.[14] The inclusion criteria for this study were patients aged 18 to 80 years, and diagnosed with STEMI onset (typical infarction of chest pain in the emergency room of Dr. Kariadi General Hospital, Semarang) ≤ 12 hours. Exclusion criteria were having an eGFR value <30 ml/min/1.73m², known to have cancer which is thought to be the main cause of death during treatment and having incomplete medical record data. Identity and demographic data were collected, as were clinical data in the form of complaints, onset, last COVID-19 status during treatment, cardiovascular risk factors, systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate, Killip class, infarction location based on ECG criteria, hemoglobin level, random blood glucose level, creatinine level, drugs administered, data related to fibrinolytic reperfusion, Primary PCI, onset to FMC time, FMC to needle time, FMC to wire crossing time, cath lab activation time, total ischaemic time, number of vessel disease, final TIMI flow, and MACE during treatment, death cause, stroke, urgent revascularization, acute pulmonary edema, and acute heart failure.

Data will be displayed in the form of mean ± standard deviation, median (min–max), frequency and percentage. An unpaired comparative test was carried out, Chi-Square test was used in categorical variables, unpaired t-test on numeric variable (parametric) or Mann Whitney (non-parametric). The normality of data distribution was tested by the Kolmogrov–Smirnov test. The p value <0.05 is a significant value. Statistical analysis used the IBM SPSS version 23.0. This study was conducted after obtaining permission from Health Research Ethics Commission No.1083/EC/KEPK-RSDK/2022 and research permission by Dr. Kariadi General Hospital No DP.02.01/I.II/3159/2022.

RESULTS

There are 332 samples of STEMI patients were obtained in the period of March 12 2019 – September 31 2021. The number of samples on the period before the COVID-19 pandemic era on March 12 2019 – March 11 2020 were 169 samples and the period during the COVID-19 pandemic era on March 12 2020 – September 31, 2021 were 163 samples (Table 1) and displayed in a graph per month (Figure 1). The baseline characteristics of the patients are shown in Table 1. There was a significant decrease in STEMI patient admissions per month, with an average of 14.1±3.1 before the pandemic compared to 8.6±4.1 during the COVID-19 pandemic. There was also a significant decrease in the use of primary PCI from 164 (97.0%) to 136 (83.4%), p 0.001, as well as a significant increase in the use of fibrinolytics from 3 (1.8%) to 14 (8.6%), p=0.010, and

TABLE 1
Baseline Characteristics

Variables		All research samples (n=332)	Before COVID-19 Pandemic (n=169)	COVID-19 Pandemic (n=163)	p
Admissions, patients per week		2,5	3.1	1.9	
Age, years		57.6±9.1	57.9±8.3	57.1±9.9	0,414[§]
Sex	Male	279 (84.0%)	135 (79.9%)	144 (88.3%)	0,051[¥]
	Female	53 (16.0%)	34 (20.1%)	19 (11.7%)	
Cardiovascular Risk Factor	Hypertension	193 (58.1%)	99 (58.6%)	94 (57.7%)	0,955[¥]
	Diabetes	160 (48.2%)	77 (45.6%)	83 (50.9%)	0,386[¥]
	Dyslipidemia	105 (31.6%)	52 (30.8%)	53 (32.5%)	0,823[¥]
	Active smoker	145 (43.7%)	72 (42.6%)	73 (44.8%)	0,143[¥]
	Ex-smoker	82 (24.7%)	36 (21.3%)	46 (28.2%)	
	Family History	30 (9.0%)	12 (7.1%)	18 (11.0%)	0,289[¥]
	Menopause	44 (14.2%)	28 (87.5%)	16 (88.9%)	0,631[£]
Presentation Method	Referred from other hospital	246 (74.1%)	114 (67.5%)	132 (81.0%)	**0,007[¥]**
	Self presenting	86 (25.9%)	55 (32.5%)	31 (19.0%)	
Systolic BP, mmHg		119 (67–180)	113 (71–175)	124 (67–180)	**0,002[‡]**
Heart Rate, bpm		79 (31–126)	80 (46–126)	78 (31–120)	**0,024[‡]**
Killip class	1	270 (81.3%)	139 (82.2%)	131 (80.4%)	
	2	42 (12.7%)	23 (13.6%)	19 (11.7%)	
	3	7 (2.1%)	3 (1.8%)	4 (2.5%)	
	4	13 (3.9%)	4 (2.4%)	9 (5.5%)	
	1		139 (82.2%)	131 (80.4%)	0,765[¥]
	2+3+4		30 (17.8%)	33 (19.6%)	
Anterior Infarction		168 (50.6%)	85 (50.3%)	83 (50.9%)	0,997[¥]
BMI, kg/m^2		24,7 (±2.9)	24,6 (±2.8)	24.8 (±3.1)	0,479[§]
Creatinine, mg/dL		1,1 (0.5–2.6)	1.1 (0.5–2.6)	1.2 (0.5–2.6)	**0,037[‡]**
Blood Glucose, mg/dL		142 (65–558)	145 (71–530)	130 (65–558)	0,419[‡]
Reperfusion Method	Primary PCI	300 (90.4%)	164 (97.0%)	136 (83.4%)	**<0,001[¥]**
	Fibrinolysis	17 (5.1%)	3 (1.8%)	14 (8.6%)	**0,010[¥]**
	None	15 (4.5%)	2 (1.2%)	13 (8.0%)	**0,007[¥]**
	Reperfusion	317 (95.5%)	167 (98.8%)	150 (92.0%)	**0,007[¥]**
	No reperfusion	15 (4.5%)	2 (0.6%)	13 (3.9%)	
Treatment	Aspirin	332 (100%)	169 (100%)	163 (100%)	
	P2Y12i	332 (100%)	169 (100%)	163 (100%)	0,568[¥]
	Ticagrelor	250 (75.3%)	130 (76.9%)	120 (73.6%)	

TABLE 1. Continued

Variables		All research samples (n=332)	Before COVID-19 Pandemic (n=169)	COVID-19 Pandemic (n=163)	p
	Clopidogrel	82 (24.7%)	39 (23.1%)	43 (26.4%)	
	Anticoagulant	213 (64.2%)	107 (63.3%)	106 (65.0%)	0,832¥
	Heparin	31 (9.3%)	7 (4.1%)	24 (14.7%)	
	Fondaparinux	165 (49.7%)	91 (53.8%)	74 (45.4%)	
	Enoxaparin	17 (5.1%)	9 (5.3%)	8 (4.9%)	
	ACEi/ARB	306 (92.2%)	155 (91.7%)	151 (92.6%)	0,914¥
	Beta blocker	263 (79.2%)	127 (75.1%)	136 (83.4%)	0,084¥
	Statin	332 (100%)	169 (100%)	163 (100%)	
COVID-19		2 (0.6%)	0 (0%)	2 (1.2%)	0,240£
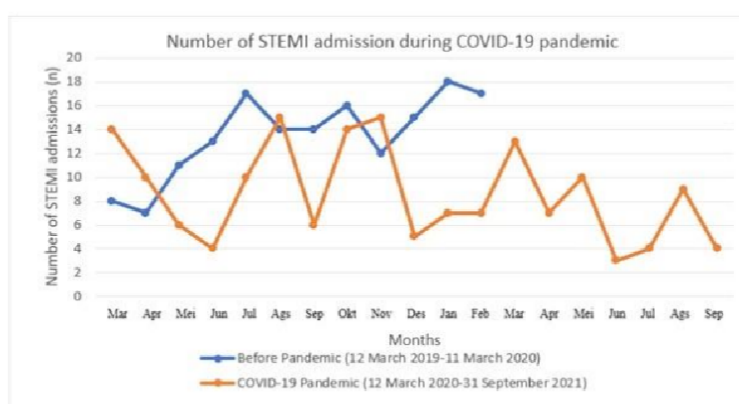
Figure 1. Monthly admission comparison of STEMI patients in one year before pandemic (12 March 2019 – 11 March 2020) and during the COVID-19 pandemic (12 March 2020 – 31 September 2021)

without reperfusion from 2 (1.2%) to 13 (8.0%), p=0.007 (Table 1, Figure 2). The majority of patients were men, with an average age of 57.9 ± 8.3 before the pandemic and 57.1 ± 9.9 during the pandemic. There were no significant differences in cardiovascular risk factors such as hypertension, diabetes, dyslipidemia, smoking, and family history. The number of patients who came to the hospital with referrals from other health facilities increased sharply from 114 (67.5%) to 132 (81.0%) p=0.007. There were 2 (0.6%) patients with a confirmed diagnosis of COVID-19 during treatment. Procedural data of patients who underwent reperfusion are included in Table 2 with details, namely that a significant prolongation of the total ischemic time component was obtained in the pre-pandemic era with 8.78 (3.22–19.68) hours compared to 10.22 (3.20–20.43) hours (Table 2, Figure 3) which includes an onset component of 5.0

(1.5–12.0) hours compared to 7.0 (1.0–12.0) hours, door to wire crossing of 3.28 (1.17–12.68) hours versus 3.66 (0.55–9.85) hours, and door to needle (on fibrinolytics) 0.58 (0.30–0.66) hours versus 1.70 (0.91–2.20) hours. Patients receive the same medical treatment before and during the COVID-19 pandemic. Major cardiovascular events significantly increased in the pandemic era with a total of 36 (22.1%) compared to 18 (10.7%) patients in the pre-pandemic era p=0.008 (Table 3, Figure 4).

DISCUSSION

During the COVID-19 pandemic period, there was a significant decrease in the average patient admission per month from the pre-pandemic era versus the pandemic era from 14.1 ± 3.1 patients per month compared to 8.6 ± 4.1 patients per month, p <0.001, mean diff 5.50, CI 95%

TABLE 2
Procedural data of patients undergoing reperfusion

Variables		Research samples (n=317)	Before COVID-19 Pandemic (n=167)	COVID-19 Pandemic (n=150)	p
Onset, hours		6.4 (1.0–12.0)	5.0 (1.5–12.0)	7.0 (1.0–12.0)	<0,001[‡]
Door-to-wire crossing, hours		3,37 (0.55–12.68)	3.28 (1.17–12.68)	3.66 (0.55–9.85)	0,046[‡]
Total ishcemic time (Primary PCI), hours		10.01 (3,22–20,43)	8.96 (3.22–19.68)	10.53 (3.95–20.43)	<0,001[‡]
Door-to-needle, hours		1.46 (0.30–2.20)	0.58 (0.30–0.66)	1.70 (0.91–2.20)	0,008[‡]
Total ishcemic time (Fibrinolitik), hours		6.70 (3.20–12.00)	5.66 (4.30–7.58)	7.00 (3.20–12.00)	0,705[‡]
Total ishcemic time (Primary PCI +fibrinolitik), hours		9.55 (3.2–20.43)	8.78 (3.22–19.68)	10.22 (3.20–20.43)	<0,001[‡]
CAD vessel disease	1	92 (29.8%)	38 (23.2%)	54 (37.2%)	
	2	92 (29.8%)	56 (34.1%)	36 (24.8%)	
	3	125 (37.7%)	70 (42.7%)	55 (37.9%)	
	1+2	184 (59.5%)	94 (42.7%)	90 (62.1%)	0,463[¥]
	3	125 (40.5%)	70 (57.3%)	55 (37.9%)	
Infarct Related Artery	LAD	158 (47.6%)	84 (51.2%)	74 (51.0%)	
	LCx	15 (4.5%)	7 (4.3%)	8 (5.5%)	
	RCA	133 (40.1%)	72 (43.9%)	61 (42.1%)	
	LAD+RCA	1 (0.3%)	1 (0.6%)	0 (0%)	
	LM	2 (0.6%)	0 (0%)	2 (1.4%)	
Final TIMI flow	3	286 (86.1%)	150 (91.5%)	136 (93.8%)	
	2	22 (6.6%)	13 (7.9%)	9 (6.2%)	
	1	1 (0.3%)	1 (0.6%)	0 (0%)	
	3	286 (86.1%)	150 (91.5%)	136 (93.8%)	0,574[¥]
	1+2	23 (7.4%)	14 (8.5%)	9 (6.2%)	

2.88–8.13 (Figure 1). This significant decrease in patient admissions also occurred globally, in London, England with a significantly decreased incidence of STEMI per week (15±3.5 in 2019 vs 10±4.4 in 2020, p=0.013).[15] Another study in Indonesia at five hospitals with primary PCI facilities stated a decrease in STEMI patient admissions in February – June 2020 (190 patients) compared to the same period in 2019 (338 patients).[7] The decline in STEMI patients during the COVID-19 pandemic may be due to several factors, including the patient's fear of going to health services at the hospital, especially with primary PCI services, where the hospital is larger and has full capacity to avoid transmission of COVID-19.[7,13,15] Some patients who want to check themselves out choose health services in places that tend

distancing, are also causes of a decrease in STEMI admissions to hospitals.[15,16] These policies can reduce stress factors, improve healthy lifestyles such as diet, sports activities, and good sleep quality, which can prevent acute myocardial infarction.[15–18] Reduction in air pollution was also reported during the policy, which could reduce exposure for individuals which is also thought to reduce the occurrence of acute myocardial infarction.[15] Focus on public education about COVID-19 and reduced education regarding awareness, signs, and symptoms of life-threatening diseases such as STEMI can cause people to perceive chest pain or shortness of breath as a respiratory symptom. This has the potential to reduce the number of patients requiring emergency care.[15,16]

This study's significant increase in patient

not to be crowded.[15] Other factors, namely the lockdown policy, orders to stay at home, and social presentation with the referral method is also similar to the registry of The International Study on Acute Coronary
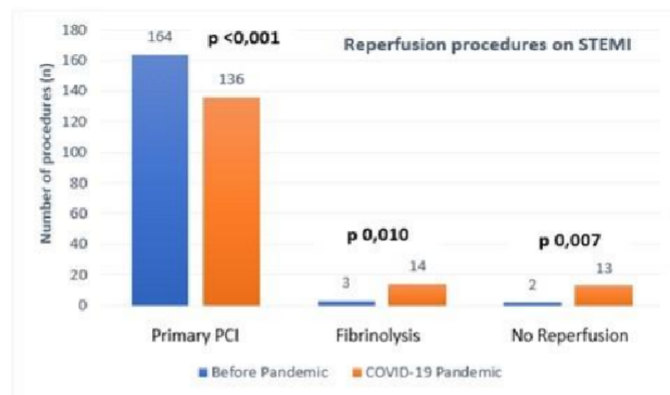
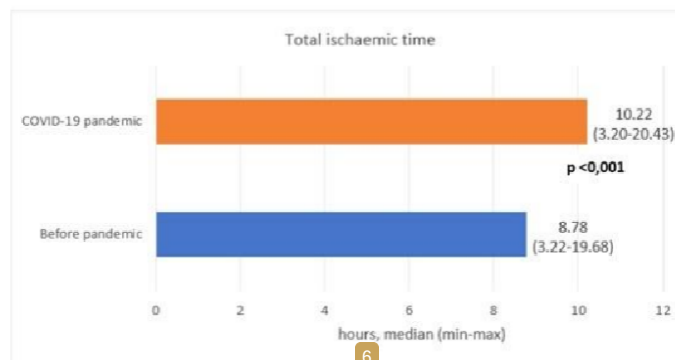**Figure 2.** Comparison of STEMI patient reperfusion methods before and during the COVID-19 pandemic.

Figure 3. Comparison of total ischemic time in STEMI patients before and during the COVID-19 pandemic.

TABLE 3
In-hospital outcomes

Variables	All Research samples (n=332)	Before COVID-19 Pandemic (n=169)	COVID-19 Pandemic (n=163)	p
MACE	54 (16,3%)	18 (10,7%)	36 (22,1%)	0,008[¥]
Death	27 (8,1%)	8 (4,7%)	19 (11,7%)	0,035[¥]
Stroke	5 (1,5%)	2 (1,2%)	3 (1,8%)	0,680[£]
Urgent Revascularization	0	0	0	
Cardiogenic shock	25 (7,5%)	7 (4,1%)	18 (11,0%)	0,030[¥]
Acute Lung Edema	23 (6,9%)	6 (3,6%)	17 (10,4%)	0,024[¥]

Note : The values displayed are mean ± SD, median (min-max), or n (%).
[‡]Mann Whitney; [§]Independent t; [¥]Chi Square, [£]Fischer. ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CAD, coronary artery disease; COVID-19, coronavirus disease 2019; BMI, body mass index; MACE, major adverse cardiac event; BP, blood pressure; TIMI, thrombolysis in myocardial infarction
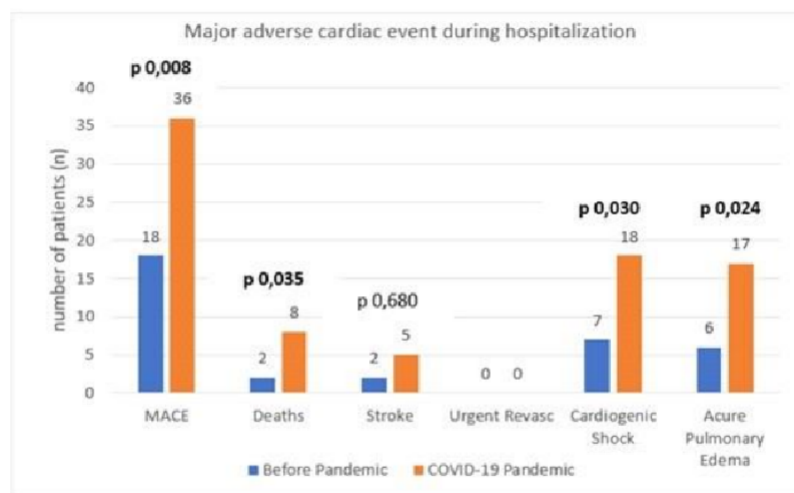
Figure 4. Comparison of the MACE components in STEMI patients before and during COVID-19 pandemic.

Syndromes- ST Elevation Myocardial Infarction COVID-19 (ISACS-STEMI COVID-19) in 6,609 patients who underwent Primary PCI in 18 countries, which stated an increase in referral rates to hospitals with Primary PCI using ambulances (from the community) from 1,893 (54.3%) patients in 2019 to 1,639 (58.3%) patients.[19,20] The increase in the number of referrals to hospitals with primary PCI facilities during this pandemic era was due to the patients' fear of avoiding transmission of COVID-19 where hospitals with primary PCI facilities are usually large hospitals, which also receive referrals for COVID-19 patients.[2,7,20] The full capacity of hospitals, especially with primary PCI facilities, also resulted in patients tending to seek health services that weren't crowded, so that the percentage of referred patients to hospitals with primary PCI increased.[2,7,20]

There was a significant decrease in the use of primary PCI in the pandemic era by 136 (83.4%) patients compared to before the COVID-19 pandemic by 164 (97.0%) patients with p<0.001; IK95% 2,210–14,185; a significant increase in the use of fibrinolytics by 14 (8.6%) patients compared to 3 (1.8%) patients with p=0.010; IK95% 1,417-16,524 (Figure 2). The ISACS-STEMI COVID-19 registry in 109 hospitals reported a consistent reduction in the use of primary PCI in STEMI patients, with an average of 559 (95% CI 514 – 607) in 2019

compared to 477 (95% CI 435 – 522) per million

population in 2020.[19,20] Whereas in Indonesia, there was also an increase in the percentage of conservative management of STEMI patients in June 2020 (33.3%) compared to the same month in 2019 (11.7%).[7] At this time, we found a shift in reperfusion strategy in STEMI as an adaptation to COVID-19 which has a high

transmission rate. The Chinese protocol recommends thrombolysis with COVID-19 in isolation wards for all acute STEMI patients (onset within 12 hours and without thrombolysis contraindications).[13] This is similar to the 1st edition of the COVID-19 management protocol in April 2020 which was also prepared by Perhimpunan Dokter Spesialis Kardiovaskular Indonesia (PERKI).[9]

However, along with the dynamic status of the COVID-19 pandemic, the latest COVID-19 management guidebook published in January 2022 (ed 4) has the principle that timely reperfusion must be pursued during the COVID-19 pandemic.[22,23] In this guideline, PERKI is guided by ESC, where reperfusion must still be carried out in STEMI patients while paying attention to the safety of health workers. In the absence of previous COVID-19 testing, all STEMI patients must be managed as if they were positive for COVID-19. This guideline also states that all primary PCI procedures are carried out in facilities capable of performing PCI in patients with confirmed COVID-19 (isolation catheterization room).[22,23] Due to the lack of isolation catheterization room facilities at Dr. Kariadi Semarang Hospital and the duration of COVID-19 screening, which requires antigen and PCR tests, all patients with STEMI onset within 12 hours and a positive COVID-19 initial screening did not receive a primary PCI strategy.

In this study, fibrinolytics were performed on

14 patients, with details on 12 patients having successful fibrinolytics, where 8 patients were continued with early routine PCI, and 2 patients with failed fibrinolytics were continued with rescue PCI. Of all the patients who underwent fibrinolytic therapy, three MACE were obtained with details of 2 patients dying and 1 patient

experiencing acute pulmonary edema. This is different from the pre-pandemic era, where only 3 fibrinolytic therapies were performed and success, with no one had MACE. Furthermore, in our study, we found 13 patients without reperfusion therapy, where two patients had confirmed COVID-19, one patient had suspected COVID-19 and three patients barely made it past the onset of 12 hours. With details of 2 patients with positive COVID-19 confirmation, the first patient with inferior STEMI KILLIP 1 underwent conservative therapy, and the second patient with anterior STEMI accompanied by ARDS pneumonia underwent conservative therapy. So that the increase in the use of fibrinolytics and without reperfusion that occurred in this pandemic era has been proven to increase the incidence of MACE.

A significant increase in duration of patient onset from first feeling infarction symptoms to first medical contact was also found in the pre-COVID-19 era, with a median mean time of 5.0 (1.5-12.0) hours compared to 7.0 (1.0-12.0) hours in the era of the COVID-19 pandemic (p<0.001). A meta-analysis that compared the characteristics and outcomes of STEMI patients said that six articles found an increase in the onset to FMC time (SMD 0.51, 95% CI, 0.24-0.78, p<0.001) during the pandemic era compared to before the COVID-19 pandemic.[12] One of the reasons for this lengthening of time is due to the patient's fear of seeking health facilities due to COVID-19 which was obtained from interviews during hospital admission.[9,12] The full capacity of hospitals during several periods during the COVID-19 pandemic in Indonesia also made it more difficult for patients to seek medical assistance, so that the onset would be even longer.

In this study, the total duration of ischemic time in patients receiving reperfusion was found to be prolonged during the COVID-19 pandemic era with a median length of 10.22 (3.20-20.43) hours compared to 8.78 (3.22-19.68)) hours in the pre-pandemic era p<0.001 (Figure 3). There was also increased median total ischemic time with fibrinolytic from 7.00 (3.20-12.00) hours compared to 5.66 (4.30-7.58) hours with p=0.705; the median door to needle time also experienced a significant increase with 1.70 (0.91-2.20) compared to 0.58 (0.30-0.66) hours with p=0.008. The ISACS-STEMI COVID-19 registry states that the total ischemic time was prolonged >12 hours for 196 (120-355) minutes in 2019 compared to 225 (135-410) in 2020 (p<0.001) and door to balloon time for 40 (25-64) minutes in 2019 compared to 40 (25-70) minutes in 2020 (p=0.01).[19] The lengthening of the total ischemic time, especially the system delay component, is seen in the significant lengthening of door to cathlab activation and door to crossing wire. Where the lengthening of time in the STEMI service system occurs due to a screening examination protocol before the patient enters the emergency unit and preparations for the use of personal protective equipment (PPE) for health workers, including

doctors, so as to delay the diagnosis and initial management of STEMI, after that the patient is still subject to a rapid test , complete blood count, chest x-ray examination, and CT scan.[7,12,24] Preparation of personnel and equipment in the isolation catheterization room is also called increasing the length of the total ischemic time.[20]

Patient delay in our study was the component that made the main contribution to the lengthening of the total ischemic time during the COVID-19 pandemic with a median difference of 5.0 (1.5-12.0) hours compared to 7.0 (1.0-12.0) hours in the era of the COVID-19 pandemic (p <0.001). As a result, health service counseling provided by health workers and the government has been critical in combating fear of COVID-19 infection, particularly in emergency situations, where STEMI patients at this time are expected to benefit from prompt and appropriate medical attention because this population has a high risk of MACE.[7]

In the era of the COVID-19 pandemic from March 12 2020 to September 31 2021 with a total of 163 patients, 2 (1.2%) had a confirmed diagnosis of COVID-19. In addition, the researchers conducted a further search on all patients and found 11 patients with STEMI who were confirmed positive for COVID-19. However, 9 patients could not be included in this study sample due to late onset (>12 hours), incomplete ischemic time data, and evidence of myocarditis. There is still a possibility that some patients will be confirmed because in the early days of the COVID-19 pandemic they only used rapid screening which included clinical data on signs and symptoms, chest x-ray, blood laboratory, and contact history and demographics. The limited and long duration of testing for COVID-19 using RT-PCR at the start of the COVID-19 pandemic also led to a reduction in the number of STEMI patients undergoing standard tests to diagnose COVID-19.

The MACE rate increased significantly during the pandemic era, rising from 36 (22.1%) to 18 (10.7%) patients prior to the COVID-19 pandemic, with p=0.008. Mortality, cardiogenic shock, and acute pulmonary edema also increased significantly, with a ratio of 19 (11.7%) vs 8 (4.7%) p=0.035, 18 (11.0%) vs 7 (4.1%) p=0.030, and 17 (10.4%) vs. 6 (3.6%) p=0.024. Meanwhile, the incidence of stroke did not increase significantly in the pandemic era, namely 3 (1.8%) compared to 2 (1.2%) with p=0.680 and there were no patients requiring urgent revascularization in both groups (Figure 4). The ISACS-STEMI COVID-19 registry also reported the same thing, namely the death rate increased significantly in 2020 compared to 2019 (481 deaths (6.5%) vs 457 deaths (5.3%); OR 1.26, CI 95% ,1.10-1.4, p<0.001).[19] As a comparison above shows, MACE rates reported in European countries were lower during the pandemic and before the pandemic, where more optimal STEMI management was able to reduce mortality and MACE compared to this

study. In addition, the differences in the assessed MACE outcomes and the different study populations are also other reasons. While the increase in MACE rates during this pandemic was mentioned in the previous study above, it could be caused by several factors, namely a long total ischemic time, changes in reperfusion strategies such as decreased use of primary PCI, inadequate health infrastructure, and concomitant infection with COVID-19.[13,19,25,26]

This study has a number of limitations, the first is that this study uses retrospective secondary data so that data collection is highly dependent on the accuracy and completeness of hospital medical records. Second, changes in examining COVID-19 status such as the use of antibodies, antigens or RT-PCR and changes in patient management policies during the COVID-19 pandemic era are very dynamic, depending on the number of cases of COVID-19 and the ability of hospital infrastructure to adapt to pandemic conditions and the availability of tools at the time. Third, our study did not include patients who died suddenly with suspected cardiac arrest which could suggest a longer onset before hospital admission. Fourth, not including the variable vaccine administration theoretically can provide external protection for sufferers of COVID-19. Fifth, this study was conducted in a single center, so the results cannot be generalized to STEMI patient populations elsewhere. Sixth, the observation time in this study was relatively short, namely only during hospitalization, so further research is needed to assess long-term outcomes.

CONCLUSION

This study shows that there is a decrease in patient admissions per month, a decrease in the use of primary PCI, an increase in the use of fibrinolytics and no reperfusion therapy, a prolonged onset and duration of total ischemic time, and a significant increase in major cardiovascular events in hospital in STEMI patients during the COVID-19 pandemic.

Public education regarding the importance of awareness of the signs and symptoms of STEMI, shortening the time for screening and antigen examination in the emergency room, increasing the availability of isolation catheterization room facilities, and improving the management of COVID-19 in general are expected to improve the morbidity and mortality of STEMI patients in the COVID-19 pandemic.

REFERENCES

1. Zhang F, Song X, Dang Y. Experience of ST segment elevation myocardial infarction management during COVID-19 pandemic from the mainland of China. Cardiovasc Revascularization Med. 2020;(xxxx).
2. Mafham MM, Spata E, Goldacre R, Gair D, Curnow P, Bray M, et al. COVID-19 pandemic and admission rates for and management of acute coronary syndromes in England. Lancet. 2020;396(10248):3819.
3. 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):1852–3.
4. Haberman R, Axelrad J, Chen A, Castillo R, Yan D, Izmirly P, et al. Reduced Rate of Hospital Admissions for ACS during Covid-19 Outbreak in Northern Italy. N Engl J Med. 2020;383(1):85–8.
5. Pessoa-Amorim G, Camm CF, Gajendragadkar P, Maria GL De, Arsac C, Laroche C, et al. Admission of patients with STEMI since the outbreak of the COVID-19 pandemic: A survey by the european society of cardiology. Eur Heart J - Qual Care Clin Outcomes. 2020;6(3):210–6.
6. Wilson SJ, Connolly MJ, Elghamry Z, Cosgrove C, Firoozi S, Lim P, et al. Effect of the COVID-19 Pandemic on ST-Segment-Elevation Myocardial Infarction Presentations and In-Hospital Outcomes. Circ Cardiovasc Interv. 2020;13(7):1–3.
7. Firman D, Mangkuanom AS, Iryuza N, Fahri I, Artha IMJR, Mulia E, 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(August).
8. Coughlan JJ, Chongprasertpon N, Arockiam S, Arnous S, Kiernan TJ. COVID-19 and STEMI: A snapshot analysis of presentation patterns during a pandemic. IJC Hear Vasc. 2020;30(xxxx):4–6.
9. Trabattoni D, Montorsi P, Merlino L. Late STEMI and NSTEMI Patients' Emergency Calling in COVID-19 Outbreak. Can J Cardiol. 2020;36(7):1161.e7–1161.e8.
10. Soylu K, Coksevim M, Yanık A, Bugra Cerik I, Aksan G. Effect of Covid-19 pandemic process on STEMI patients timeline. Int J Clin Pract. 2021;75(5):1–6.
11. Reinstadler SJ, Reindl M, Lechner I, Holzknecht M, Tiller C, Roithinger FX, et al. Effect of the COVID-19 pandemic on treatment delays in patients with st-segment elevation myocardial infarction. J Clin Med. 2020;9(7):1–10.
12. Zhu Y, Xing W, Wang H, Song J, Sun Z, Li X. Characteristics of patients with ST-segment elevated myocardial infarction (STEMI) at the initial stage of the COVID-19 pandemic: a systematic review and meta-analysis. Infect Dis (Auckl). 2021;53(11):865–75.
13. Dingcheng Xiang, Xin Xiang, Wei Zhang, Shaodong Yi JZ. Management and Outcomes of Patients With STEMI During the COVID-19 Pandemic in China. J Am Coll Cardiol. 2020;76(January).
14. Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2018;39(2):119–77.
15. Neil R, Vasileios P. The missing acute coronary syndromes in the COVID-19 era. Ther Adv Cardiovasc Dis. 2020;14(6):1–5.
16. Ashraf S, Ilyas S, Alraies MC. Acute coronary syndrome in the time of the COVID-19 pandemic. Eur Heart J. 2020;41(22):2089–91.
17. Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Vol. 140, Circulation. 2019.596–646 p.
18. Chi JS, Kloner RA. Stress and myocardial infarction. Heart. 2003;89(5):475–6.
19. De Luca G, Algowhary M, Uguz B, Oliveira DC, Ganyukov V,

Zimbakov Z, *et al.* COVID-19 pandemic, mechanical reperfusion and 30-day mortality in ST elevation myocardial arction. Heart. 2022;108(6):458–66.

20. De Luca G, Verdoia M, Cercek M, Jensen LO, Vavlukis M, Calmac L, *et al.* Impact of COVID-19 Pandemic on Mechanical Reperfusion for Patients With STEMI. J Am Coll Cardiol. 2020;76(20):2321–30.

21. Erlina B, Agus Dwi S, Sally A N, Eka G, Isman F, Anwar S, *et al.* Protokol Tatalaksana Covid-19 Edisi 1 April 2020. 2020;26–7.

22. Daniele 8 Elena A, Emanuele B, Antonio L, Baumbach A, Elijah B. ESC Guidance for the Diagnosis and Management of CV Disease during the COVID-19 Pandemic. Eur Heart J. 2020;1–115.

23. Firdaus I, Sukmawan R, Santoso A, Juzar DA. Panduan Diagnosis dan Tatalaksana Penyakit Kardiovaskular pada Pandemi COVID-19. 2020;1–117.

24. Ng S, Juzar DA. Tantangan Penatalaksanaan STEMI di andemi Covid-19. Indones J Cardiol. 2020;41(2):92–7.

25. Rodriguez-Leor O, Cid-Alvarez B, Ojeda S, Martin-Moreiras J, Ramon Rumoroso J, Lopez-Palop R, *et al.* Impact of the COVID-19 pandemic on interventional cardiology activity in Spain. REC Interv Cardiol. 2020;2(2):82–9.

26. Chew NWS, Ow ZGW, Teo VXY, Heng RRY, Ng CH, Lee CH, *et al.* The Global Effect of the COVID-19 Pandemic on STEMI Care: A Systematic Review and Meta-analysis. Can J Cardiol. 2021;37(9):1450–9.

In-Hospital Major Adverse Cardiovascular Events

9% SIMILARITY INDEX

7% INTERNET SOURCES

4% PUBLICATIONS

5% STUDENT PAPERS

PRIMARY SOURCES

1	Submitted to Laureate Higher Education Group Student Paper	1%
2	Submitted to Harvard Medical School Student Paper	1%
3	Submitted to University of Southampton Student Paper	1%
4	journal.nzma.org.nz Internet Source	1%
5	Submitted to SDM Universitas Gadjah Mada Student Paper	1%
6	www.researchsquare.com Internet Source	1%
7	pubmed.ncbi.nlm.nih.gov Internet Source	<1%
8	lusiadasscientificjournal.pt Internet Source	<1%
9	referencecitationanalysis.com Internet Source	<1%

10 Submitted to Aristotle University of Thessaloniki
Student Paper
<1 %

11 journal.scardio.ru
Internet Source
<1 %

12 jcancer.org
Internet Source
<1 %

13 publichealth.jmir.org
Internet Source
<1 %

14 www.infmed.dk
Internet Source
<1 %

15 www.springermedizin.de
Internet Source
<1 %

16 jemdsa.co.za
Internet Source
<1 %

17 Elita Chamdimba, Alister Munthali, Caroline W Kabiru, Chrissie Thakwalakwa, Boniface Ayanbekongshie Ushie, Anthony Idowu Ajayi. "Self-report of mental health distress among pregnant and parenting adolescents during the COVID-19 pandemic in Malawi", Research Square Platform LLC, 2022
Publication
<1 %

18 acamedicine.org
Internet Source
<1 %

19 www.manilatimes.net
Internet Source
<1%

20 J. Corey Williams, Molly Ball, Nora Roscoe, Jenna Harowitz et al. "Widening Racial Disparities During COVID-19 Telemedicine Transition: A Study of Child Mental Health Services at Two Large Children's Hospitals", Journal of the American Academy of Child & Adolescent Psychiatry, 2023
Publication
<1%

21 academic.oup.com
Internet Source
<1%

22 thefinancialexpress.com.bd
Internet Source
<1%

23 www.hkmj.org
Internet Source
<1%

24 Maciej Kempa, Marcin Gułaj, Michał M. Farkowski, Andrzej Przybylski, Maciej Streliński, Przemysław Mitkowski. "An opinion of the Heart Rhythm Section of the Polish Cardiac Society (with an update) on electrotherapy and electrophysiology procedures during the COVID-19 epidemic", Kardiologia Polska, 2020
Publication
<1%

25   Rujin Tian, Zhengtong Qiao, Ziliang Zhou, Jiazhen Zhang, Siyue Sa, Kai Liu. "Effect of Active and Passive Stretching on Symptoms in Stable COPD: A Systematic Review and Meta-Analysis", Research Square Platform LLC, 2023
Publication

<1%

26   Yun Qiu, Ying-Fan Zhang, Liang-Ru Zhu, Jin-Shen He et al. "Impact of COVID-19 on the Healthcare of Patients With Inflammatory Bowel Disease: A Comparison Between Epicenter vs. Non-epicenter Areas", Frontiers in Medicine, 2020
Publication

<1%

27   journals.plos.org
Internet Source

<1%

28   repository.uhamka.ac.id
Internet Source

<1%

29   worldwidescience.org
Internet Source

<1%

30   www.science.gov
Internet Source

<1%

31   J. T. Parissis. "Plasma B-type natriuretic peptide and anti-inflammatory cytokine interleukin-10 levels predict adverse clinical outcome in chronic heart failure patients with depressive symptoms: a 1-year follow-up

<1%

study", European Journal of Heart Failure, 10/01/2009

Exclude quotes	Off	Exclude matches	Off
Exclude bibliography	Off		