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Impact of COVID-19 pandemic on STEMI undergoing primary PCI treatment in Beijing, China



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ABSTRACT

Objective: Strict control measures under the COVID epidemic have brought an inevitable impact on ST-segment elevation myocardial infarction (STEMI)'s emergency treatment. We investigated the impact of the COVID on the treatment of patients with STEMI undergoing primary PCI.

Methods: In this single center cohort study, we selected a time frame of 6 month after declaration of COVID-19 infection (Jan 24-July 24, 2020); a group of STEMI patients in the same period of 2019 was used as control. Finally, a total of 246 STEMI patients, who were underwent primary PCI, were enrolled into the study (136 non COVID-19 outbreak periods). The impact of COVID on the time of symptom onset to the first medical contact (symptom-to-FMC) and door to balloon (D-to-B) was investigated. Moreover, the primary outcome was in-hospital major adverse cardiac events (MACE), defined as a composite of cardiac death, heart failure and malignant arrhythmia.

Results: Compared with the same period in 2019, there was a 19% decrease in the total number of STEMI patients undergoing primary PCI at the peak of the pandemic in 2020. The delay in symptom-to-FMC was significantly longer in COVID Outbreak period (180 [68.75, 342] vs 120 [60,240] min, P = 0.003), and the D-to-B times increased significantly (148 [115–190] vs 84 [70–120] min, P < 0.001). However, among patients with STEMI, MACE was similar in both time periods (18.3% vs 25.7%, p = 0.168). On multivariable analysis, COVID was not independently associated with MACE; the history of diabetes, left main disease and age>65 years were the strongest predictors of MACE in the overall population.

Conclusions: The COVID pandemic was not independently associated with MACE; suggesting that active primary PCI treatment preserved high-quality standards even when challenged by a severe epidemic.

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1. Introduction

As a public health emergency of international concern, novel Coronavirus Disease 2019 (COVID-19) is an unprecedented health crisis in the contemporary era [1,2]. COVID-19 has inevitable impact for medical care of other systemic diseases, especially the cardiovascular disease [3]. During the COVID-19 pandemic, many hospitals gave priority to treating COVID-19 patients and even reduced in-person ambulatory care [4]. Moreover, screening for COVID-19 will delay the time of management. More importantly, Health care workers (HCWs), especially those in the front-line of the epidemic, are under tremendous workload and psychological pressure. Their knowledge and attitudes towards COVID are also key factors [5]. However, our hospital provides good personal protective equipment and working environment for medical staff, HCWs have good knowledge of COVID and can provide patients with timely medical help.

As we all known, ST-segment elevation myocardial infarction (STEMI) is one of the most common severe emergent cardiovascular diseases, which has the characteristics of acute onset, high mortality, and short optimal treatment time. "Time is myocardium and Time is outcomes" [6]. However, strict control measures under the COVID epidemic have brought an inevitable impact on STEMI's emergency treatment system. The current study represents the experience of a cardiac

Abbreviations: STEMI, ST-segment elevation myocardial infarction; COVID, novel Coronavirus Disease; PCI, percutaneous coronary intervention; MACE, major adverse cardiac events; HF, heart failure; HCWs, Health care workers; CTnI, Cardiac troponin 1; CTnT, Cardiac troponin T; CK-MB, creatine kinase-myocardial band; NT-proBNP, N terminal pro brain natriuretic peptide; D-to-B, door to balloon; symptom-to-FMC, symptom onset to the first medical contact.

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center in China in regard to the influence of COVID-19 pandemic on patients with STEMI.

2. Methods

2.1. Study design and patients

We performed a retrospective analysis of a cohort of STEMI patients undergoing primary PCI from January 24 to July 24, 2020 (COVID-19 Outbreak period) at Beijing Friendship Hospital. We designated January 24, 2020 as the start of the COVID-19 era since Beijing raised the public health incident response to the highest level on that date [7]. A group of STEMI patients from a similar time period of last year (January 24–July 24, 2019; Non outbreak period) was used as control. STEMI patients who were already in hospital during symptom onset were excluded. And only STEMI patients who underwent primary PCI were included in this study. The study protocol was approved by the ethics committee of our hospital. Patient flow of the study is shown in Fig. 1.

2.2. Study outcomes

The outcome was door-to-balloon (D-to-B) time, symptom onset to first medical contact (Symptom-to-FMC) time. Characteristics of the STEMI cases, including demographic data (age, sex, BMI), history of past illness (hypertension, diabetes, hyperlipemia, old myocardial infarction and other diseases), conditions of smoking and drinking, family histories of coronary heart disease were recorded.

The peak values of cardiac troponin (cTnl and cTnT), creatine kinasemyocardial band (CK-MB) were used as indicators of myocardial injury. Moreover, cTnl and cTnT level on admission was also recorded. Serum peak concentration of N terminal pro brain natriuretic peptide (NTproBNP) was used to reflect heart function. These cardiac markers were measured on admission and every 24 h until the peaks occurred.



Fig. 1. Flow chart of patient enrollment. CBD bank: Cardiovascular Center Beijing Friendship Hospital Database Bank.

The left ventricular ejection fraction (LVEF) was determined using 2-dimensional echocardiography within 3 days after primary PCI.

The major adverse cardiac events (MACE) in hospital were defined as cardiac death, malignant arrhythmia and heart failure (HF). Malignant arrhythmia was defined as a tachyarrhythmia requiring electrical cardioversion therapy or a bradyarrhythmia requiring pacemaker therapy. Moreover, HF was determined by symptom, physical sign and the result of echocardiography (EF<50%).

2.3. Statistical analysis

Data analysis was performed with SPSS, version 25.0 (IBM Corporation, Armonk, NY) and Metaninf function in Stata 12.0. Categorical variables were summarized as numbers and percentages and compared using Pearson χ 2 test. Continuous variables were expressed as a mean \pm SD (standard deviation) or median with IQR (interquartile range) and compared using Student *t*-test, Mann-Whitney test or Wilcoxon tests as appropriate. Logistic regression analysis was used to analyze the factors that affect MACE. P value <0.05 was considered statistically significant.

3. Results

3.1. Population characteristics

A total of 246 patients were included during the described time frames (136 Non COVID-19 outbreak periods and 110 COVID-19 Outbreak periods). No patient showed positive results by CT or throat swab test. There was a 19% decrease in the total number of STEMI patients undergoing primary PCI in the outbreak period. Patients presenting with STEMI were similar in terms of demographics (age, gender, BMI) and comorbidities (Hypertension, Hyperlipidemia, Previous history of Coronary Heart Disease and PCI) during both time periods. However, the proportion of patients with diabetes was higher, and the proportion of old myocardial infarctions was reduced in 2020. Moreover, the location of myocardial infarction and TIMI risk score in the two groups are comparable. During the COVID epidemic, the average hospital stay decreased (8 [6,10] vs 9 [8,11], p<0.001). In terms of drug use, the proportion of patients treated with dual antiplatelet therapy (DAPT), statins and β -blockers were similar among the two groups. However, compared with the non-COVID period, the proportion of ACEI/ARB application during the COVID period has decreased(56.4% VS 69.9, p = 0.029). The baseline clinical characteristics are shown in Table 1.

3.2. Myocardial enzymes and cardiac function during the COVID-19 outbreak

The peak values of cTnI, cTnT and CK-MB were used as indicators of myocardial injury, we found no difference between the two groups. However, the index of cTnI (0.11 ng/ml vs 0.08 ng/ml) and cTnT (0.05 ng/ml vs 0.02 ng/ml) in admission has a rising trend, although there is no statistical difference.

From the perspective of cardiac function assessed by echocardiography, the LVEF and end-diastolic dimension (EDD) between the two groups were also similar, as shown in Table 1. Lastly, there was no difference in the peak concentration of NT-proBNP levels.

3.3. Symptom-to-FMC and D-to-B times

The delay in symptom-to-FMC was significantly longer in COVID outbreak period (180 [68.75, 342] vs 120 [60,240] min, P = 0.003) compared to no outbreak period group. The proportion of patient presenting 12 h after onset of symptom was higher (10% vs 3.7%) in 2020 (Fig. 2 A). Moreover, in the COVID outbreak period, patients had significantly

Table 1

Baseline clinical characteristics of STEMI patients underwent PCI according to the study period.

Variable	Non outbreak period	Outbreak period	Р
	Jan 24, 2019,	Jan 24, 2020,	
	Through	Through	
	July 24, 2019	July 24, 2020	
	(n = 136)	(n = 110)	
Age, years	61 ± 13	58 ± 13	0.087
Male, n (%)	105(77.2)	79(71.8)	0.333
BMI, Kg/m ²	25.28 ± 3.54	25.78 ± 3.62	0.283
Hypertension, n (%)	78(57.4)	67(60.9)	0.573
Diabetes, n(%)	29(21.3)	39(35.5)	0.014
Hyperlipidemia, n (%)	43(31.6)	44(40)	0.172
Smoking, n (%)	87(64)	71(64.5)	0.925
Drinking, n(%)	19(14)	16(14.5)	0.898
Previous history of CAD, n(%)	22(16.2)	13(11.8)	0.331
Previous history of OMI, n(%)	13(9.6)	3(2.7)	0.031
Previous history of PCI, n (%)	16(11.8)	8(7.3)	0.238
Previous history of Stroke, n (%)	15(11)	15(13.6)	0.534
Family history of CAD, n (%)	41(30.1)	36(32.7)	0.664
T,°C	36.3 ± 0.3	36.3 ± 0.3	0.397
SBP, mmHg	123 ± 26	121 ± 20	0.472
DBP, mmHg	76 ± 19	74 ± 13	0.349
HR, bpm	76 ± 15	75 ± 14	0.72
GFR<60 ml/min, n (%)	13(9.6)	10(9.1)	0.9
Killip≥2, n (%)	31(22.8)	19(17.3)	0.285
LVEDD, cm	5.1 ± 0.4	5.1 ± 0.4	0.742
LVEF	0.57 ± 0.08	0.58 ± 0.08	0.594
CK-MB max, ng/ml	93.2(41.98,173.05)	91.4(43.03,151.6)	0.982
cTnI max, ng/ml	50(29.32,50)	50(21.7,50)	0.68
cTnT _{max, ng/ml}	3.95(2,7.75)	4.8(1.9,8.93)	0.499
NT-pro BNP max, pg/ml	1660	1447.5	0.647
	(769.75,2910.75)	(749.25,2949)	
cTnI on admission, ng/ml	0.08(0.01,0.6)	0.11(0.02,0.6)	0.72
cTnT on admission, ng/ml	0.02(0.01,0.15)	0.05(0.01,0.21)	0.098
Location of MI, n (%)			0.343
Anterior	70(51.5)	47(42.7)	
Inferior	59(43.4)	58(52.7)	
Lateral	7(5.1)	5(4.5)	
Hospital days	9(8,11)	8(6,10)	< 0.001
TIMI risk score	3.88 ± 2.34	3.77 ± 2	0.715
Medical therapy			
DAPT, n(%)	136(100)	110(100)	1
Beta-blocker, n (%)	99(72.8)	91(82.7)	0.065
ACEI/ARB, n (%)	95(69.9)	62(56.4)	0.029
Statin, n (%)	128(94.1)	103(93.6)	0.875

BMI: body mass index; CAD: coronary artery disease; OMI: Old myocardial infarction; SBP: systolic blood pressure; DBP: diastolic blood pressure; GFR: glomerular filtration rate; LVEDD: left ventricular end-diastolic dimension, LVEF: left ventricular ejection fraction; PCI: percutaneous coronary intervention, TIMI: Thrombolysis in Myocardial Infarction; DAPT: dual antiplatelet therapy; ACEI/ARB: Angiotensin-converting enzyme inhibitor/ Angiotensin receptor blockers.

p values for comparisons between the two groups. Significance level was 0.05.

prolonged D-to-B times (148 [115–190] vs 84 [70–120] min, P<0.001). The scatter chart shows this trend more intuitively (Fig. 2 B).

3.4. Coronary angiographic and lesion characteristics

No significant differences in the proportion of three vessel disease, left main disease (LM disease) and infarction related artery were seen as shown in Table 2. However, the use of thrombus aspiration equipment has decreased significantly in the 2020 COVID period (10.9% vs 40.4%, p<0.001).

3.5. Clinical outcomes

The hospital cardiac death occurred in 4 patients (1.6%) in the overall population. No significant differences were observed in the incidence of cardiac death, heart failure, and malignant arrhythmia (Table 3). Moreover, the 30 days mortality rate was 1.5% (non COVID-19 outbreak periods) and 3.6% (COVID-19 outbreak periods) respectively, and there was also no statistical difference (p = 0.274). The correlates of MACE in multivariable analysis are presented in Fig. 3; there were no significant associations between the COVID period and MACE; while, the history of diabetes; left main disease and age>65 years were the strongest predictors of MACE in the overall population.

4. Discussion

Coronavirus disease (COVID-19) pandemic have greatly affected healthcare services around the world. The current study highlights the impact of COVID-19 outbreak on STEMI patient undergoing primary PCI. We found that the primary PCI volume seems to be reduced by 19% during the pandemic; moreover, the symptom-to-FMC and D-to-B times were delayed. However, there were no significant associations between the COVID period and MACE. Active and effective primary PCI may improve the prognosis of STEMI patients during the special epidemic period.

In terms of comorbidities, our data showed that the proportion of STEMI patients with previous myocardial infarction decreased in COVID period; this may be related to the fact that such patients pay more attention to heart health, coupled with the decrease in activity during the epidemic, which all caused a reduction in the predisposing factors of myocardial infarction. However, a higher proportion of patients in the COVID outbreak period presented with diabetes compared with the non-outbreak period. During the epidemic, medical treatment was not standardized or even interrupted due to inconvenient medical treatment. This may increase the risk of acute myocardial infarction in diabetic patients.

STEMI is the most acute manifestation of coronary artery disease and is associated with great morbidity and mortality, primary PCI is the typical recommended therapy. Immediate reperfusion of coronary arteries related to infarction can better improve patient prognosis [8,9]. However, the public health emergencies such as COVID will inevitably have an impact on the treatment of STEMI patients. Many cardiac catheterization laboratories in China have scaled down the number of cases; we carried out PCIs continuously to treat high-risk ACS patients in need of interventions under modified approaches aiming at minimizing the nosocomial infection risk. Patients treated in our hospital will undergo the "3 + 1" screening model, include complete blood count, chest CT, throat swab nucleic acid test and epidemiological investigation, which will inevitably lead to the prolonged D-to-B time. In the current study, the delay in D-to-B during the COVID period is substantial, with an increase in the median from 84 to 148 min compared with no COVID period.

On the other hand, the willingness of patients to present to the emergency department is also the focus of our observation, we found that the symptom-to-FMC time was increased also, the proportion of patient presenting 12 h after onset of symptom increased from 3.7% to 10%; this may be related to factors such as fear of COVID exposure and delays in public transportation. Similar patterns of delay in seeking medical care from the United States [10] and British [11] were observed during the current pandemic. To our knowledge, this is the first report from the China mainland highlighting the problem. This suggests that the society should increase publicity for COVID and cardiovascular emergency. Moreover, due to fear of the epidemic and prohibition of visits in our hospital, the average hospital stay of patients with STEMI also decreased in the COVID period.

Our study also examined the baseline cTnI and cTnT level on admission. Although there is no statistical difference, the index of cTnI and cTnT in admission has a rising trend in the 2020 COVID period, we believe that this difference may become statistically significant as the sample size expands.

In terms of drug use, the use of ACEI /ARB were different between two groups, the proportion of ACEI/ARB application during the COVID period has decreased. This difference was not associated with COVID pandemic



Fig. 2. The distribution of time delays in minutes for the 2019 and 2020 groups. A: The proportion of patient presenting 12 h after onset of symptom was higher in 2020; B: The scatter plot reflects the extended D to B time in 2020.

impact. First of all, the patients in our study are non-COVID patients. Second, although some recent experimental studies have found that SARS-CoV-2 uses ACE2 as the receptors for entry. On the other side, some evidences suggest that the ACE2 receptor is not necessary for SARS-CoV-2 entry into the cell and suggested that there is a cofactor that play part, human studies showed that there is no association between ACEI/ARB with SARS-CoV-2 infectivity and mortality. In conclusion, there is still insufficient data to stop the use of ACEI/ARB in COVID patients [12].

The research views on COVID and ACEI/ARB have not affected our decision-making on the application of ACEI/ARB. The use of ACEI/ARB were different in our study, this may be related to the condition of the patients. In clinical practice, for patients with myocardial infarction, we will give priority to antihypertensive drugs that can improve the prognosis, such as ACEI/ARB and β -blockers. The blood pressure level and heart rate are factors that affect the use of these drugs. We speculated that he blood pressure of STEMI patients in the COVID group may be low, and ACEI/ARB drugs cannot be added. Moreover, As the research sample size expands, this difference may disappear.

Notably, there was no significant difference in the characteristics of coronary artery lesions by coronary angiography between the two groups. However, in the 2020 COVID period, the use of thrombus aspiration equipment during PCI was decreased significantly; this may be related to the autolysis or organization of thrombosis caused by the delayed symptom-to-FMC time and D to B time.

Table 2

Coronary angiographic, lesion characteristics, S-to-FMC and D-to-B time in 2019 and 2020.

	5 6 6 1	-		
Varia	ble	Non outbreak period	Outbreak period	Р
		Jan 24, 2019, Through July 24, 2019	Jan 24, 2020, Through July 24, 2020	
		(n = 136)	(n = 110)	
three	e vessel disease, n (%)	94(69.1)	71(64.5)	0.448
LM d	isease, n (%)	12(8.8)	6(5.5)	0.313
Infar	ction related artery, n (%)			0.254
LAD		71(52.2)	49(44.5)	
LCX		22(16.2)	15(13.6)	
RCA		43(31.6)	46(41.8)	
Thro n (mbus aspiration device, %)	55(40.4)	12(10.9)	< 0.001
Door [IQ	to Balloon, min (median [R])	84(70,120)	148(115,190)	< 0.001
Symj [IQ	ptom-to-FMC, min (median [R])	120(60,240)	180(68.75,342)	0.003

LM: left main coronary artery; LAD: left anterior descending artery; LCX: left circumflex artery; RCA: right coronary artery; FMC, first medical contact;

p values for comparisons between the two groups. Significance level was 0.05.

Although the epidemic has affected patients' willingness to visit a doctor and medical treatment, we did not find differences in hospital MACE and 30 days mortality between the two groups of patients, the MACE includes malignant arrhythmia, heart failure and cardiac death.

Table 3

Comparison of clinical MACE during hospitalization and 30 days mortality between study groups.

Variable	Non outbreak period	Outbreak period	Р
	Jan 24, 2019, Through June 24, 2019	Jan 24, 2020, Through June 24, 2020	
	(n = 136)	(n = 110)	
MACE, n(%)	35(25.7)	20(18.3)	0.168
Cardiac death, n(%)	2(1.5)	2(1.8)	0.83
Malignant arrhythmia, n(%)	16(11.8)	8(7.3)	0.238
Heart failure, n(%)	22(16.2)	14(12.8)	0.464
30 days mortality, n(%)	2(1.5)	4(3.6)	0.274

MACE: major adverse cardiovascular events;

p values for comparisons between the two groups. Significance level was 0.05.



Fig. 3. Factors associated with MACE in multivariable analysis. Variables associated with MACE are shown along the vertical axis. The strength of effect is shown along the horizontal axis with the vertical line demarcating an odds ratio (OR) of 1 (i.e., no association); estimates to the right (i.e., > 1) are associated with a greater likelihood of MACE, whereas those to the left (i.e., < 1) indicate a reduced likelihood of MACE. Each dot represents the point estimate of the effect of that variable in the model, whereas the line shows the 95% confidence interval (Cl).

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In this study, there was a large increase in D to B time (148 vs 84 min) in 2020 compared to 2019 and yet no difference in outcomes. This is a surprising result. More importantly, we believed that active and effective primary PCI improved patient prognosis when challenged by a severe epidemic. The strongest predictors of MACE were the history of diabetes, left main disease and age>65 years. Further studies are necessary to determine whether the delayed symptom-to-FMC time and D to B time will lead to differences in long-term prognosis.

4.1. Limitations

Our present study had limitations inherent to its nonrandomized, observational design. First, this is a single center observational experience; the research sample size is relatively small. Second, the followup time was still short; patients were only followed up during hospitalization and one month after discharge. The long-term effect of delayed "Symptom-to-FMC and D-to-B" during COVID-19 pandemic is yet to be determined, such as newly diagnosed heart failure cases and even increased mortality. Third, the onset of symptom is a subjective parameter and might not be precisely recorded.

5. Conclusion

During the current the COVID-19 outbreak, the primary PCI volume seems to be reduced, the "door to Balloon and Symptom-to-FMC" were delayed, but the prognosis of STEMI patients is not different. When there are symptoms of discomfort, the patient should seek medical attention in time instead of staying at home, especially for patients with STEMI. More importantly, Active primary PCI treatment under effective protection is the key to improving the prognosis of patients.

Author contributors

Conception and drafting the article: HWL and XHG. Data collection, analysis, and interpretation: XHG, LZ, THD and XSD. Revising the article: HC and HQZ. Final approval of the manuscript to be published: all authors.

Ethics approval

This study was approved by the Institutional Review Board of Beijing Friendship Hospital. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Declaration of Competing Interest

None.

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