ORIGINAL ARTICLE

Effect of the COVID-19 pandemic on access to primary percutaneous coronary intervention for ST-segment elevation myocardial infarction

COVID-19 pandemisinin ST-segment yükselmeli miyokart enfarktüsü nedeniyle yapılan primer perkütan koroner girişim zamanlamasına etkisi

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ABSTRACT

Objective: The coronavirus disease 2019 (COVID-19) pandemic caused by the emergence of severe acute respiratory syndrome coronavirus 2 has resulted in a health crisis and a significant number of deaths worldwide. The full effect on access to medical care and the treatment for patients with chronic diseases and acute conditions is still unknown. This is an investigation of access to primary percutaneous coronary intervention (PPCI) for patients diagnosed with ST-segment myocardial infarction (STEMI) during the pandemic.

Methods: Consecutive patients who were diagnosed with STEMI and underwent PPCI during the ongoing COVID-19 pandemic were included in the study. Clinical and angiographic characteristics of the patients were assessed. A control group of patients diagnosed with STEMI and who underwent PPCI during the same time interval a year prior to the outbreak of the disease was analyzed retrospectively for comparison.

Results: There was a significant reduction in the number of STEMI cases during the COVID-19 crisis period. Furthermore, these patients had a prolonged ischemic time; they were more likely to have a longer pain-to-balloon (Odds ratio [OR]: 2.0, 95% confidence interval [CI]: 1.1–10.2) and door-to-balloon time (OR: 5.4, 95% CI: 3.1–22.8).

Conclusion: Patients diagnosed with STEMI during the pandemic experienced a significant delay between the onset of symptoms and PPCI.

ÖZET

Amaç: COVID-19 pandemisi dünya genelinde bir sağlık krizine neden olmuş ve çok sayıda ölüme yol açmıştır. Pandeminin kronik durumu olan ya da acil hastaların medikal tanı ve tedavi zamanlamasına olan etkisi bilinmemektedir. Biz bu çalışmada, COVID-19 döneminde ST-segment yükselmeli miyokart enfarktüsü (STYME) tanısı alan hastaların primer perkütan koroner girişim (PPKG) yapılana kadar geçen sürelerini değerlendirdik.

Yöntemler: COVID-19 döneminde ev kısıtlamasının en yoğun olduğu zamanda STYME tanısı alan ve bu nedenle PPKG işlemi yapılan ardışık hastalar çalışmaya alındı. Hastaların klinik ve anjiyografik özellikleri değerlendirildi. Kontrol grubu olarak geçen yıl aynı dönemde aynı tanı nedeniyle hastaneye başvuran hastalar çalışmaya dahil edilerek iki grup karşılaştırıldı.

Bulgular: Geçen sene aynı dönemde göre COVID-19 döneminde STYME ile başvuran ve PPKG yapılan hasta sayıda önemli derecede azalma olduğu saptandı (174 ve 90). COVID-19 döneminde başvuran hastalarda önceki süreç başvuranlara göre ağrı-balon [Odds oranı (OO) 2.0, %95 güven aralığı (GA) 1.1–10.2) ve kapı-balon (OO 5.4, %95 GA 3.1–22.8] sürelerinin daha uzun olduğu görüldü. Bu hastaların miyokart iskemisi sürelerinin daha uzun olduğu değerlendirildi.

Sonuç: COVID-19 pandemisi sırasında STYME tanısıyla başvuran hastalarda semptom başlangıcı ile PPKG arasında geçen sürede artış mevcuttur.

Coronavirus disease 2019 (COVID-19) is currently a rapidly spreading infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] Significant morbidity and mortality has occurred around the world since the first cases were diagnosed in December 2019. Healthcare sys-

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tems and policies have primarily focused on reducing transmission of the disease and treatment of confirmed cases.[2,3] Reports have suggested that there may also be a simultaneous reduction in the number of patients presenting with ST-segment elevation myocardial infarction (STEMI) at emergency departments.[4,5] Concerns have been raised regarding late presentation of patients with STEMI due to restrictions on going outside (lockdown conditions) and the fear of viral transmission in hospitals.

The objective of the present study was to investigate the clinical and angiographic characteristics of patients who presented with STEMI during a peak period of the COVID-19 pandemic and to compare them with patients who presented during the same time period a year earlier, prior to the pandemic.

METHODS

Between March 5, 2020 and April 6, 2020, when the number of new cases was high and strict lockdown measures were adopted in Turkey, consecutive patients who presented at Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital, Istanbul, Turkey, with the diagnosis of STEMI and underwent primary percutaneous coronary intervention (PPCI) were included. Patients with the same diagnosis who underwent PPCI during the same time interval a year earlier were included as a control group. The hospital electronic database was searched retrospectively to retrieve the characteristics of the control group. This study was conducted in accordance with the Declaration of Helsinki and the study was approved by the local ethical committee.

A STEMI diagnosis was made according to the current European Society of Cardiology guideline for the management of acute myocardial infarction in patients presenting with ST-segment elevation.[6] The periprocedural pharmacotherapy and the revascularization technique used were left to the discretion of the primary operator. Successful PPCI was defined as achievement of Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow, resolution of ischemic chest pain, and ST-segment elevation (>70% at 60 min). TIMI calculations and other angiographic evaluations were performed by a cardiologist who was blinded to other clinical data.

Abbreviations:

CI	*Confidence interval*
COVID-19	*Coronavirus disease 2019*
IQR	*Interquartile ratio*
OR	*Odds ratio*
PPCI	*Primary percutaneous coronary intervention*
STEMI	*ST-segment myocardial infarction*
TIMI	*Thrombolysis in Myocardial Infarction*

The technique for the PPCI and pre-, intra-, and post-procedural medications were left to the discretion of the primary operator. All of the patients underwent transthoracic echocardiographic evaluation a day after the PPCI performed by a cardiologist who was blinded to other clinical data. The left ventricular ejection fraction was calculated according to the modified Simpson's method. The TIMI flow before and after the PPCI was assessed in accordance with the established definition.[7]

We defined symptom onset as the start of ischemic symptoms based on patient reporting. Balloon time was defined as the time of the first balloon inflation during the PPCI procedure. Pain-to-balloon and door-to-balloon time were defined as the time interval between the onset of symptoms to balloon inflation and arrival at the hospital and balloon inflation, respectively.

Statistical analysis

The study population was divided into 2 groups according to the time period of the procedure: COVID-19 era (n=90) and non-COVID-19 era (n=174). The demographic features and clinical characteristics of the study groups were compared. The Kolmogorov-Smirnov test was used to assess normality. Quantitative variables were presented as mean value±SD. Continuous variables were presented as median and interquartile range (IQR) or mean±SD using a t-test or the Mann-Whitney U test, as appropriate. A p value of <0.05 was considered statistically significant. Categorical variables were presented as numbers and percentages. Analyses of categorical variables were performed using Pearson's chi-square test or Fisher's exact test. Logistic regression models were used to examine the effect of a door-to-balloon time of >90 minutes and a pain-to-balloon time of >12 hours according to the time period of the admission and PPCI procedure (Table 2). The results of regression analysis were presented as the odds ratio (OR) with a 95% confidence interval (CI). Two models were used in the logistic regression analysis: model I, which was unadjusted, and model II, which was adjusted. Mod-

el II was adjusted for the baseline demographics and risk factors, with 2019 admissions serving as a reference group. The covariates used in model II were age, gender, hypertension, diabetes mellitus, smoking, hyperlipidemia, chronic obstructive pulmonary disease, coronary artery disease, and chronic renal failure. The analyses were performed using Statistical Package for Social Sciences software (IBM, Armonk, New York, USA).

RESULTS

During the period of March 5, 2020 to April 6, 2020, 96 patients presented at the study hospital with the initial diagnosis of STEMI and underwent coronary angiography. Of those, 6 had no critical stenosis in the coronary arteries and were excluded from the study. The remaining 90 patients were included for analysis. The clinical and angiographic characteristics of the

Table 1. Comparison of patient demographic and clinical characteristics according to time period

	Non-COVID-19 era STEMI March 5–April 6, 2019 (n=174)	COVID-19 era STEMI March 5–April 6, 2020 (n=90)	*p*-value
Age (years), mean±SD	63.7±13.3	59.3±13.4	0.002
Male gender, n (%)	149 (85.6)	73 (81.1)	0.346
Hypertension, n (%)	88 (50.6)	41 (45.6)	0.439
Diabetes mellitus, n (%)	60 (34.5)	24 (26.7)	0.196
Insulin dependency, n (%)	25 (14.4)	6 (6.7)	0.055
Smoking, n (%)	117 (67.2)	43 (47.8)	0.002
Hyperlipidemia, n (%)	26 (14.9)	13 (14.4)	0.914
COPD, n (%)	9 (5.2)	7 (7.8)	0.409
Coronary artery disease, n (%)	57 (32.8)	21 (23.3)	0.112
Chronic renal failure, n (%)	8 (4.6)	4 (4.4)	1.000
Cerebrovascular accident, n (%)	4 (2.3)	5 (5.6)	0.281
Infarct-related artery (IRA), n (%)			
Left main coronary artery	0 (0.0)	5 (5.6)	0.004
Left anterior descending artery	92 (52.9)	43 (47.8)	0.791
Circumflex artery	32 (18.4)	18 (20.0)	0.753
Right coronary artery	43 (24.7)	22 (24.4)	0.962
Saphenous vein graft	7 (4.0)	2 (2.2)	0.722
Pre-PCI TIMI flow in IRA, n (%)			
TIMI 0	123 (70.7)	64 (71.1)	0.943
TIMI 1	23 (13.2)	12 (13.3)	0.979
TIMI 2	12 (6.9)	6 (6.7)	0.944
TIMI 3	16 (9.2)	8 (8.9)	0.934
Pain-to-balloon, hours, median	4.0 [2.0–5.5]	6.0 [2.0–10.0]	0.003
Pain-to-balloon >12 hours, n (%)	7 (4.0)	22 (24.4)	<0.001
Door-to-balloon, minutes	26.4 [11.0–40.0]	54.6 [9.0–55.0]	0.004
Door-to-balloon >90 minutes, n (%)	2 (1.1)	16 (17.8)	<0.001
Post-PCI TIMI flow <3, n (%)	6 (3.4)	8 (8.9)	0.081
Ejection fraction (%), mean±SD	50.6±8.1	47.8±9.6	0.027
In-hospital mortality, n (%)	6 (3.4)	6 (6.7)	0.349

COPD: Chronic obstructive pulmonary disease; STEMI: ST-segment elevation myocardial infarction; SVG: Saphenous vein graft; TIMI: Thrombolysis in Myocardial Infarction; SD: Standard deviation.

patients are provided in Table 1. The mean age was 59.3±13.4 years and 81.1% of the patients were male. Hypertension and diabetes were present in 45.6% and 26.7%, respectively. The infarct-related artery was the left anterior descending artery in 47.8%, the circumflex artery 20%, and the right coronary artery in 24.4% of the patients. The median pain-to-balloon duration was 6 hours (IQR: 4.0–12.0 hours). In 24.4% of the patients, the pain-to-balloon time was >12 hours. The median door-to-balloon time was 54.6 minutes (IQR: 35.0–80.0 minutes) and in 17.8% of the patients, the door-to-balloon time was 90 minutes. The mean left ventricular ejection fraction was 47.8±9.6% and 6 patients died during hospitalization.

In order to compare the clinical and angiographic characteristics of patients who presented during the COVID-19 outbreak with routine practice, patients who had presented with STEMI and underwent PPCI during the same time interval 1 year earlier were included. Characteristics of the control group are provided in Table 1. A significant reduction in the number of patients who were diagnosed with STEMI and underwent PPCI was observed during the COVID-19 period.

Logistics regression models were created to evaluate pain-to-balloon time of >12 hours and door-to-balloon time of >90 minutes among patients who presented at the hospital during the COVID-19 era and the non-COVID-19 era (Table 2). The door-to-balloon time was more than 90 minutes for 2 and 16 patients during the non-COVID-19 and COVID-19 periods, respectively. After covariate adjustment, it was revealed that the patients who presented during the pandemic were more likely to have a door-to-balloon time of >90 minutes (OR: 5.4, 95% CI: 3.1–22.8) and a pain-to-balloon time of >12 hours (OR: 2.0, 95% CI: 1.1–10.2) (Table 2).

DISCUSSION

In the present study, we found that patients who were diagnosed with STEMI and underwent PPCI during the COVID-19 crisis period presented later following the onset of ischemic symptoms. In addition, they were more likely to have a door-to-balloon time of >90 minutes. Our findings suggest that although the in-hospital mortality risk was similar, the ischemic duration of the patients in the COVID-19 era group was longer compared with those who had presented during the non-COVID-19 era.

The COVID-19 pandemic has caused a significant health crisis, during which the major focus of governments, healthcare policy makers, and hospital administrations has been reducing transmission of the virus and treating infected patients. Strict lockdown

Table 2. Logistic regression models for door-to-balloon time >90 minutes and pain-to-balloon time >12 hours

	Non-COVID-19 era STEMI March 5–April 6, 2019 (n=174)	COVID-19 era STEMI March 5–April 6, 2020 (n=90)
Door-to-balloon >90 minutes		
Number of patients	2	16
Case rate, %	1.1	17.8
Door-to-balloon >90 minutes, OR (95% CI)		
Model 1: unadjusted	[Reference]	13.9 (4.1–92.5)
Model 2: adjusted for all covariates[a]	1[Reference]	5.4 (3.1–22.8)
Pain-to-balloon time >12 hours		
Number of patients	7	22
Case rate, %	4.0	24.4
Pain-to-balloon time >12 hours, R (95% CI)		
Model 1: unadjusted	[Reference]	5.9 (2.4–26.2)
Model 2: adjusted for all covariates	1[Reference]	2.0 (1.1–10.2)

aAdjusted for age, gender, hypertension, diabetes mellitus, smoking, hyperlipidemia, chronic obstructive pulmonary disease, coronary artery disease, and chronic renal failure. CI: Confidence interval; STEMI: ST-segment elevation myocardial infarction; OR: Odds ratio.

regulations were one of the measures implemented during the pandemic. Unfortunately, difficulty accessing medical contact may have had an adverse impact on patients with chronic diseases who need frequent hospital visits and individuals who developed acute conditions that required urgent treatment. This was particularly true in countries where digital solution strategies, such as telehealth services, were not ready for deployment to supplement the healthcare system. Other studies have also reported that the number of patients with STEMI decreased during the pandemic.[4,5] An expanded analysis from the United States indicated that activation of the catheter laboratory declined 29% during the pandemic.[8] In the context of STEMI, establishing coronary flow by performing PPCI is of utmost importance since "time is muscle." Each half an hour of delay has been demonstrated to increase the 1-year mortality risk by 7.5%.[9]

Aside from a decrease in the number of patients presenting with STEMI during the pandemic, a study has reported that the interval between the onset of symptoms and the first medical contact increased.[10] Furthermore, comparable to our findings, an analysis from the United States reported that door-to-balloon time increased 20%.[8] In contrast, a report from Austria found an increase in the total ischemic time but not in door-to-balloon time.[11] The authors speculated that patient-related delays were the major contributor to delayed reperfusion. Possible reasons for this delay include reluctance to seek medical contact due to fear of virus transmission or difficulties accessing healthcare facilities due to lockdown restrictions. Although we did not evaluate the time from pain onset to first medical contact, the total ischemic duration assessed by pain-to-balloon time and door-to-balloon time was greater in the pandemic patients in our study. Reasons for extended pain-to-balloon time not only include patient delay in seeking medical care but also system-related delays, such as the initial triage and transportation to the catheter lab. The Turkish Cardiology Association Consensus Report: COVID-19 Pandemic and Cardiovascular Diseases noted a significant deviation in the initial management of patients with STEMI during the pandemic.[12] In particular, changes in the STEMI triage system in the emergency department during the pandemic can cause significant delays in door-to-balloon time. The majority of hospitals canceled the direct transfer of patients with suspected STEMI to the catheterization lab and instead used computed tomography and echocardiography for COVID-19 triage. In addition, reports have indicated that noteworthy ST-segment changes may be observed in patients with COVID-19 in the absence of significant stenosis in the coronary arteries. This could cause diagnostic challenges during triage.[13] Significant delays might occur due the need to prepare the catheterization lab personnel with the proper protective equipment. Although we did not observe an increase in the number patients with a post-PCI TIMI grade of <3 or in-hospital mortality, the number of patients in this study was limited. Previously, it has been demonstrated that total ischemic time prolongation in the context of STEMI increased the risk of no-reflow and in-hospital mortality rates.[14] Reinstadler et al.[11] observed that patients who presented during the COVID-19 outbreak had lower post-PCI TIMI flow grades and higher peak troponin levels, which might adversely impact the long-term prognosis.

Given these findings, the pharmacoinvasive strategy of early fibrinolytic therapy may be a reasonable approach if significant delays in the ability to perform the PPCI are expected.[15] It might be possible to complete COVID-19 screening tests during the interval between initiating fibrinolytic treatment and the rescue PCI, if required. However, it should be kept in mind that the role of secondary hemostasis during the course of COVID-19 is complex and not yet well defined.[16]

This is not the first pandemic that the world has been through and it likely will not be the last. Several important measures should be taken to overcome issues that have been observed during the COVID-19 crisis. First, efforts to inform the public that they should seek medical attention as soon as possible in the context of emergency conditions should be emphasized, and it should be highlighted that 24/7 facilities are available for coronary angiography. Second, digital tools, including telehealth systems and mobile applications, should be adopted quickly by healthcare systems. The necessary legal issues should be resolved and technological infrastructure should be improved. Finally, more sophisticated organization and strategy should be implemented to reduce in-hospital delays in triage and transportation of the patients.

Limitations

This was a single-center study with a limited number of patients. We only evaluated in-hospital mortality;

there was no long-term follow-up. Retrospective analysis of the control group includes inherent limitations.

Conclusion

We observed a significant reduction in the number of patients who were diagnosed with STEMI and underwent PPCI during a peak of the COVID-19 pandemic. Patients who were diagnosed during the outbreak had a longer ischemic time: They were more likely to have a pain-to-balloon time of >12 hours and a door-to-balloon time of >90 minutes.

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