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## Impact in total ischemic time and ST-segment elevation myocardial infarction admissions during COVID-19

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### ABSTRACT

**Background:** Despite the COVID-19 pandemic, cardiovascular disease is still the main cause of death in developed countries. Of these deaths, acute coronary syndromes (ACS) account for a substantial percentage of deaths. Improvement in ACS outcomes, are achieved by reducing the time from symptom onset until reperfusion or total ischemic time (TIT). Nevertheless, due to the overwhelming reality at the beginning of the pandemic, acute coronary syndrome (ACS) care may have been compromised.

**Objectives:** We evaluated delays in TIT based on the date and timing of admissions in patients with STEMI, by a timeline follow-up form, before and during the current COVID-19 pandemic.

**Methods:** Between July 2018 and June 2020, two hundred and twelve patients diagnosed with ST-segment elevation myocardial infarction (STEMI) were admitted to our medical center. Upon presentation, cases were assigned a timeline report sheet and each time interval, from onset of symptoms to the catheterization lab, was documented. The information was later evaluated to study potential excessive delays throughout ACS management. **Results:** Our data evidenced that during the COVID-19 pandemic ACS admissions were reduced by 34.54%, in addition to several in-hospital delays in patient's ACS management including delays in door-to-ECG time ( $9.43 \pm 18.21$  vs.  $18.41 \pm 28.34$ ,  $p = 0.029$ ), ECG-to-balloon ( $58.25 \pm 22.59$  vs.  $74.39 \pm 50.30$ ,  $p = 0.004$ ) and door-to-balloon time ( $57.41 \pm 27.52$  vs.  $69.31 \pm 54.14$ ,  $p = 0.04$ ).

**Conclusions:** During the pandemic a reduction in ACS admissions occurred in our hospital that accompanied with longer in-hospital TIT due to additional tests, triage, protocols to protect and prevent infection within hospital staff, and maintenance of adequate standards of care. However, door-to-balloon time was maintained under 90 min.

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### 1. Introduction

Cardiovascular diseases (CVD) are the number one cause of death globally [1]. In Israel, CVD were the second most common cause of death, after cancer, representing 15% of all deaths in 2016 [2]. Considered one of the most representative CVD, acute coronary syndrome (ACS) is characterized by sudden and severe reduction of coronary flow and tissue perfusion followed by cardiomyocytes loss and tissue necrosis [1,3,4]. The total ischemic time (TIT) is one of the most critical

parameters that determine patient prognosis defined as the time from symptoms onset until reperfusion [3,5,6]. The underlying ACS perfusion deficit or ischemia can be classified into a ST-segment elevation myocardial infarction (STEMI) and a non-ST-segment elevation myocardial infarction (NSTEMI) by electrocardiographic (ECG) assessment [7,8]. STEMI is the electrical manifestation of transmural ischemia secondary to a complete absence of perfusion to the previously perfused myocardium [5]. Expedited treatment of STEMI with percutaneous coronary intervention (PCI) or thrombolysis, has been shown to improve outcomes [9]. According to the 2018 Acute Coronary Syndrome Israeli Survey (ACSIS), about 36–40% of all ACS were associated with electrocardiographic evidence of STEMI [10,11]. The door-to-balloon time within 90 min of presentation is recommended by the current guidelines [5].

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However, the PCI-within-90 min goal is commonly hampered by patient-related factors, delayed presentation, commuting times, and in-hospital system-associated challenges.

The ongoing outbreak of coronavirus disease 2019 (COVID-19), an infectious disease caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has become a rapidly evolving global pandemic that impacted millions of people worldwide. From a clinical standpoint, current reports emphasize that COVID-19 outbreak limit the application of the standards of care for STEMI patients with altered procedures at all levels, unforeseen delays with dramatic consequences in ACS management. Furthermore, during the current pandemic, hospitals around the world have reported a substantial reduction in ACS admissions and reduced number of cardiac procedures [12,13].

In this study, we evaluated the impact of COVID-19 on the TIT in patients with STEMI undergoing primary PCI at our hospital.

## 2. Methods

### 2.1. Study design

The study was performed at Barzilai Medical Center, a 617-bed hospital, in Ashkelon area in southern Israel. The hospital serves a population of 500,000, with more than 100,000 admissions annually. For this single centered, retrospective study, TIT ACS intervals for STEMI patients were recorded from July 2018 until June 2020 using a pre-determined time report spreadsheet. TIT intervals and delays assessment were simplified by dividing TIT into three different stages 1) symptom's onset-to-first medical contact (FMC), 2) FMC-to-catheter lab activation, and 3) catheter lab activation-to-PCI (Fig. 1) [6]. Based on reports by the Ministry of Health, February 2020 was selected as the beginning of the coronavirus outbreak as reports of infected patients were noted from hospitals around the country. The study population included 212 patients with STEMI on which primary PCI was performed. The cohort was further divided into two groups, 176 patients with a conventional STEMI protocol (before COVID-19) and 36 with STEMI protocol during the COVID-19 pandemic (COVID-19).

### 2.2. Pre-revascularization protocol

We registered TIT intervals from onset of symptoms to PCI procedure. Pre-hospital data was provided by the emergency medical service (EMS) upon patient arrival. Patient admission to the emergency department (ED), and initial evaluation and ECG assessment was performed by the nursing staff. Upon STEMI diagnosis by the ER physician, the on-call cardiologist was notified for further patient evaluation. If the decision to

proceed to primary PCI is made, the Cath lab team is activated and assumes the responsibility of recording the time interval information into the time report spreadsheet. The route from the ED to the Cath lab at our hospital is approximately 200 m and involve the use of an elevator in a two stories ride. When a STEMI diagnosis is known prior to hospital arrival, the cardiologist is informed in advance to wait for the patient at the ED. After the procedure, the timeline report spreadsheet is revised and signed by the chief interventional cardiologist and transferred to our institutional quality control department. The study protocol adhered to the declaration of Helsinki and was approved by the institutional review board of Barzilai Medical Center (BRZ-0113-20).

### 2.3. Statistical analysis

The results are presented as the mean  $\pm$  standard deviation (SD) for continuous variables with normal distribution, and as number and percentage for categorical data. *t*-test was used for comparison of continuous variables. Proportions were compared with contingency tables followed by either Fisher's exact test or Chi-square depending of the variable category. A two-sided *p*-value  $<0.05$  was considered statistically significant. Statistical analysis was performed with GraphPad Prism version 8.4.3 for Mac, GraphPad Software, La Jolla California USA.

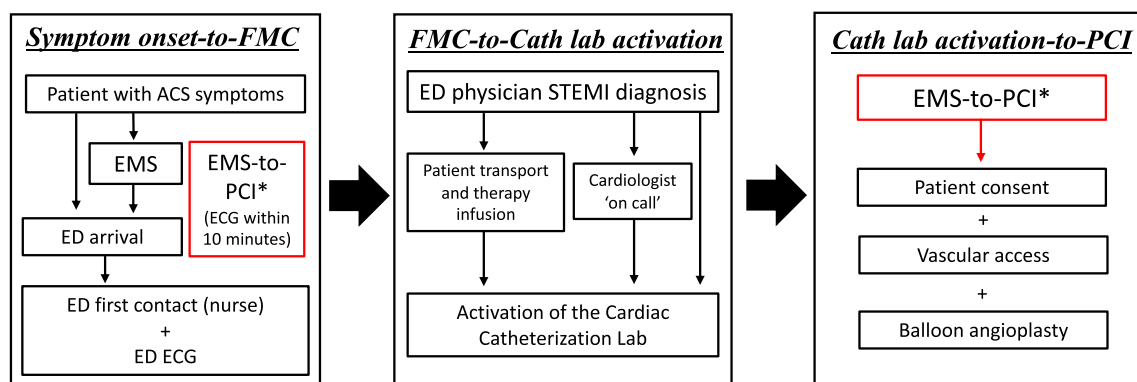
## 3. Results

We analyzed data from 212 patients further divided into two groups, 176 patients with STEMI before the COVID-19 (Before COVID-19 group)

**Table 1**  
Characteristics of patients admitted to the emergency department with STEMI before and during the COVID-19 pandemic.

	Before COVID-19 (n = 176)	COVID-19 (n = 36)	<i>p</i> -value
Male gender	146 (83)	32 (89)	0.46
Age (mean $\pm$ SD)	61 $\pm$ 12.9	59 $\pm$ 11.73	0.62
BMI (mean $\pm$ SD)	27.67 $\pm$ 4.55	27.67 $\pm$ 4.15	0.99
Hyperlipidemia	82 (46.5)	13 (36)	0.27
Past family history	22 (12.5)	5 (14)	0.78
Smoking (Current)	77 (44)	12 (33)	0.27
Past CAD or cerebrovascular accident	45 (25.5)	5 (14)	0.19
Hypertension	86 (49)	13 (36)	0.20
Diabetes mellitus	60 (34)	9 (25)	0.33
Peripheral vascular disease	9 (5)	0 (0)	0.36
Troponin T negative at admission	30 (17)	6 (17)	0.99

SD, standard deviation. BMI, body mass index. CAD, coronary artery disease.



**Fig. 1.** Classification of total ischemic time during COVID-19 pandemic. The different stages of time delays from onset of symptoms until reperfusion therapy. TIT intervals are divided into hospital independent delays (symptom onset-to-FMC) and in-hospital delays (FMC-to-cath lab activation, and cath lab activation-to-PCI). \*A clear EMS-STEMI diagnosis even during COVID-19 pandemic mandates direct and immediate catheterization lab activation to minimize total ischemic time at any given time as before COVID-19 pandemic. ECG should be performed within 10 min upon arrival. TIT, total ischemic time. FMC, first medical contact. EMS, emergency medical service. STEMI, ST-segment elevation myocardial infarction. ECG, electrocardiogram. ED, emergency department. PCI, percutaneous coronary intervention.

and 36 with STEMI during the COVID-19 pandemic (COVID-19 group). Patients in both groups were predominantly male (83% vs. 89%), and older (61 vs. 59 years old). No significant differences between the two groups were observed in gender, age, BMI or comorbidities including hyperlipidemia, past cardiac family history, smoking, past ischemic heart disease or cerebrovascular accident, hypertension, diabetes mellitus, peripheral vascular disease, and Troponin T negative results at admission (Table 1). During the COVID-19 pandemic, we observed a significant increase in STEMI hospitalizations during the morning shift, however, before the pandemic hospitalizations were evenly distributed throughout the day ( $p = 0.043$ , Table 2). STEMI cases were also evenly distributed throughout the week, with a slightly increased percentage of STEMI cases on Thursdays ( $p = 0.69$ ). The time interval from symptom onset to hospital arrival, obtained during history taking

in the ED, accounted for an average of  $174.6 \pm 213.8$  min compared to  $158.5 \pm 162.3$  min during the COVID-19 pandemic. Despite a reduction in 16 min, no significant statistical differences were observed ( $p = 0.698$ ). Time from symptoms onset to PCI was  $231 \pm 199$  min compared to  $229 \pm 157.4$  min recorded during COVID-19 pandemic ( $p = 0.949$ ). In-hospital time intervals indicated a 9 min delay in door-to-ECG time ( $9.43 \pm 18.21$  vs.  $18.41 \pm 28.34$ ,  $p = 0.029$ , Table 2, Fig. 2). The average time-interval from ECG-to-balloon increased by 16 min ( $58.25 \pm 22.59$  vs.  $74.39 \pm 50.30$ ,  $p = 0.004$ , Table 2, Fig. 2). In addition, the door-to-balloon time experienced a 12 min delay ( $57.41 \pm 27.52$  vs.  $69.31 \pm 54.14$ ,  $p = 0.04$ , Table 2, Fig. 2). No increased mortality, from admission to PCI, was observed when both time periods were compared (15 vs. 0,  $p = 0.08$ ).

#### 4. Discussion

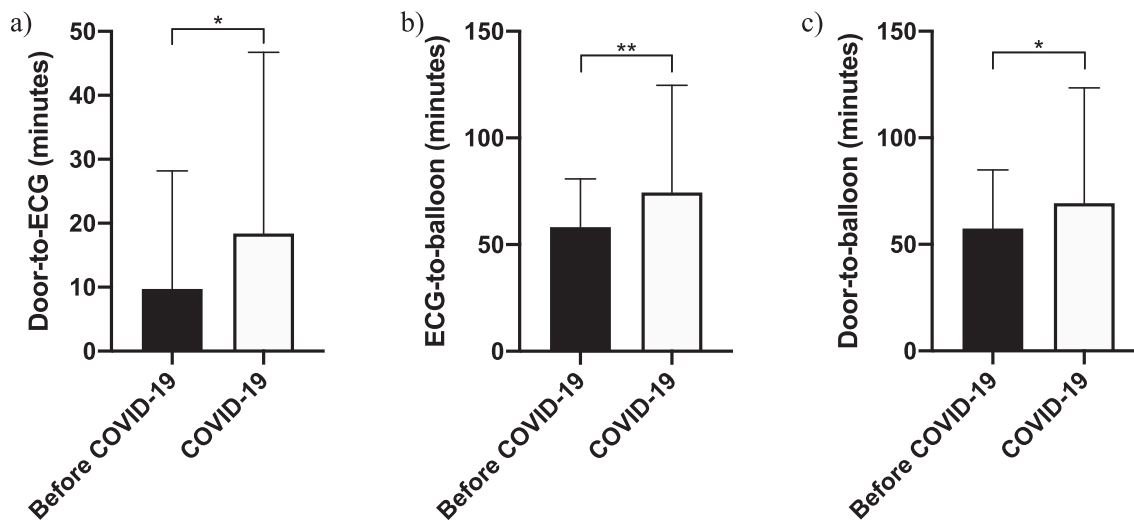
The impact of COVID-19 on ACS presentation and management has shaped the clinical scenario in our daily hospital practice. In line with other hospitals worldwide [12–14], we observed a reduction of hospitalization for STEMI, which in our hospital accounted for a 34.54% reduction. In this new clinical scenario, we hypothesized that the reduction in STEMI is caused by a less stressful home-based work environment and a patient's fear of being admitted to the hospital, especially during lockdown.

The best ACS clinical outcomes are achieved by reducing the time from symptom onset until reperfusion or TIT. TIT is one of the most critical parameters that strongly correlated with infarct size and mortality [6,15,16]. The current guidelines of the European Society of Cardiology (ESC) and the American Heart Association (AHA) for the management of patients with STEMI emphasize the importance in TIT reduction strategies [5,17]. In particular, the ESC guidelines advocate for an ECG diagnosis within 10 min upon chest pain presentation, and a door-to-balloon time within 90 min of STEMI diagnosis [5]. In fact, TIT can be divided into three different stages 1) symptom's onset-to-FMC, 2) FMC-to-catheter lab activation, and 3) catheter lab activation-to-PCI [6]. Despite that our study did not show an overall reduction in TIT, no substantial delays were evidenced during the COVID-19 pandemic. As far as stage 1 is concerned, our study evidenced significant delays from symptoms onset to first medical contact. Despite a 16-min reduction in stage 1 delays during COVID-19, the results did not prompt statistically significant outcomes. The shorter symptom-to-FMC time

**Table 2**  
Comparison of time intervals in STEMI patients before and during the COVID-19 pandemic.

	Before COVID-19	COVID-19	p-value
Time of day (daytime), n (%)			0.043
AM	87 (49%)	24 (66%)	
PM	89 (51%)	11 (33%)	
Day of the week			0.69
1	26 (15%)	7 (19%)	
2	22 (13%)	5 (14%)	
3	27 (15%)	2 (5%)	
4	23 (13%)	3 (8%)	
5	30 (17%)	8 (22%)	
6	25 (14%)	5 (14%)	
7	23 (13%)	6 (17%)	
Time from symptoms onset to first medical contact/nurse, minutes±SD, (95% CI)	$174.6 \pm 213.8$ (95% CI, 135.4–213.7)	$158.5 \pm 162.3$ (CI, 99.02–218.1)	0.698
Time from symptoms onset to PCI, minutes±SD, (95% CI)	$231.1 \pm 199$ (CI 198.1–264.1)	$229 \pm 157.4$ (CI 181.2–276.9)	0.949
Door-to-ECG time, minutes±SD, (95% CI)	$9.43 \pm 18.21$ (CI 6.19–12.67)	$18.41 \pm 28.34$ (CI 8.95–27.85)	0.029
ECG-to- balloon time, minutes ±SD, (95% CI)	$58.25 \pm 22.59$ (CI 54.37–61.12)	$74.39 \pm 50.30$ (CI 58.51–90.27)	0.004
Door-to-balloon time, minutes ±SD, (95% CI)	$57.41 \pm 27.52$ (CI 53.06–61.76)	$69.31 \pm 54.14$ (CI 54.09–84.54)	0.04

1, Sunday. 2, Monday. 3, Tuesday. 4, Wednesday. 5, Thursday. 6, Friday. 7, Saturday. PCI, percutaneous coronary intervention. ECG, electrocardiogram. SD, standard deviation. 95% CI, confidence interval.



**Fig. 2.** Comparison of In-hospital times before the pandemic (Before COVID-19) and during the pandemic (COVID-19). ECG, electrocardiogram. \* $p < 0.05$ . \*\* $p < 0.005$ .

observed during COVID-19 is in sharp contrast to data reported from US and Europe where this time interval was excessively prolonged [14,17–20]. This reduction can be explained by a relatively milder impact of the pandemic medium-sized metropolis, combined with a faster commuting times caused by 'lock-down' restrictions issued by the government inviting citizens to stay at home, unless urgent needs should arise. Nevertheless, stage 1 still continues to be a major player in increased TIT interval overall. As far as the stage 2 delays are concerned, our catheterization lab is within walking distance to the ED, hence no significant delays were noted. Interestingly, our study shows that COVID-19 pandemic caused significant delays in stage 3, including ECG-to-balloon and door-to-balloon time. This fact can be explained by the additional tests carried out, the extra time for staff preparation to protect themselves with personal protection equipment against COVID-19, and delays on PCI-related activities. Detailed analysis of the three stages evidenced that despite no substantial delays were observed in stage 1, the delays accounted in stages 2 and 3 delays were due to COVID-19 protocols set in place at our facility which maintained TIT as before the pandemic. In addition, we maintained a door-to-balloon time under 90 min as prior to the pandemic hence, no increase primary PCI procedure time or increased mortality was observed and the quality of care was preserved. One of the reasons for this success is based on the 'STEMI code' set in place at our facility, thus when a STEMI diagnosis is made in the ER, a direct activation of the Cath lab team can be made by the ED physician [21–23]. The readiness of the patient for transport to the catheterization lab begins shortly after diagnosis, concomitantly to treatment in the ED. When the lab is ready, the ED is notified and the patient is urgently transferred, accompanied by a cardiologist (Fig. 1).

#### CRedit authorship contribution statement

**Sharon Bruoha:** Investigation, Methodology, Data curation, Visualization, Writing - review & editing. **Chaim Yosefy:** Supervision, Funding acquisition, Writing - review & editing. **Enrique Gallego-Colon:** Investigation, Writing - original draft, Formal analysis. **Jonathan Rieck:** Supervision, Writing - review & editing. **Yan Orlov:** Resources, Writing - review & editing. **Azriel Osherov:** Validation, Data curation, Writing - review & editing. **Abu Hamed Jihad:** Validation, Data curation, Writing - review & editing. **Yaniv Sherer:** Resources, Data curation, Writing - review & editing. **Nasi Viki:** Methodology, Writing - review & editing. **Jamal Jafari:** Conceptualization, Project administration, Writing - review & editing.

#### 5. Conclusion

During the COVID-19 pandemic, we observed a reduction in STEMI hospitalizations. Despite the delays observed throughout patient's cardiovascular care along with the additional extraordinary measures to protect staff and patients from viral transmission, the delays were within the 90 min door-to-balloon window with no associated increased mortality.

#### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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