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Change in Hospitalizations and 30-Day Mortality of Patients With Acute Myocardial Infarction During the First COVID-19 Lockdown – A Pure Social Isolation Effect?

Gil Lavie^{a,c}, Erez Battat^a, Walid Saliba^{a,c}, Moshe Y. Flugelman^{b,c,*}

^a Division of Planning and Strategy, Clalit Health Services, Tel Aviv, Israel

^b The Department of Cardiovascular Medicine, Lady Davis Carmel Medical Center, Haifa, Israel

^c Ruth and Bruce Rappaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel

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ABSTRACT

Background: The COVID-19 pandemic has had diverse effects on population health and psychology in relation to non-COVID-19 diseases, as well as on COVID-19 infection. Fewer patients with acute myocardial infarction (AMI) sought medical attention during the first lockdown of the pandemic.

Methods and results: We conducted a retrospective cohort study of Clalit Health Services patients treated in multiple hospitals for AMI. We examined the numbers and characteristics of the patients and 30-day mortality during three 5-week phases of the first wave of the COVID-19 pandemic in Israel: pre-lockdown ($N = 702$), lockdown ($N = 584$), and lockdown-lift ($N = 669$). We compared data for the same period in 2018 and 2019. We stratified the data by ST-elevation myocardial infarction (STEMI) and non-STEMI. AMI hospitalizations during the lockdown were 17% lower than in the pre-lockdown period (rate ratio-0.83, 95% CI 0.74–0.93), and 22% and 31% lower than in the corresponding periods in 2018 and 2019, respectively. The reduction was mainly attributed to non-STEMI hospitalizations (26% lower than the pre-lockdown period in 2020). Hospitalizations due to both STEMI and non-STEMI were moderately reduced during the post-lockdown period compared to the corresponding periods in 2018 and 2019. Thirty-day mortality rate was similar for all the periods assessed.

Conclusions: The number of hospitalized patients with AMI during the first COVID-19 lockdown and post-lockdown periods was significantly reduced, without significant changes in 30-day mortality rates.

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1. Introduction

The immediate and direct global effects of the COVID-19 pandemic on public health have been dreadful [1,2]. As of August 2021, 4 million individuals have succumbed to the viral disease [3]. During the pandemic, the regulations and measures taken to reduce viral transmission and the associated psychology of the global pandemic have forced multiple changes in behaviors and resulted in devastating indirect effects on public health [4–6]. On one hand, persons with acute and chronic diseases have been reluctant to seek medical help, fearing that visits to emergency rooms and medical institutes could expose them to COVID-19. On the other hand, the medical system has been stretched to its limits and depleted from resources to deal with both COVID-19 and non-COVID-19 conditions.

While cardiac involvement in COVID-19 is highly significant in many patients [7,8], we focused on the indirect, collateral effects of the pandemic on patients with acute myocardial infarction (AMI) who were

free of COVID-19 infection. The data we accumulated may contribute to preparing health services to prevent delays in diagnosis and therapies for noninfectious diseases during the current and future pandemics. The number of COVID-19 patients was low in the first wave of COVID-19 in Israel, and the lockdown was strictly applied. This period of time, in which pandemic psychology prevailed over actual COVID-19 disease, provided a unique opportunity to examine the possible psychological effects of the lockdown on hospitalization for AMI.

2. Methods

In this study, we examined hospitalizations for AMI of insureds of Clalit Health Services in all Israeli hospitals during different phases of the first wave of the COVID-19 pandemic. As the largest healthcare organization in Israel, Clalit Health Services insures and provides medical services to 52% of Israel's population (nearly 4.5 million). A single and comprehensive electronic record database is used for all the insureds of Clalit Health Services, which covers all medical data including hospitalizations of the insureds in any hospital in Israel [9]. We examined the numbers and characteristics of persons hospitalized from February 9,

* Corresponding author at: Department of Cardiovascular Medicine, Lady Davis Carmel Medical Center, 7 Michal Street, Haifa 34632, Israel.

E-mail address: myf@technion.ac.il (M.Y. Flugelman).

2020 to May 31, 2020 due to AMI, and the 30-day mortality of these patients. These 15 weeks included 5 weeks before the first lockdown period, the 5 weeks of lockdown, and the 5 weeks after the lockdown-lift. Using the database of Clalit Health Services, we identified patients with AMI who were hospitalized in non-COVID-19 wards. The patients were classified as having ST-elevation myocardial infarction (STEMI – ICD-9 codes 41011, 41021, 41031, 41041, 41051, 41061, and 41081) and non-STEMI (ICD-9 codes 41071 and 41091).

We compared the hospitalization rate and 30-day all-cause mortality between the pre-lockdown, lockdown, and lockdown-lift periods in 2020. AMI-related hospitalizations during these three periods in 2020 (5 weeks each) were compared to the corresponding 5 weeks periods in 2018 and 2019.

AMI-related hospitalization was expressed as the number per 100,000 patient-years. We compared patient age, sex, and 30-day all-cause mortality rates between the phases of the pandemic in 2020, and between each of these periods and the corresponding periods in 2018 and 2019.

3. Statistical methods

Continuous variables were summarized as means and standard deviations, and categorical variables were summarized as counts and proportions. Baseline categorical variables, cumulative hospitalizations, and 30-day all-cause mortality were compared between phases of the pandemic in 2020 (pre-lockdown, lockdown, and lockdown-lift); and between these periods and the corresponding periods in 2018 and 2019, using the chi-square test. One-way ANOVA was used to compare continuous variables between groups.

AMI hospitalization was estimated for each 5-week period of the study by dividing the number of patients by the total follow-up time. Hospitalization rates were presented with 95% confidence intervals (CIs). AMI hospitalizations were compared pairwise using the mid-p exact test. The group effect was estimated using rate ratios (RRs) and presented with 95% confidence intervals. Statistical analyses were performed using IBM SPSS Statistics 24.0 (IBM, New York, NY) and OpenEpi [10]. For all analyses, $p < 0.05$, for the 2-tailed tests was considered statistically significant. All CIs were calculated using the mid-p exact limits provided by the OpenEpi software. The Breslow-Day test was used to examine the interactions between the study periods and study year in their associations with AMI-related hospitalizations and 30-day all-cause mortality.

4. Results

4.1. Patient demographics

For all nine 5-week periods analyzed (the pre-lockdown, lockdown, and lockdown-lift phases of the pandemic in 2020) and the corresponding periods in 2018 and 2019, the mean age of the patients was similar, 66–68 years, as was the proportion of males, 71%–76% (Table 1). For all

nine 5-week periods, the mean age was lower, and the proportion of males was higher among patients hospitalized with STEMI than among those with non-STEMI (Table 1). Among both patients with STEMI and non-STEMI, statistical differences were not found in mean age or sex distribution between each of the three periods examined in 2020 and the corresponding periods in 2018 and 2019.

4.2. Myocardial infarction hospitalization rate and 30-day mortality during the phases of the pandemic in 2020

Table 2 and Fig. 1 present data of all hospitalizations with AMI, and separately for STEMI and non-STEMI, for the nine periods examined.

The total number of AMI hospitalizations during the lockdown phase of the pandemic was 17% lower than in the pre-lockdown period (RR 0.83; 95% CI, 0.74–0.93). Total AMI hospitalizations did not differ significantly between the lockdown-lift and pre-lockdown periods (RR 0.95; 95% CI 0.86–1.06).

Hospitalization rates of non-STEMI patients during the examined periods in 2020 were similar to those of total AMI. STEMI hospitalization rates in the lockdown and post-lockdown periods were similar to those of the pre-lockdown period; the RR was slightly less than 1.0.

Thirty-day all-cause mortality did not differ significantly between the three periods examined in 2020 (Table 3). Thirty-day mortality of patients hospitalized with STEMI was significantly lower in the lockdown and lockdown-lift periods, RR 0.46 (0.26–0.84) and 0.56 (0.33–0.98), respectively, compared to the pre-lockdown period. Thirty-day mortality rates for patients hospitalized with non-STEMI in 2020 were higher in the lockdown and lockdown-lift periods than in the pre-lockdown period, RR 2.99 (1.05–8.5) and 2.54 (0.90–7.16), respectively.

4.3. Comparison of rates of myocardial infarction hospitalization and 30-day mortality between the year 2020 and the years 2018 and 2019

Data for the years 2018 and 2019 are presented in Tables 2 and 3, and in Fig. 1. Rates of AMI hospitalization were lower during the phases of the pandemic in 2020 than during the corresponding periods in the years 2018 and 2019 ($p < 0.01$, for both 2018 and 2019) (Table 2). Compared to 2018 and 2019, total AMI hospitalizations were decreased during the pandemic in 2020 (p for interaction < 0.05 , for 2018 and < 0.01 for 2019) (Table 2).

For non-STEMI hospitalization, the RR was less than 1.0 for the each of the three periods in 2020 compared to the corresponding periods in 2018 and 2019. However, significant interactions were detected only for the pre-lockdown and lockdown-lift periods in 2020 relative to their corresponding periods in 2019; RR 1.35 (1.16–1.57) (P for interaction < 0.001) (Table 2).

Thirty-day all-cause mortality rates of patients hospitalized with AMI did not differ significantly between the lockdown phases in 2020 and the corresponding 5-week-periods in 2018 and 2019 (Table 3).

Table 1

Age and gender of patients hospitalized with acute myocardial infarction during 5-week periods of three phases of the COVID-19 pandemic in Israel in 2020 (pre-lockdown, lockdown, and post lockdown), and the corresponding periods in 2018 and 2019. The data are presented for all the patients with acute myocardial infarction, and separately for those with ST-elevation myocardial infarction (STEMI) and non-STEMI.

	2018			2019			2020		
	All	STEMI	Non-STEMI	All	STEMI	Non-STEMI	All	STEMI	Non-STEMI
Age, years									
Period 1	67.5 (n = 645)	64.8 (n = 269)	69.5 (n = 376)	67.4 (n = 673)	64.3 (n = 291)	69.9 (n = 382)	67.4 (n = 702)	65.9 (n = 279)	68.3 (n = 423)
Period 2	67.9 (n = 693)	66.8 (n = 296)	68.8 (n = 397)	66.6 (n = 830)	64.0 (n = 356)	68.6 (n = 474)	66.3 (n = 584)	64.5 (n = 272)	67.9 (n = 312)
Period 3	67.5 (n = 731)	66.4 (n = 314)	68.3 (n = 417)	67.6 (n = 844)	64.8 (n = 392)	70.0 (n = 452)	66.4 (n = 669)	63.9 (n = 270)	68.1 (n = 399)
The proportion of males (%)									
Period 1	73.2	76.2	71.0	71.5	73.5	69.9	71.5	72.4	70.9
Period 2	73.9	73.6	74.1	76.0	78.9	73.8	74.8	77.9	72.1
Period 3	71.1	69.7	72.2	72.0	72.4	71.7	73.1	77.8	69.9

Table 2
Incidence of acute myocardial infarction (per 100,000 patient years) in three 5-week phases of the COVID-19 pandemic in 2020 and their corresponding periods in 2018 and 2019: pre-lockdown, lockdown, and after lockdown-lift.

	No	Incidence rate (95% CI) (per 100,000 p-y) 2018	RR (95% CI)	No	Incidence rate (95% CI) (per 100,000 p-y) 2019	Incidence rate (95% CI) (per 100,000 p-y) 2019	RR (95% CI)	No	Incidence rate (95% CI) (per 100,000 p-y) 2020	RR (95% CI)
Period 1, total AMI	645	149 (138–161)	Reference	673	153 (142–165)	153 (142–165)	Reference	702	157 (146–169)	Reference
Period 2, total AMI	693	160 (148–172)	1.07 (0.96–1.20)	830	189 (176–202)	189 (176–202)	1.23 (1.11–1.36)	584	131 (121–142)	0.83 ^{a,b} (0.74–0.93)
Period 3, total AMI	731	169 (157–181)	1.13 (1.02–1.26)	844	192 (179–206)	192 (179–206)	1.25 (1.13–1.39)	669	150.0 (139–162)	0.95 ^{c,d} (0.86–1.06)
Period 1, STEMI	269	62.1 (54.9–69.9)	Reference	291	66.2 (58.9–74.3)	66.2 (58.9–74.3)	Reference	279	62.5 (55.4–70.3)	Reference
Period 2, STEMI	296	68.3 (60.7–76.5)	1.10 (0.93–1.3)	356	81.0 (72.8–89.9)	81.0 (72.8–89.9)	1.22 (1.05–1.43)	272	61.0 (53.9–68.7)	0.97 (0.82–1.15)
Period 3, STEMI	314	72.5 (64.7–80.9)	1.17 (0.99–1.37)	392	89.2 (80.6–98.5)	89.2 (80.6–98.5)	1.35 (1.16–1.57)	270	60.5 (53.5–68.2)	0.96 ^e (0.82–1.14)
Period 1, non-STEMI	376	86.7 (78.2–96.0)	Reference	382	87.0 (78.5–96.1)	87.0 (78.5–96.1)	Reference	423	94.8 (86–104.3)	Reference
Period 2, non-STEMI	397	91.6 (82.8–101.1)	1.06 (0.92–1.22)	474	107.9 (98.4–118.1)	107.9 (98.4–118.1)	1.21 (1.08–1.42)	312	69.9 (62.4–78.1)	0.74 ^{f,g} (0.64–0.85)
Period 3, non-STEMI	417	96.2 (87.2–105.9)	1.11 (0.96–1.28)	452	102.9 (93.6–112.8)	102.9 (93.6–112.8)	1.18 (1.03–1.34)	399	89.4 (80.9–98.7)	0.94 ^h (0.82–1.08)

RR, rate ratio; CI, confidence interval; p-y, patient year; AMI, acute myocardial infarction; STEMI, ST-elevation myocardial infarction Period 1: pre-lockdown or the corresponding period; Period 2: lockdown or the corresponding period; Period 3: lockdown-lift or the corresponding period.

- ^a Lockdown vs. pre-lockdown 2020 vs. 2018 < 0.01.
- ^b Lockdown vs. pre-lockdown 2020 vs. 2019 < 0.01.
- ^c Lockdown-lift vs. pre-lockdown 2020 vs. 2018 < 0.05.
- ^d Lockdown-lift vs. pre-lockdown 2020 vs. 2019 < 0.01.
- ^e Post-lockdown vs. pre-lockdown 2020 vs. 2019 < 0.01.
- ^f Lockdown vs. pre-lockdown 2020 vs. 2018 < 0.01.
- ^g Lockdown vs. pre-lockdown 2020 vs. 2019 < 0.01.
- ^h Lockdown vs. pre-lockdown 2020 vs. 2019 < 0.05.

Thirty-day mortality rates of patients hospitalized with STEMI did not differ significantly between each of the three phases of the pandemic in 2020 and their corresponding periods in 2018 and 2019. Although the magnitude of the RRs in 2020 differed substantially from those in 2018 and 2019, a significant interaction was observed only for the comparison of the lockdown-lift period with the corresponding period in 2019 (Table 3).

For patients with non-STEMI, the magnitudes of the RRs for 30-day mortality for the three phases of the pandemic in 2020 were considerably higher than for the corresponding periods in 2018 and 2019. However, a significant interaction was observed only for the lockdown phase compared to the corresponding period in 2019 (Table 3).

5. Discussion

This study showed that significantly fewer patients were hospitalized with AMI during the lockdown and post-lockdown phases of the pandemic in 2020 than in the corresponding periods in 2018 and 2019. These reductions were mainly attributed to the hospitalization of patients with non-STEMI. Hospitalizations of patients with STEMI were significantly reduced only during the post-lockdown period. Thirty-day mortality of patients with STEMI was significantly lower in the lockdown period in 2020 than in the corresponding period in 2018. In contrast, 30-day mortality of patients with non-STEMI was higher in the lockdown period than in the corresponding period in 2019.

Our findings collaborate reports of lower numbers of patients with AMI during social confinement and lockdowns due to the COVID-19 pandemic globally [11–16], and lower occurrences of other, non-COVID-19 diseases [17–20]. The findings were ascribed to the reluctance of patients to arrive at clinics and hospitals despite symptoms, due to fear of contracting coronavirus infection in these centers. Increased occurrence of AMI during lockdown has also been reported [21].

February–May 2020 represents a unique period in Israel, as the number of COVID-19 patients was low, but social distancing and mask wearing were strictly enforced. Thus, the effects of the lockdown and lockdown-lift on cardiovascular and other diseases were apparently due to social isolation and psychological effects of the pandemic. Accordingly, the epidemiology of AMI during this period presumably reflects direct effects of delayed treatment, life changes and stress, and social isolation measures that were imposed by the pandemic. Treatment may have been delayed due to reluctance of patients to arrive at

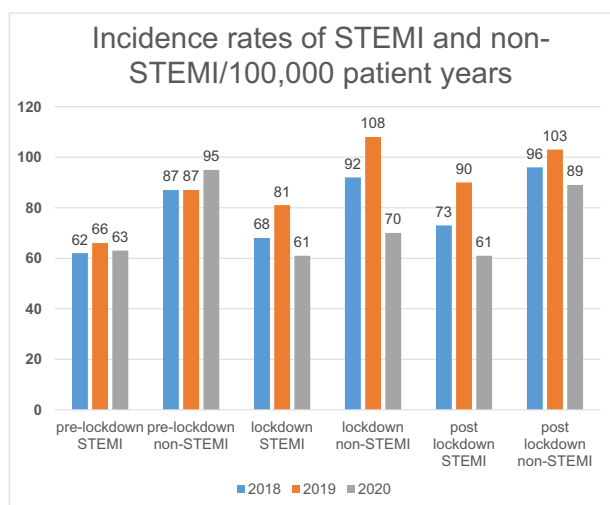


Fig. 1. Hospitalizations of patients with ST-elevation myocardial infarction (STEMI) and non-STEMI during three phases of the COVID-19 pandemic in 2020 and during corresponding periods in 2018 and 2019. The data are presented for occurrence per 100,000 person years. Three 5-week time periods are presented for each year: 1) pre-lockdown in 2020 and the corresponding periods in 2018 and 2019; 2) lockdown in 2020 and the corresponding periods in 2018 and 2019; and 3) post-lockdown in 2020 and the corresponding periods in 2018 and 2019.

Table 3
Thirty-day mortality rates of patients hospitalized with acute myocardial infarction.

Total	2018			2019			2020		
	Death/total	Risk (95% CI)	RR (95% CI)	Death/total	Risk (95% CI)	RR (95% CI)	Death/total	Risk (95% CI)	RR (95% CI)
Period 1, total AMI	50/645	7.8% (5.9–10.1)	Reference	46/673	6.8% (5.1–9.0)	Reference	38/702	5.4% (4.0–7.4)	Reference
Period 2, total AMI	50/693	7.2% (5.5–9.4)	0.93 (0.64–1.36)	53/830	6.4% (4.9–8.3)	0.93 (0.64–1.37)	26/584	4.5% (3.0–6.5)	0.82 (0.51–1.34)
Period 3, total AMI	49/731	6.7% (5.1–8.8)	0.86 (0.59–1.26)	53/844	6.3% (4.8–8.1)	0.92 (0.63–1.35)	30/669	4.5% (3.0–6.5)	0.82 (0.51–1.34)
Period 1, STEMI	28/269	10.4% (7.3–14.7)	Reference	30/291	10.3% (7.3–14.4)	References	33/279	11.8% (8.5–16.2)	References
Period 2, STEMI	29/296	9.8% (6.9–13.8)	0.94 (0.58–1.54)	40/356	11.2% (8.3–15.0)	1.09 (0.7–1.7)	15/272	5.5% (3.3–9.0)	0.46 ^a (0.26–0.84)
Period 3, STEMI	31/314	9.8% (7.0–13.7)	0.94 (0.58–1.54)	34/392	8.6% (6.2–11.9)	0.84 (0.53–1.34)	18/270	6.7% (4.2–10.4)	0.56 (0.33–0.98)
Period 1, non-STEMI	22/376	5.9% (3.9–8.7)	Reference	16/382	4.2% (2.5–6.7)	References	5/423	1.18% (0.42–2.82)	References
Period 2, non-STEMI	21/397	5.3% (3.4–7.9)	0.9 (0.5–1.6)	13/474	2.7% (1.6–4.7)	1.5 (0.74–3.13)	11/312	3.5% (1.9–6.3)	2.99 ^b (1.05–8.5)
Period 3, non-STEMI	18/417	4.3% (2.7–6.7)	0.73 (0.4–1.35)	19/452	4.2% (2.7–6.5)	1.0 (0.52–1.9)	12/399	3.0% (1.67–5.24)	2.54 (0.9–7.16)

Period 1: pre-lockdown or the corresponding period; Period 2: lockdown or the corresponding period; Period 3: lockdown-lift or the corresponding period. RR, rate ratio; CI, confidence interval.

^a Lockdown vs. pre-lockdown 2020 vs. 2019 $p < 0.05$.

^b Lockdown vs. pre-lockdown 2020 vs. 2019 $p < 0.005$.

the hospital. Interestingly, increased numbers of Google searches for chest pain and for alternative therapies to hospital-based therapies have been noted during the COVID-19 pandemic [22–23]. Assuming that the occurrence of AMI during the pandemic was similar to previous years, individuals who stayed home despite symptoms of AMI would presumably seek medical attention at a later point, with symptoms related to untreated AMI, such as heart failure. This is expected to increase morbidity and mortality in the coming months and years. Future studies should examine this phenomenon and its long-term consequences.

Disasters are usually associated with immediate and direct stress, and with insufficient control of threats; however, even high-profile sports events were reported to be associated with increased cardiovascular events [24–28]. Although the first-wave COVID 19 lockdown in Israel was characterized by a low number of patients hospitalized with COVID-19, the pandemic was an acute stressful situation and an increase in cardiovascular events could have been expected. A possible explanation for the differences observed between STEMI and non-STEMI hospitalizations during the lockdown is that STEMI usually presents as a dramatic event, while non-STEMI often presents as a relatively minor event. Individuals with a dramatic presentation are more likely to receive medical attention, particularly at a time that hospitals seem risky to visit. The effect of social isolation on the occurrence of AMI during a pandemic is unclear. Social isolation has been reported to increase the risk of fatality in a cardiovascular event, although it did not affect the risk of developing the event [29].

During the COVID-19 pandemic, the primary medical focus has been on patients with coronavirus. This population has dominated healthcare attention and resources at the expense of patients with cardiovascular and other diseases. Some symptoms of heart pathologies, such as dyspnea and exhaustion, are among the possible presenting symptoms of COVID-19 infection. Patients with such symptoms could decide to stay home for fear that being tested for COVID-19 requires immediate isolation and hospitalization in corona-confined departments. For patients with non-STEMI, we and others have shown that avoidance of angiography and revascularization is detrimental to the prognosis [30,31]. These findings were echoed in the AMI guidelines [32].

Pandemics play a major role in the behavior of communities and individuals. Media and community leaders may inform and misinform. Together with personal beliefs, this may influence behavior. While the medical community has focused on the pandemic and allocated most resources to treat patients with COVID-19, other disease entities have received insufficient attention [17,19,20]. Limitations on face-to-face meetings with physicians, and the transition to telemedicine have also contributed to the neglect of non-COVID-19 diseases.

Health services should be prepared to address the non-COVID-19 outcomes of the pandemic. The increased 30-day mortality rate of non-STEMI patients, which we observed during the lockdown compared to 2019, may indicate delayed arrival to the hospital of these patients. Our finding of lack of change during the pandemic, in 30-day

mortality following STEMI, concurs with a meta-analysis [33]. Similar findings regarding mortality in patients with myocardial infarction were reported in another cohort of Israeli patients and in Germany [34,35]. Although we investigated the effects of the pandemic on AMI during a more limited time period than in other studies [36,37], a unique aspect of our report is that during our study period, only very few hospitalized patients had COVID-19 infection. This enabled investigating the psychological effects of social distancing, and the reluctance to seek medical care on the occurrence of AMI. During the early pandemic period, medical teams were caught by surprise; and methods to treat patients with symptoms and findings of both AMI and COVID-19 infection were lacking. Only following scientific reports from Italy and later from other countries were guidelines established for treating patients with COVID-19 who also had symptoms and laboratory findings of AMI.

Limitations of the current study arise from the exclusive reliance on the Clalit electronic database. This database may have missed individuals who were hospitalized in non-Clalit hospitals and whose health status was inadvertently not updated. In addition, the use of the abovementioned ICD classifications for non-STEMI may erroneously have increased the number of patients reported to have non-STEMI, as some patients with increased troponin levels could have been misdiagnosed as having non-STEMI. Due to the focus on the first wave of the pandemic, patients with COVID-19 infection were absent from our cohort. This contrasts with a study of patients with COVID-19 infection, myocardial injury and an abnormal troponin level [38]. Notably, we assessed all-cause and not cardiovascular mortality rates. Data on out-of-hospital mortality as the primary event were unavailable for analysis.

In conclusion, we observed a significant reduction in the number of hospitalized patients with AMI during the first COVID-19 lockdown and post-lockdown periods, without a significant change in 30-day mortality rates. Future studies should evaluate the long-term consequences of these findings on public health.

Ethics approval and consent to participate

Not applicable.

Consent for publication

All authors reviewed the manuscript and consented to its publication.

Availability of data and material

Data are available upon request.

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CRediT authorship contribution statement

Gil Lavie, MD initiated the project, supervised data acquisition, analyzed the data, and participated in writing the manuscript.

Erez Batta, MBA, worked on data acquisition and analyzed the data. Walid Saliba, MD, MPH, analyzed the data and reviewed the manuscript.

Moshe Y. Flugelman, MD participated in planning, analyzing the data, and writing the manuscript.

Period 1: pre-lockdown or the corresponding period; Period 2: lockdown or the corresponding period; Period 3: post-lockdown or the corresponding period.

Declaration of competing interest

There are no competing interests of any authors.

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