

Article

Treatment Times and In-Hospital Mortality Among Patients with ST-Elevation Myocardial Infarction Throughout the Waves of the COVID-19 Pandemic: Lessons Learned

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Abstract

Previous studies about the COVID-19 pandemic on STEMI patient outcomes have conflicting results. It remains unclear if this may be attributed to regional differences and/or differences during COVID-19 wave periods. Using the American Heart Association Get With The Guidelines—Coronary Artery Disease registry data, we evaluated (1) time metrics related to STEMI system goals and (2) regional variation in STEMI incidence and in-hospital mortality during pandemic wave time periods. The study included all patients 18–100 years old admitted with STEMI ($n = 72,516$) to 1 of 435 American Heart Association Get With The Guidelines—Coronary Artery Disease hospitals (1 October 2019–31 December 2021). Of these, 70.8% were male and 73.0% non-Hispanic White, with a median age of 63 (IQR 18) years. Compared to pre-pandemic time frames, patients with STEMI had a higher risk profile, delayed time to treatment, were treated with fibrinolytic therapy or primary PCI, and were transferred for primary PCI at similar rates, and had higher adjusted in-hospital mortality (during the second wave in the South and Midwest). Preservation of STEMI systems of care resulted in an overall lower in-hospital mortality rate than predicted, although opportunities exist to improve treatment delays. Regional differences in mortality rates require further study.

Keywords: COVID-19; ST-segment elevation myocardial infarction (STEMI); STEMI systems of care; outcomes

1. Introduction

ST-elevation myocardial infarction (STEMI) is a life-threatening emergency requiring rapid diagnosis and reperfusion therapies to prevent immediate and long-term devastating patient outcomes. Timely identification and treatment of STEMI are critical because delayed therapy or misdiagnosed MI doubles the risk of death [1].

The coronavirus (SARS-CoV-2) emerged in 2020 as a new threat to individuals with cardiac disease: emergency medical services (EMS) calls, emergency department (ED) visits, and hospital admissions for acute cardiac conditions decreased substantially [2–4]. Prior to the pandemic, there were over 3.5 million ED visits for STEMI per year in the United States (US) for suspected STEMI [5]. In the first 10 weeks of the COVID pandemic (mid-March 2020 through May 2020), ED visits for MI declined by 23% compared with the preceding 10-week period (January 2020–mid-March 2020) [6]. EMS calls and hospital admissions decreased sharply for conditions such as acute coronary syndrome (ACS), decompensated heart failure, and atrial fibrillation [2,4,7] while out-of-hospital sudden cardiac arrest and resultant death increased [7]. Of the >500,000 total deaths reported in the US between March and April 2020 (i.e., early pandemic period), 87,001 were considered excess deaths, of which >50% were attributed to causes other than COVID-19, including heart disease, diabetes, Alzheimer’s disease, and cerebrovascular disease [8]. The direct impact of COVID-19 on STEMI outcomes remains unclear, in part related to the unknown number of patients who did not seek care.

In response to this concern, and within Mission: Lifeline, the American Heart Association’s (AHA) national initiative to advance the systems of care for patients with STEMI [9], the AHA issued guidance to ensure that patients with STEMI continue to receive life-saving treatments while maintaining patient and healthcare worker safety [10]. The American Heart AHA Get With The Guidelines–Coronary Artery Disease registry (GWTG-CAD) [11] enrolls patients admitted with STEMI in over 700 participating hospitals across the US. Using these national data, the purpose of our study was to describe (1) time metrics related to STEMI system of care goals and (2) regional variation related to the incidence of STEMI and in-hospital mortality of patients presenting to hospitals pre-pandemic and during specified pandemic wave time frames. We hypothesized there would be a delay in STEMI diagnosis and treatment, and an increase in in-hospital mortality during pandemic wave periods compared to pre-pandemic. Moreover, we hypothesized that there would be geographical variation in mortality related to specific wave periods. This is a comprehensive report of national data to describe the impact of the COVID-19 pandemic on STEMI systems of care.

2. Materials and Methods

2.1. Data Sources and Collection

The AHA GWTG-CAD Registry is a voluntary quality improvement program in the US that has been described previously [12,13]. Participating hospitals upload clinical data of consecutive patients admitted with STEMI or non-ST-elevation myocardial infarction (NSTEMI). Program information and data elements collected in the case report form are available at: <https://www.heart.org/en/professional/quality-improvement>. Because data were used primarily at the local site for quality improvement, sites were granted a waiver of informed consent under the Common Rule. Patients, therefore, are neither recruited nor consented, and no patient identifiers are collected. The data collection and coordination for

GTWG programs are managed by IQVIA (Parsippany, NJ, USA). The data for the social vulnerability index (SVI), ranging from 0 (least vulnerable) to 1 (most vulnerable), were from the Center for Disease Control (CDC)/Agency for Toxic Substances and Disease Registry (ATSDR) SVI database at: https://www.atsdr.cdc.gov/placeandhealth/svi/data_documentation_download.html (accessed on 2 July 2025). Patient-level GTWG-CAD data and SVI data are linked by county. Characteristics of the CAD registry hospitals are shown in Supplementary Table S1. The number of hospitals within the registry by CDC region is shown in Supplementary Table S2. Supplementary Table S3 includes the number of STEMI patients in the CAD registry during analogous pre-pandemic time frames.

2.2. Study Period, Population, and Patient Selection

The study population included all patients between 18 and 100 years old admitted to GTWG-CAD hospitals from 1 October 2019 to 31 December 2021 (Figure 1). A discharge diagnosis of STEMI or STEMI equivalent was defined as STEMI of the anterior wall, inferior wall, other sites, or unspecified site. Patients diagnosed with STEMI and discharged from the hospital with valid data for sex (male and female; other excluded $n = 58$), race/ethnicity, and disposition status, and who were admitted to hospitals with patients from all wave time frames were included. A total of 72,516 patients from 435 sites were included in the study after applying the inclusion–exclusion criteria.

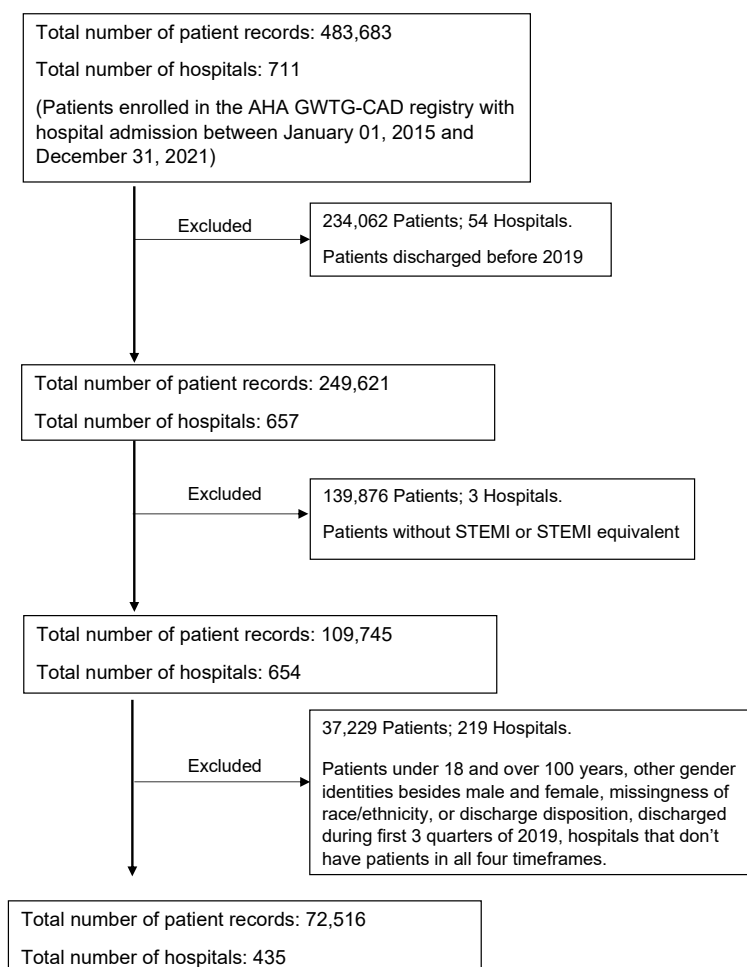


Figure 1. Inclusion–exclusion criteria flowchart of the study.

2.3. Outcomes and Covariates

The primary outcomes included the following timed process metrics: for receiving centers only, first medical contact (FMC) to cardiac catheterization lab (Cath Lab) activation for EMS patients; door-to-Cath Lab activation for walk-in patients; FMC-to-device time for EMS patients; door-to-device time for walk-in patients; symptom onset-to-device time for EMS and walk-in patients. For both receiving and referral centers, FMC-to-electrocardiogram (ECG) time for EMS patients; door-to-ECG time for walk-in patients; and ED dwell time for both EMS and walk-in patients. In-hospital all-cause mortality was the secondary outcome. Only date times that have a precision of hours and minutes are used to calculate timed process metrics (e.g., Cath Lab activation date time, arrival date time, and EMS FMC date time for FMC to Cath Lab activation). Values for all timed process metrics less than 0 or greater than 1440 min are excluded [10,11]. Categorical variables of five time intervals, including FMC to device ≤ 90 min for EMS patients, door-to-device ≤ 90 min for walk-in patients, door to ECG ≤ 10 min for walk-in patients, ED ≤ 30 min for EMS patients, and ED ≤ 30 min for walk-in patients, were created. COVID-19 pandemic waves included time frames to encompass specific CDC COVID-19 peaks and case trends. Time frames were (1) pre-pandemic: 1 October 2019–29 February 2020; (2) wave 1: 1 March 2020–31 October 2020; (3) wave 2: 1 November 2020–31 March 2021; and (4) wave 3: 1 April 2021–31 December 2021 [14]. Each COVID-19 pandemic wave was the main independent variable, with pre-pandemic as the reference group. The reason for the non-system delay was defined as the need for additional personal protective equipment (PPE) for suspected/confirmed infectious disease.

2.4. Statistical Analysis

Descriptive statistics were presented as percentages for categorical variables and medians (with interquartile range) for continuous variables. Characteristics of patients and hospitals were stratified by pre-pandemic and COVID-19 waves. Missing values of insurance status were assigned to the “other/not documented” category. Missing values of SVI are imputed by the median. Missing values of cardiac arrest prior to arrival, heart failure on FMC, and cardiogenic shock on FMC were managed by multiple imputations by chained equations. Between-group differences were assessed using a chi-square test for categorical variables and Kruskal–Wallis followed by the Dunn test for continuous variables. Kruskal–Wallis, a non-parametric test, ranks all the observations from two or more groups and sums the ranks from one of the groups, which is then compared with the expected rank sum. It should be noted that with a sufficient sample size, the difference in ranks will be large enough to be significant even though the medians are equal. A linear trend of the in-hospital mortality across pre-pandemic and pandemic waves was assessed for each CDC region using the Mann–Kendall test. For in-hospital mortality, generalized estimating equations (GEE) were used to calculate odds ratios (ORs) for different pandemic waves, accounting for within-hospital clustering, using robust sandwich estimators for the variance. Three models were fitted, including unadjusted, multivariable-adjusted (adjusting for age, race/ethnicity, cardiac arrest prior to arrival, cardiogenic shock on FMC, and heart failure on FMC), and extended multivariable-adjusted (adjusting for all covariates from the multivariable-adjusted model and diabetes, hypertension, left ventricular function (LVF) assessment, insurance, and SVI). Additional models were also fitted on different subsets of the study population, including sex (male and female) and different regions (Midwest, Northeast, South, West). Sensitivity analyses excluding cardiac arrest prior to arrival and cardiogenic shock on FMC (attributed to the pandemic) from the adjusted covariate list stratified by males and females were also performed. Statistical significance was assessed

at $\alpha = 0.05$. Data analysis was performed using the open-source software R (4.2.0) and Python (3.7.16) by the American Heart Association's Data Science Analytics team.

3. Results

3.1. Patient Population

Between 1 October 2019, through 31 December 2021, a total of 72,516 patients hospitalized with STEMI and entered into the GWTG-CAD registry were evaluated (Table 1). The cohort had a median age of 63 years (IQR: 18), with 29.2% female, 73.0% non-Hispanic White, 11.3% Black, and 7.7% Hispanic. Most had health insurance coverage (including 46.8% with private insurance, 25.5% with Medicare, 11.4% with Medicaid) and median SVI was 0.5 (IQR: 0.4). Compared to the pre-pandemic cohort (8.3%), patients in waves 2 and 3 had higher proportions of heart failure on FMC (9.6%, 9.7%). Patients in wave 3 also had significantly higher rates of cardiogenic shock (8.3%) compared to pre-pandemic rates (7.5%). More individuals were transported by EMS during all waves (waves 1–3 [49.4, 48.9%, 48.9%]) compared to pre-pandemic (46.9%). The overall SARS-CoV-2 infection rate at admission was 1.3%.

Table 1. Baseline characteristics of patients hospitalized with STEMI by established pre-pandemic vs. pandemic wave time periods.

Variable	Pre-Pandemic: 1 October 2019– 29 February 2020 (N = 13,603)	Pandemic Wave 1: 1 March 2020– 31 October 2020 (N = 21,026)	Pandemic Wave 2: 1 November 2020– 31 March 2021 (N = 13,627)	Pandemic Wave 3: 1 April 2021– 31 December 2021 (N = 24,260)	Total (N = 72,516)	<i>p</i> -Value (Pre-Pandemic vs. Wave 1)	<i>p</i> -Value (Pre-Pandemic vs. Wave 2)	<i>p</i> -Value (Pre-Pandemic vs. Wave 3)
Age, years (median, IQR)	63.0 (17)	63.0 (18)	63.0 (18)	63.0 (18)	63.0 (18)	0.309	0.958	0.963
Male (n, %)	9563 (70.3%)	14,993 (71.3%)	9662 (70.9%)	17,147 (70.7%)	51,365 (70.8%)	0.132	0.551	0.739
Female (n, %)	4040 (29.7%)	6033 (28.7%)	3965 (29.1%)	7113 (29.3%)	21,151 (29.2%)	0.045 *	0.281	0.444
Race/Ethnicity (n, %)								
Hispanic	1023 (7.5%)	1541 (7.3%)	1071 (7.9%)	1960 (8.1%)	5595 (7.7%)	0.520	0.304	0.055
Non-Hispanic White	10,024 (73.7%)	15,640 (74.4%)	9903 (72.7%)	17,355 (71.5%)	52,922 (73.0%)	0.153	0.060	<0.001
Black	1525 (11.2%)	2260 (10.7%)	1552 (11.4%)	2878 (11.9%)	8215 (11.3%)	0.184	0.656	0.060
Asian	491 (3.6%)	739 (3.5%)	528 (3.9%)	1021 (4.2%)	2779 (3.8%)	0.663	0.262	0.005 *
American Indian/Alaskan Native	78 (0.6%)	145 (0.7%)	83 (0.6%)	121 (0.5%)	427 (0.6%)	0.211	0.760	0.374
Native Hawaiian/Pacific Islander	31 (0.2%)	52 (0.2%)	36 (0.3%)	86 (0.4%)	205 (0.3%)	0.804	0.630	0.042 *
Unable to Determine/Untold	431 (3.2%)	649 (3.1%)	454 (3.3%)	839 (3.5%)	2373 (3.3%)	0.692	0.468	0.141
Social Vulnerability Index (SVI) (median, IQR)	0.5 (0.4)	0.5 (0.4)	0.5(0.4)	0.5 (0.4)	0.5 (0.4)	0.964	0.137	0.286
CDC Region (n, %)								
Midwest	2000 (14.7%)	2942 (14.0%)	1787 (13.1%)	3325 (13.7%)	10,054 (13.9%)	0.067	<0.001 *	0.008 *
Northeast	3007 (22.1%)	4482 (21.3%)	2876 (21.1%)	5184 (21.4%)	15,549 (21.4%)	0.084	0.047 *	0.097
South	6382 (46.9%)	10,031 (47.7%)	6533 (47.9%)	11,543 (47.6%)	34,489 (47.6%)	0.153	0.092	0.218
West	2177 (16.0%)	3481 (16.6%)	2384 (17.5%)	4107 (16.9%)	12,149 (16.8%)	0.180	0.001 *	0.021 *
Missing	37 (0.3%)	90 (0.4%)	47 (0.3%)	101 (0.4%)	275 (0.4%)	0.024 *	<0.001 *	0.032 *
Insurance Status (n, %)								
Medicare	3709 (27.3%)	5291 (25.2%)	3444 (25.3%)	6051 (24.9%)	18,495 (25.5%)	<0.001 *	<0.001 *	<0.001 *
Medicaid	1387 (10.2%)	2307 (11.0%)	1587 (11.6%)	2978 (12.3%)	8259 (11.4%)	0.023 *	<0.001 *	<0.001 *
Private/VA/Champus/Other	6241 (45.9%)	9990 (47.5%)	6404 (47.0%)	11,269 (46.5%)	33,904 (46.8%)	0.003 *	0.066	0.290
Self-pay/No Insurance	1025 (7.5%)	1572 (7.5%)	995 (7.3%)	1735 (7.2%)	5327 (7.3%)	0.856	0.477	0.175
Other/Not Documented/Unable to Determine	1241 (9.1%)	1866 (8.9%)	1197 (8.8%)	2227 (9.2%)	6531 (9.0%)	0.441	0.338	0.868
Medical History (n, %)								
Cerebrovascular disease	696 (5.1%)	1188 (5.7%)	806 (5.9%)	1532 (6.3%)	4222 (5.8%)	0.102	0.016 *	<0.001 *
Diabetes mellitus	2864 (21.1%)	4749 (22.6%)	3233 (23.7%)	5773 (23.8%)	16,619 (22.9%)	0.004 *	<0.001 *	<0.001 *

Table 1. Cont.

Variable	Pre-Pandemic: 1 October 2019– 29 February 2020 (N = 13,603)	Pandemic Wave 1: 1 March 2020– 31 October 2020 (N = 21,026)	Pandemic Wave 2: 1 November 2020– 31 March 2021 (N = 13,627)	Pandemic Wave 3: 1 April 2021– 31 December 2021 (N = 24,260)	Total (N = 72,516)	p-Value (Pre-Pandemic vs. Wave 1)	p-Value (Pre-Pandemic vs. Wave 2)	p-Value (Pre-Pandemic vs. Wave 3)
Hypertension	6352 (46.7%)	10,941 (52.0%)	7210 (52.9%)	13,091 (54.0%)	37,594 (51.8%)	<0.001 *	<0.001 *	<0.001 *
Heart failure	495 (3.6%)	980 (4.7%)	676 (5.0%)	1241 (5.1%)	3392 (4.7%)	<0.001 *	<0.001 *	<0.001 *
Prior MI	1401 (10.3%)	2410 (11.5%)	1495 (11.0%)	2839 (11.7%)	8145 (11.2%)	0.003 *	0.199	<0.001 *
Prior CABG	447 (3.3%)	725 (3.4%)	448 (3.3%)	791 (3.3%)	2411 (3.3%)	0.718	1.000	0.991
Prior PCI	1596 (11.7%)	2803 (13.3%)	1753 (12.9%)	3276 (13.5%)	9428 (13.0%)	<0.001 *	0.018	<0.001 *
SARS-CoV-2 infection at admission	0 (0%)	219 (1.0%)	380 (2.8%)	310 (1.3%)	909 (1.3%)	<0.001 *	<0.001 *	<0.001 *
Active or prior Smoking	5082 (37.4%)	7785 (37.0%)	4903 (36.0%)	8751 (36.1%)	26,521 (36.6%)	0.991	0.028 *	<0.001 *
Patient characteristics on FMC (n, %)								
Cardiac Arrest Prior to Arrival	1286 (9.5%)	2072 (9.9%)	1395 (10.2%)	2426 (10.0%)	7179 (9.9%)	0.959	0.598	0.848
Heart failure on FMC	1134 (8.3%)	1747 (8.3%)	1303 (9.6%)	2353 (9.7%)	6537 (9.0%)	0.998	<0.001 *	<0.001 *
Cardiogenic Shock on FMC	1016 (7.5%)	1599 (7.6%)	1104 (8.1%)	2010 (8.3%)	5729 (7.9%)	0.837	0.090	0.007 *
Left Ventricular Ejection Fraction								
<30%	1158 (8.5%)	1933 (9.2%)	1291 (9.5%)	2396 (9.9%)	6778 (9.3%)	0.032 *	0.006 *	<0.001 *
30–39%	1934 (14.2%)	3070 (14.6%)	2072 (15.2%)	3457 (14.2%)	10,533 (14.5%)	0.329	0.022 *	0.943
40–49%	2971 (21.8%)	4698 (22.3%)	2988 (21.9%)	5363 (22.1%)	16,020 (22.1%)	0.277	0.875	0.558
50–59%	4068 (29.9%)	6150 (29.2%)	3883 (28.5%)	7171 (29.6%)	21,272 (29.3%)	0.195	0.011 *	0.487
60–69%	2227 (16.4%)	3284 (15.6%)	2094 (15.4%)	3692 (15.2%)	11,297 (15.6%)	0.063	0.024 *	0.003 *
70%+	72 (0.5%)	148 (0.7%)	94 (0.7%)	154 (0.6%)	468 (0.6%)	0.059	0.104	0.227
Transportation characteristics (n, %)								
EMS (ambulance and air)	6386 (46.9%)	10,397 (49.4%)	6660 (48.9%)	11,851 (48.9%)	35,294 (48.7%)	<0.001 *	0.002 *	<0.001 *
Walk-in	3686 (27.1%)	5212 (24.8%)	3431 (25.2%)	6091 (25.1%)	18,420 (25.4%)	<0.001 *	<0.001	<0.001 *
Transfer	3093 (22.7%)	4706 (22.4%)	3092 (22.7%)	5488 (22.6%)	16,379 (22.6%)	0.447	0.937	0.806
Prehospital ECG obtained (EMS)	5449 (85.3%)	9021 (86.8%)	5795 (87.0%)	10,429 (88.0%)	30,694 (87.0%)	0.009 *	0.006 *	<0.001 *
Reperfusion (n, %)								
Fibrinolytic Therapy	700 (5.1%)	1062 (5.1%)	697 (5.1%)	1197 (4.9%)	3656 (5.0%)	0.931	1.000	0.739
PCI	11,870 (87.3%)	18,319 (87.1%)	11,772 (86.4%)	21,031 (86.7%)	62,992 (86.9%)	0.991	0.072	0.393
No PCI and no fibrinolysis	1157 (8.5%)	1737 (8.3%)	1250 (9.2%)	2137 (8.8%)	6281 (8.7%)	0.764	0.105	0.495

Table 1. Cont.

Variable	Pre-Pandemic: 1 October 2019– 29 February 2020 (N = 13,603)	Pandemic Wave 1: 1 March 2020– 31 October 2020 (N = 21,026)	Pandemic Wave 2: 1 November 2020– 31 March 2021 (N = 13,627)	Pandemic Wave 3: 1 April 2021– 31 December 2021 (N = 24,260)	Total (N = 72,516)	<i>p</i> -Value (Pre-Pandemic vs. Wave 1)	<i>p</i> -Value (Pre-Pandemic vs. Wave 2)	<i>p</i> -Value (Pre-Pandemic vs. Wave 3)
Documented non-system delay (need for additional PPE for suspected infectious disease)	0 (0.0%)	836 (4.0%)	429 (3.1%)	281 (1.2%)	1550 (2.1%)	<0.001 *	<0.001 *	<0.001 *
Discharge Disposition (n, %)								
In-hospital raw mortality	929 (6.8%)	1420 (6.8%)	1087 (8.0%)	1774 (7.3%)	5210 (7.2%)	0.963	0.001 *	0.216

Note: *p*-values do not correspond to the table exactly as it is presented here. *p*-values were calculated by comparing only non-missing row values of pre-pandemic to other waves. *p*-value < 0.05—significant; * indicates statistically significant.

3.2. Reperfusion Therapy

Patients with STEMI during waves 1–3 received reperfusion therapy (i.e., fibrinolytics 5%, primary PCI 86.9%) at similar rates as pre-pandemic. There were no differences in the proportion of patients transferred from a STEMI referring hospital to a STEMI receiving center during the pandemic waves compared with the pre-pandemic period (22.7%). There were higher rates of non-system reasons for delay, specifically of need for additional PPE for suspected/confirmed infectious disease across waves 1–3 compared to the pre-pandemic period.

3.3. Time Metrics

We compared timed process metrics among all STEMI patients hospitalized pre- and during pandemic waves 1–3. Median and interquartile range (IQR) values for timed process metrics and the proportion of patients achieving recommended time metrics are presented in Table 2. FMC-to-Cath lab activation times among patients transported by EMS to receiving hospitals were longer for each pandemic wave compared to the pre-pandemic period ($p < 0.002$). For walk-in patients, door-to-Cath Lab activation median times were significantly longer in wave 3 compared to the pre-pandemic period. FMC-to-device times in receiving centers for EMS patients were longer among waves 1–3 compared to the pre-pandemic period ($p < 0.001$). A significantly higher proportion of EMS patients met the target FMC-to-device time of ≤ 90 min pre-pandemic compared to each of the pandemic waves ($p < 0.001$). Among walk-in patients, a significantly higher proportion of pre-pandemic patients met the target of door-to-device time of ≤ 90 min compared to pandemic waves 2 and 3 ($p < 0.001$). In receiving centers, symptom onset-to-device times for EMS transported patients were longer for waves 1–3 compared to the pre-pandemic period ($p < 0.001$). Among walk-in patients, symptom onset-to-device times were lower pre-pandemic compared to all waves 1–3 ($p < 0.016$). In both receiving and referral centers, there was no significant difference between pandemic waves for FMC to ECG time among EMS patients, but waves 2–3 had a significantly longer door-to-ECG time among walk-in patients. In both receiving and referral centers, for walk-in patients, there was a significantly higher proportion of patients meeting the target of ≤ 10 min for door-to-ECG times in the pre-pandemic period compared to waves 2–3. In both receiving and referral centers, for both EMS and walk-in patients, the ED time of the three pandemic waves was significantly longer than the pre-pandemic period. Among EMS patients, a significantly higher proportion of pre-pandemic patients met the target of ≤ 30 min for ED time compared to those in waves 1–3 ($p < 0.001$). Among walk-in patients, a significantly higher proportion of pre-pandemic patients met the target of ≤ 30 min for ED time compared to waves 1–2.

Table 2. Timing metrics of all patients hospitalized with STEMI by established pre-pandemic vs. pandemic wave time periods.

Variable	Pre-Pandemic: 1 October 2019– 29 February 2020 (N = 13,603)	Pandemic Wave 1: 1 March 2020– 31 October 2020 (N = 21,026)	Pandemic Wave 2: 1 November 2020– 31 March 2021 (N = 13,627)	Pandemic Wave 3: 1 April 2021– 31 December 2021 (N = 24,260)	p-Value (Pre-Pandemic vs. Wave 1)	p-Value (Pre-Pandemic vs. Wave 2)	p-Value (Pre-Pandemic vs. Wave 3)
First medical contact to Cath Lab activation (EMS) (minutes) (N = 25,899) (median, IQR) (receiving center only)	25.0 (25.0)	27.0 (26.0)	27.0 (26.0)	27.0 (27.0)	<0.001 *	0.005 *	0.002 *
Doo- to-Cath Lab activation (Walk-in) (minutes) (N = 14,047) (median, IQR) (receiving center only)	15.0 (19.0)	15.0 (21.0)	16.0 (22.0)	16.0 (23.0)	1.000	0.167	0.034 *
First medical contact to device (EMS) (minutes) (N = 29,125) (median, IQR) (receiving center only)	86.0 (38.0)	90.0 (37.0)	90.0 (38.0)	89.0 (38.0)	<0.001 *	<0.001 *	<0.001 *
First medical contact to device ≤ 90 min (EMS) (n, %) (receiving center only)	3043 (57.5)	4419 (51.4)	2814 (51.6)	5170 (52.9)	<0.001 *	<0.001 *	<0.001 *
Door-to-device (Walk-in) (minutes) (N = 16,255) (median, IQR) (receiving center only)	74.0 (36.0)	76.0 (34.0)	77.0 (39.0)	77.0 (38.0)	0.001 *	<0.001 *	<0.001 *
Door-to-device ≤ 90 min (Walk-in) (n, %) (receiving center only)	2298 (71.8)	3221 (70.1)	2062 (67.4)	3690 (68.4)	0.113	<0.001 *	<0.001 *
Symptom onset-to-device (EMS) (N = 25,522) (minutes) (median, IQR) (receiving center only)	147.0 (115.0)	154.0 (118.0)	154.0 (124.0)	153.0 (121.0)	<0.001 *	<0.001 *	<0.001 *
Symptom onset-to-device (Walk-in) (N = 12,563) (median, IQR) (receiving center only)	193.0 (226.0)	201.0 (231.5)	209 (243.3)	209.0 (245.8)	0.016 *	<0.001 *	<0.001 *
First medical contact to ECG (EMS) (N = 30,339) (minutes) (median, IQR) (referral and receiving centers)	7.0 (10.0)	7.0 (9.0)	7.0 (9.0)	7.0 (9.0)	1.000	1.000	0.056
Door-to-ECG (Walk-in) (minutes) (N = 16,800) (median, IQR) (referral and receiving centers)	7.0 (7.0)	7.0 (7.0)	7.0 (7.0)	7.0 (8.0)	0.197	<0.001 *	<0.001 *
Door-to-ECG ≤ 10 min (Walk-in) (n, %) (referral and receiving centers)	2483 (74.1)	3426 (72.1)	2188 (69.6)	3814 (68.7)	0.058	<0.001 *	<0.001 *

Table 2. Cont.

Variable	Pre-Pandemic: 1 October 2019– 29 February 2020 (N = 13,603)	Pandemic Wave 1: 1 March 2020– 31 October 2020 (N = 21,026)	Pandemic Wave 2: 1 November 2020– 31 March 2021 (N = 13,627)	Pandemic Wave 3: 1 April 2021– 31 December 2021 (N = 24,260)	<i>p</i> -Value (Pre-Pandemic vs. Wave 1)	<i>p</i> -Value (Pre-Pandemic vs. Wave 2)	<i>p</i> -Value (Pre-Pandemic vs. Wave 3)
Emergency department time (EMS) (N = 29,389) (minutes) (median, IQR) (referral and receiving centers)	29.0 (33.0)	32.0 (33.0)	31.0 (32.0)	31.0 (33.0)	<0.001 *	<0.001 *	<0.001 *
Emergency department time ≤ 30 min (EMS) (n, %) (referral and receiving centers)	2758 (52.3)	4113 (47.3)	2736 (49.0)	4729 (48.1)	<0.001 *	<0.001 *	<0.001 *
Emergency department time (Walk-in) (minutes) (N = 16,622) (median, IQR) (referral and receiving centers)	47.0 (34.0)	49.0 (35.0)	49.0 (39.0)	49.0 (40)	0.027 *	<0.001 *	<0.001 *
Emergency department time ≤ 30 min (Walk-in) (n, %) (referral and receiving centers)	662 (20.1)	824 (17.5)	549 (17.7)	1013 (18.4)	0.003 *	0.019 *	0.059

* indicates statistically significant.

3.4. In-Hospital Mortality

Patients had higher rates of mortality during pandemic wave 2 (8.0%) compared to the pre-pandemic period (6.8%) ($p < 0.001$) (Table 1), with a higher odds ratio (OR 1.12 [CI 1.01, 1.25], $p = 0.030$) compared with the pre-pandemic period, after adjusting for age, race/ethnicity, diabetes, hypertension, cardiac arrest prior to arrival, heart failure at FMC, cardiogenic shock at FMC, LVF assessment, insurance status, and SVI (Table 3). This increase was limited to males (OR 1.19 [CI 1.04, 1.36]) and not seen in females (Supplementary Table S4a,b). Sensitivity analysis also demonstrated mortality increase for males only (OR 1.22 [CI 1.08, 1.39]) (Supplementary Table S5a,b). Figure 2 shows observed in-hospital mortality and adjusted odds ratios with 95% confidence intervals by pandemic waves and CDC regions after adjusting for age, race/ethnicity, diabetes, hypertension, cardiac arrest prior to arrival, heart failure at FMC, cardiogenic shock at FMC, LVF assessment, insurance status, and SVI. There were significantly higher proportions of in-hospital mortality among the South (7.0%) and West (8.5%) regions compared to the Northeast (reference 6.2%) region (Table 4). The Midwest and South regions exhibited a higher odds ratio of in-hospital mortality in pandemic wave 2 compared to the pre-pandemic period (Supplementary Table S6a–d).

Table 3. Multivariable analysis of in-hospital mortality among COVID waves.

In-Hospital Mortality (Expired at Discharge)	Unadjusted		Adjusted for Age, Race/Ethnicity, Cardiac Arrest Prior to Arrival, Heart Failure on FMC, and Cardiogenic Shock on FMC		Adjusted for Age, Race/Ethnicity, Diabetes Mellitus, Hypertension, Cardiac Arrest Prior to Arrival, Heart Failure on FMC, LVF, Cardiogenic Shock on FMC, Insurance Status, and Social Vulnerability Index	
	Odds Ratio [95% CI]	<i>p</i> -Value	Odds Ratio [95% CI]	<i>p</i> -Value	Odds Ratio [95% CI]	<i>p</i> -Value
Pre-pandemic (reference)	ref	ref	ref	ref	ref	ref
Pandemic wave 1	0.99 [0.90 1.08]	0.079	0.99 [0.89 1.10]	0.833	0.98 [0.88 1.08]	0.672
Pandemic wave 2	1.18 [1.08 1.30]	<0.001 *	1.15 [1.03 1.28]	0.009 *	1.12 [1.01 1.25]	0.030 *
Pandemic wave 3	1.08 [0.99 1.17]	0.089	1.03 [0.93 1.14]	0.550	1.01 [0.91 1.12]	0.880

p-value < 0.05—significant; * indicates statistically significant.

Table 4. Proportion of in-hospital mortality rate per CDC region. * indicates statistically significant.

CDC Region	In-Hospital Mortality (n)	STEMI (n)	Proportion of In-Hospital Mortality	<i>p</i> -Value
Northeast (reference)	969	15,549	6.2%	ref
Midwest	669	10,054	6.7%	0.186
South	2420	34,489	7.0%	0.001 *
West	1034	12,149	8.5%	<0.001 *
Total	5210	72,516	7.2%	

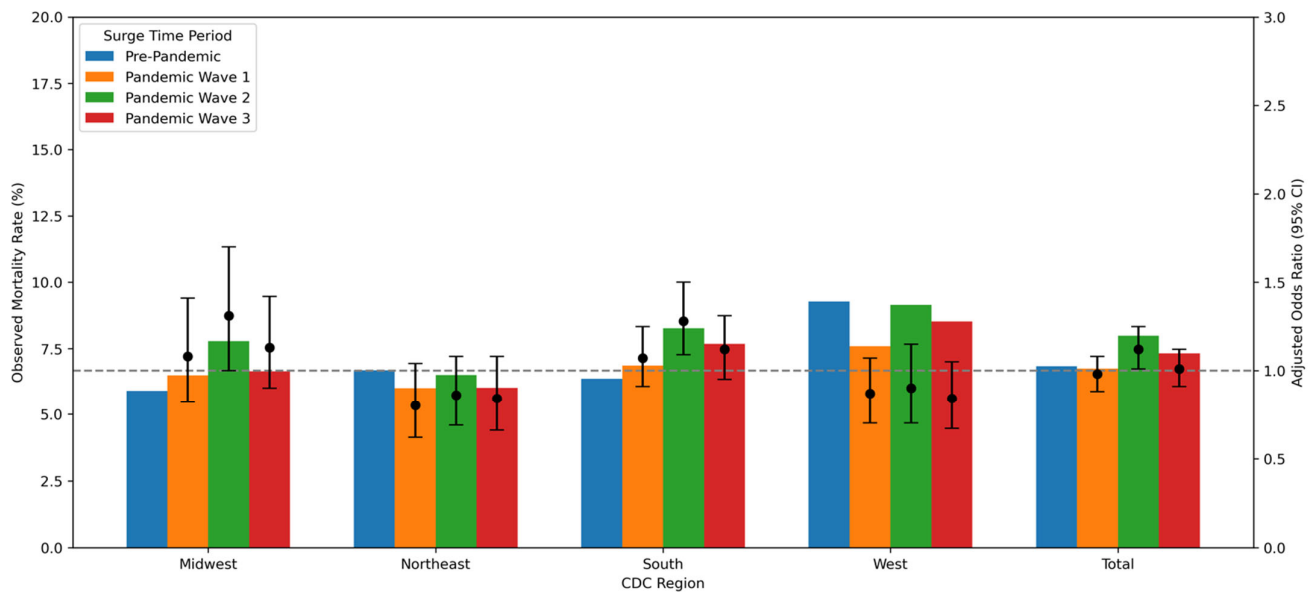


Figure 2. Observed in-hospital mortality rates and adjusted odds ratios with 95% confidence intervals by COVID-19 wave and CDC region (adjusted for age, race/ethnicity, diabetes mellitus, hypertension, cardiac arrest prior to arrival, heart failure on FMC, LVEF, cardiogenic shock on FMC, insurance status, and Social Vulnerability Index). The primary (left) y-axis represents the observed mortality rate (%), and the secondary (right) y-axis represents the adjusted odds ratio. Each bar corresponds to the observed mortality rate within a wave, while the scatter points indicate the adjusted odds ratios with error bars showing the 95% confidence intervals. The dashed horizontal line at odds ratio = 1 serves as a reference.

4. Discussion

In this large-scale study of patients with STEMI during the COVID-19 pandemic in the US, unique in its size and evaluation of STEMI system goals and outcomes across the country during waves of COVID-19 infection between 1 March 2020 and 31 December 2021, patients had a higher risk profile, delayed FMC to device despite presenting via EMS more often, similar treatment with reperfusion therapy, and higher in-hospital mortality only during one wave period compared to the pre-pandemic period, with higher adjusted in-hospital mortality in the Midwest and South, although the overall incidence of documented SARS-CoV-2 virus was only 1.3%.

Many studies have previously reported on patients experiencing STEMI during the SARS-CoV-2 outbreak. Several of these studies, however, were limited to patients with concomitant SARS-CoV-2 infection during the early period of the pandemic. Within the North American COVID-19 Myocardial Infarction (NACMI) Registry, 230 patients with COVID-19 infection and 495 with suspected infection, all presenting with STEMI, exhibited a higher risk profile, were less likely to undergo coronary angiography and PCI, experienced increased time to treatment (door-to-balloon time) and higher in-hospital mortality (of 33.0%) compared to matched control patients with STEMI pre-pandemic [15]. In another study of NACMI patients with STEMI and COVID-19, 74% had one culprit lesion, 14% had multiple culprits, and 12% had no culprit identified [16]. Investigators discovered this cohort had thrombus grade burden, multivessel thrombotic disease, and post-PCI thrombus-related complications. Similarly, within the AHA COVID-19 Cardiovascular Disease Registry, of 15,621 COVID-19 hospitalizations in 2020, 54 patients (0.4%) had STEMI, of whom only 50.0% received reperfusion therapy [17]. In-hospital mortality was 41% in patients with STEMI compared to 16% in those without STEMI.

During the waves of the COVID pandemic, patients who presented with STEMI had a higher risk factor profile compared to the pre-pandemic patients. This may be partly attributable to barriers in access to care throughout the waves of the pandemic and to less effective, more delayed treatment. These data demonstrate delays in presentation (e.g., symptom onset-to-device) and delays in care on arrival, as described in other studies [18]. Delays in time to treatment for STEMI have also been noted, both in patients with and without COVID-19 infection [19,20]. In a study within the Vancouver Coastal Health Authority STEMI database, while the incidence of STEMI was similar, FMC-to-balloon time was delayed compared to pre-pandemic, and the delay increased across the three waves of the pandemic [21]. In a more recent study of patients transported by EMS to the ED for suspected ACS, however, there were no significant differences in ECG markers of ischemia (ST-elevation, ST-depression, T-wave inversion, and/or Q-waves), adverse events (death, heart failure, reinfarction), or prehospital time intervals (9-1-1 call to EMS arrival or to ED arrival) between pre-pandemic and pandemic periods [22].

Most prior studies have also noted an increase in in-hospital mortality in patients with STEMI with [19] and without [23,24] COVID-19 infection. In a retrospective, cross-sectional study of all 15,244 hospitalizations involving 14,724 patients with acute MI in a large multistate healthcare system, the risk-adjusted mortality rate among patients with STEMI increased substantially throughout 2020 [23]. However, the COVID-19 infection rate and time to treatment were not reported. In the International Study on Acute Coronary Syndromes–ST-elevation Myocardial Infarction (ISACS-STEMI) COVID-19 worldwide registry, designed to estimate the impact of the COVID-19 pandemic on patients with STEMI treated by PCI [24], among 16,683 patients undergoing PCI in 109 centers located on four continents during the pandemic in 2020, there was a significant age-related reduction in procedures and longer ischemic time, with a larger effect in elderly than in younger patients. There was also a significantly higher 30-day mortality during the pandemic period, especially among elderly patients compared to young patients [24].

In the present study, limited by a questionably low COVID-19 infection rate in patients with STEMI, it is of interest to note that adjusted in-hospital mortality was increased in wave 2 compared to the pre-pandemic period. Whether this can be attributed in part to an increased COVID-19 infection rate and/or a low vaccination rate in wave 2 compared to wave 3 is unknown; therefore, these ideas are hypothesis-generating. In the NACMI registry, none of the 22 vaccinated patients expired in the hospital, whereas an in-hospital death was recorded in 37 (22%) of unvaccinated patients ($p = 0.009$) [19]. It is also unclear why the mortality increase only occurred in men, but etiologies of STEMI other than plaque rupture and coronary occlusion in women may play a role. Possible further explanations include sex-specific differences in STEMI pathophysiology (plaque morphology and thrombus burden) [25,26] and delay in seeking care for fear of exposure to healthcare-seeking behaviors [27]. Within the COVID-19 NACMI Registry, women more often had STEMI without an identified culprit lesion than men (33% vs. 18%, $p < 0.001$). The use of PCI was significantly higher in men, whereas medical therapy was higher in women, although in-hospital mortality was similar [28]. However, with respect to increased time to treatment across all waves (albeit absolute differences in several metrics were small and less likely to be clinically significant), it was anticipated that mortality would be increased in all waves compared with the pre-pandemic period. Furthermore, as shown in the observational cohort study using data from the National Center for Health Statistics, there was an increase in ischemic heart disease deaths in the early phases of the pandemic [18]. Although the incidence of OHCA was similar throughout the waves of the pandemic to pre-pandemic, perhaps there was a decrease in the survival rate prior to hospital arrival. This may also explain the observation that mortality was decreased during wave 1 compared to pre-

pandemic in the Northeast and West. Delayed care-seeking or overwhelmed EMS may have contributed to an increase in OHCA; therefore, patients with less severe presentations may have reached the hospital during the initial wave, resulting in survival bias. In the Lombardia Cardiac Arrest Registry in Italy, patients with COVID-19 accounted for 77.4% of the increase in cases of out-of-hospital cardiac arrest observed in 2020, and an increase of 14.9% in out-of-hospital deaths in 2020 compared with 2019 among patients in whom resuscitation attempts by EMS were unsuccessful [7]. Moreover, a prior study within the AHA GWTG-CAD registry from 2018 to 2021 [29] in all patients with STEMI, including those with non-system delays, noted that although both time to treatment and mortality had increased during the pandemic (attributed to inherent delays related to EMS, PPE, decreased staffing), mortality during quarter 4 of 2019, pre-pandemic, was 7.2%, which was higher than previously reported in the earlier registry studies [12,30]. The earlier studies, however, excluded patients with non-system reasons for delay; thus, in-hospital mortality may have been significantly increased. Nonetheless, importantly, when time-to-treatment goals were met, mortality was significantly lower.

It is also difficult to determine why changes in mortality differed across geographical regions, but the prevalence of SARS-CoV-2 infection, the proportion of rurality, differences in transfer and transport time, and variations in the development of STEMI systems of care may play a role. Notably, there was no change in the proportion of STEMI patients in the South and an increased proportion in the West throughout the pandemic in comparison to pre-pandemic and the absolute number of patients with STEMI decreased in comparison to analogous pre-pandemic time periods for all waves in all regions (Supplementary Table S3). In a study across 51 New York State hospitals during the early pandemic, PCI for STEMI was decreased, and symptom onset-to-arrival increased in high-density COVID areas but not in low-density areas [31]. It has also been suggested that the geographic areas most impacted by COVID-19 may not remain stable due to changing public health mandates both over time and in different geographic regions [32]. A study using an emerging hot spot analysis to examine the spatiotemporal trends in COVID-19 death rates in the US from March 2020 to May 2021 revealed that, over the three phases of the pandemic (first wave, second wave, and post-vaccine deployment), hot spots shifted from high-density population areas with more socially vulnerable individuals to the states with less strict social distancing and then to the states with low vaccination rates [32]. These data suggested that the factors associated with COVID-19 death rates, including local infection and testing rates, social distancing interventions, and other social, environmental, geographical (urban versus rural), and health risk factors, varied over time. It was noted that these findings can inform the planning of public health initiatives. However, since the COVID-19 infection rate was low on admission in this study population, it is unclear how these regional changes would affect mortality in patients with STEMI.

It is important to highlight several findings from this AHA voluntary, quality improvement registry that support the importance of STEMI systems of care. Despite the inherent delays in care during the pandemic noted above, there was no change in the proportion of patients receiving reperfusion therapy with either fibrinolytic agents or, importantly, with primary PCI, although the overall reperfusion incidence of 83% is lower than in the earlier AHA registry studies. In addition, there was no change in the proportion of patients transferred to a STEMI receiving center for PCI throughout the pandemic waves compared to pre-pandemic, which likely relates to the relatively stable in-hospital mortality. Indeed, within the AHA functioning regional STEMI systems of care, with regular meetings of all stakeholders, including STEMI Referral Hospitals, Receiving Centers, and EMS, planning of how best and where to care for STEMI patients during the pandemic could occur. Certainly, what we have learned from the review of the process metrics and outcomes

throughout the waves of the pandemic across the country will allow us to best prepare and respond to the next (ongoing) pandemic or disaster [33], and continue to maintain and optimize the quality of care and outcomes for patients with STEMI. It should be noted, however, that long transfer delays both pre-pandemic and during the pandemic provide key opportunities for systems improvement.

Limitations

This study has several limitations. The registry is a voluntary quality improvement project with the objective of assisting participating hospitals to improve their processes of care. It uses hospital-reported data, although audits are performed, and the sample of the study is not from random sampling. There is potential for selection bias given the voluntary nature of the registry. All multivariable analyses are subject to potential confounding. They, moreover, do not include any hospital-level covariates. Small and rural hospitals that rely on fibrinolysis and frequently need to transfer patients to PCI-capable facilities are underrepresented in the registry. This suggests that the findings may not be generalizable. It is possible that hospitals most impacted by the pandemic were less likely to voluntarily report data, in which case, we may underestimate the overall impact of the pandemic on STEMI patients. Hospitals under greater pandemic-related stress may have been less able to participate consistently or submit complete data, potentially leading to underrepresentation of more severely impacted institutions. We may, furthermore, not fully understand the true rate of COVID-19 infection or vaccinations in our data, given the various sources of reporting used, including a lack of reporting from individuals using home testing to determine infection.

5. Conclusions

In conclusion, among a US national sample of STEMI patients presenting to the hospital during waves of the COVID-19 pandemic compared to those pre-pandemic, patients had a higher risk profile, delayed time to treatment despite presenting via EMS more often, similar proportions treated with reperfusion therapy and transfer rates for primary PCI, and higher in-hospital mortality only during one wave period, with adjusted mortality increased in the Midwest and South. The latter finding emphasizes the importance of addressing regional disparities in patient outcomes. Treatment delays during the pandemic underscore the need for targeted strategies to enhance timely STEMI management and inform future planning. Regionalization of STEMI care has remained an important systems approach to address gaps in care and suboptimal outcomes during the COVID-19 pandemic and allows us to prepare for the next pandemic or national disaster.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/covid5080114/s1>, Table S1: Characteristics of CAD registry hospitals; Table S2: CAD registry hospitals by CDC region; Table S3: STEMI patients of CAD registry by pre-pandemic periods; Table S4: (a) Multivariable analysis of in-hospital mortality among COVID waves for females, (b) Multivariable analysis of in-hospital mortality among COVID waves for males; Table S5: (a) Sensitivity Analysis: Multivariable analysis of In-hospital mortality among COVID waves for females, (b) Sensitivity Analysis: Multivariable analysis of in-hospital mortality among COVID waves for males; Table S6: (a) Multivariable analysis of in-hospital mortality among COVID waves for Midwest region, (b) Multivariable analysis of in-hospital mortality among COVID waves for Northeast region, (c) Multivariable analysis of in-hospital mortality among COVID waves for South region, (d) Multivariable analysis of in-hospital mortality among COVID waves for West region.

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Abbreviations

The following abbreviations are used in this manuscript:

COVID-19	Coronavirus disease of 2019
STEMI	ST-elevation myocardial infarction
PCI	Percutaneous coronary intervention
EMS	Emergency medical services
ACS	Acute coronary syndrome

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