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Original Article

Disparities by sex, race, and region in acute myocardial infarction-related outcomes during the early COVID-19 pandemic: the national inpatient sample analysis

Harshith Thyagaturu[1], Amro Taha[2], Shafaqat Ali[3], Nicholas Roma[4], Sanchit Duhan[5], Neel Patel[6], Yasar Sattar[1], Karthik Gonuguntla[1], Harigopal Sandhyavenu[2], Irisha Badu[7], Erin D Michos[8*], Sudarshan Balla[1*]

[1]Department of Cardiology, West Virginia University, Morgantown, WV, USA; [2]Department of Internal Medicine, Weiss Memorial Hospital, Chicago, IL, USA; [3]Department of Medicine, Louisiana State University, Shreveport, LA, USA; [4]Department of Internal Medicine, St Luke's University Hospital, Bethlehem, PA, USA; [5]Department of Internal Medicine, Sinai Hospital of Baltimore, Baltimore, MD, USA; [6]Department of Internal Medicine, New York Medical College/Landmark Medical Center, Woonsocket, RI, USA; [7]Department of Medicine, Onslow Memorial Hospital, Jacksonville, NC, USA; [8]Division of Cardiology, Johns Hopkins University School of Medicine, Baltimore, MD, USA. [*]Equal contributors and co-senior authors.

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Abstract: Background: Disparities in acute myocardial infarction (AMI)-related outcomes have been reported before the COVID-19 pandemic. We studied in-hospital outcomes of AMI across demographic groups in the United States during the early COVID-19 pandemic. Methods: The National Inpatient Sample (NIS) database was queried for 2020 to identify AMI-related hospitalizations based on appropriate ICD-10-CM codes categorized by sex, race, and hospital region categories. The primary outcome was in-hospital mortality in females, racial and ethnic minority groups, and Northeast hospital region compared with males, White patients, and Midwest hospital region, respectively. Multivariable regression analysis was used to calculate the adjusted odds ratio and mean difference. Results: A total of 820,893 AMI-related hospitalizations were identified during the study period. On adjusted analysis, during the early COVID-19 pandemic, females had lower odds of in-hospital mortality [aOR 0.89 (0.85-0.92); P < 0.01] and revascularization [aOR 0.68 (0.66-0.69); P < 0.01] than males. Racial and ethnic based analysis showed that Asian/Pacific Islander patients had higher odds of in-hospital mortality [aOR 1.13 (1.03-1.25); P < 0.01] than White patients. During the early COVID-19 pandemic, Northeast and Western region hospitals had higher odds of in-hospital mortality, lower odds of revascularization, longer length of stay, and higher total hospitalization costs than Midwest region hospitals. Conclusions: Our study disclosed disparities in AMI-related mortality and revascularization by sex, race and ethnic, and region during the early COVID-19 pandemic. Special attention should be given to at-risk populations. Whether these disparities continue in the post-vaccination era warrants further study.

Keywords: COVID-19, SARS-CoV-2, acute myocardial infarction, percutaneous coronary intervention

Introduction

The COVID-19 pandemic has resulted in more than 1,090,000 deaths in the United States as of January 2023. Data from the Centers for Disease Control and Prevention (CDC) suggest a differential impact of the pandemic on different racial and ethnic groups and age groups in the United States. A higher mortality rate has been observed in Black and Hispanic populations, and people aged 65-74 years have the highest mortality rate across all racial and ethnic groups [1]. A similar disparity has been seen in contemporary studies of acute myocardial infarction (AMI) outcomes, with a higher mortality rate observed in middle-aged adults, non-Hispanic Black adults, and residents of rural counties than in their counterparts [2]. Although there was a declining trend of AMI mortality rates between 1999 and 2019 across all sexes, racial and ethnic groups, and geographical regions in the United States [2], recent studies indicate a reversal in this trend, with an increased cardiovascular disease mortality rate

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in 2020 [3]. The exact reason behind this rise and the observed disparities is still unclear, although the pandemic likely played a substantial role. The explanation for the overall increase in AMI mortality rates is likely multifactorial. First, reduced access to healthcare, and delays in reperfusion during the lockdown have been reported [4]. Second, the pandemic lockdown was associated with increased rates of smoking (30% increase) and alcohol use (20% increase), which are known risk factors for cardiovascular disease [5]. The pervasive disparities among different racial and ethnic groups have been ascribed to social determinants of health in addition to differences in prevalence of cardiovascular risk factors. Further, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is associated with higher thrombogenicity, especially in African American patients, which may have predisposed this group to worse outcomes [6].

Data regarding sex, racial and regional disparities in outcomes of AMI during the COVID-19 pandemic are lacking. We performed a National Inpatient Sample (NIS) analysis to examine the impact of the early COVID-19 pandemic (January-December 2020) on AMI outcomes across demographic groups and geographic regions in the United States.

Methods

Data source

The NIS is a subset of the Healthcare Cost and Utilization Project (HCUP) databases. These databases are sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NIS database comprises nearly 95% of the US population and encompasses 20% of discharge patient data from 1,000 hospitals. The AHRQ undergoes annual quality assessments, which help confirm its internal validity. Additionally, NIS is a publicly available database with de-identified data; therefore, Institutional Review Board approval was not required for our study. Author HT had full access to all the data in this study and takes responsibility for its integrity and the data analysis.

Study cohort

Using the 2020 NIS database, a nationally weighted sample of all patients 18 years old or older hospitalized with AMI (both ST-segment elevation MI [STEMI] and non-ST-segment elevation MI [NSTEMI]) was identified in both primary and secondary diagnosis categories using the appropriate International Classification of Disease, Tenth Edition, Clinical Modification (ICD-10-CM) codes, as shown in Supplementary Table 1. We excluded the patients who were electively admitted or transferred from outside the State. The AMI cohort was stratified based on sex (male and female), racial or ethnic group (White, Black, Hispanic, and Asian/Pacific Islander), and hospital region (Northeast, West, South, and Midwest) categories. We extracted baseline demographics, primary payer, hospital characteristics (bed size, location, and teaching status), discharge location status, median household income, and comorbidities using variables available within the dataset. The baseline demographics including sex, race/ethnicity and regions are available within the database based on electronic health record coding. In addition, the NIS 2019 database was similarly analyzed to evaluate the baseline sex, race, and regional disparities in AMI outcomes immediately prior to the COVID-19 pandemic. Note that NIS is only currently released through 2020, so we could not examine outcomes in the post-COVID vaccination years of 2021 and 2022.

Outcomes

The primary outcome of our study was in-hospital mortality stratified by sex, race, and hospital region. Secondary outcomes were rates of revascularization (percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG]), length of stay, and total costs among AMI hospitalizations. Revascularization was identified using ICD10 PCS codes for PCI or CABG (see Supplementary Table 1).

Statistical analysis

All analyses were performed using Stata software package, release version 17.0 (StataCorp LLC, College Station, Texas, USA) [8]. In accordance with HCUP regulations, we conducted our analysis through appropriate stratifying, clustering, and weighting of samples. The discharge weights provided in NIS were applied for all analyses to provide the national estimates

for this study. We reported categorical variables as numbers with percentages and compared them using Pearson's Chi-square test. We reported continuous variables as weighted means with standard deviation (SD) (normal distribution) or median with interquartile ranges (IQR) for skewed distribution and compared them using independent *t*-tests. We calculated unadjusted odds ratios and mean differences for outcomes using logistic or linear regression. Multiple variables were included in the models based on the literature and significant associations found in the univariate analysis with a *p*-value < 0.2. For the adjusted analysis, we used two models (Model 1 and Model 2) to determine the impact of COVID-19 infection in the AMI cohorts on the study's primary outcome. Model-1 included all significant variables along with COVID-19 infection status in AMI patients, whereas Model-2 did not adjust for COVID-19 infection. Adjusted odds ratios (aOR) and adjusted mean differences (aMD) were calculated using multivariable logistic and linear regression analyses. All *P*-values were calculated based on 2-tailed tests, with 0.05 as a threshold for statistical significance.

Results

Sex disparities in baseline characteristics and outcomes of AMI

In 2020, a total of 820,893 AMI-related adult hospitalizations were identified, of which 508,104 (61.9%) were males and 312,789 (38.1%) were females (**Figure 1A**). Females with AMI were more likely to be older (mean age in years ± SD; 70.2 ± 13.4 vs. 66.2 ± 13.1; P < 0.01), Black (14.1% vs. 10.7%; P < 0.01), and beneficiaries of Medicare (69.3% vs. 17.8%; P < 0.01) compared with males. Chronic ischemic heart disease was more prevalent in males than in females (78.8% vs. 68.8%; P < 0.01), while the prevalence of COVID-19 infection in both groups was similar (3.9% vs. 3.9%; P = 0.97) (**Table 1**). Trends in AMI hospitalizations categorized by sex, race, and hospital regions are summarized in **Figure 1A-C**.

Females with AMI had higher unadjusted mortality than males. However, after adjusting for age and other comorbidities, females had lower odds of in-hospital mortality than males [9.9% vs. 8.8%; aOR 0.89 (0.85-0.92); P < 0.01]. In addition, compared with males hospitalized with AMI, females with AMI had lower odds of procedural interventions such as revascularization [37.1% vs. 51.1%; aOR 0.68 (0.66-0.69); P < 0.01] and coronary angiography [60.8% vs. 52.1%; aOR 0.93 (0.91-0.95); P < 0.01] along with lower total hospitalization costs (24,831 ± 33,926 vs. 28,513 ± 35,143) (**Table 2** and **Figure 2**). These findings remained significantly lower in females than in males in our Model-2 analysis (Supplementary Table 2).

Ethnic and racial subgroup analysis

White patients were predominant among AMI-related hospitalizations with a prevalence of 72%, followed by Black (11.9%), Hispanic (9.3%), and Asian/Pacific Islander (< 5%) patient subgroups (**Figure 1B**). Adult Black AMI patients were relatively younger, with more than half being < 64 years of age. Black, Hispanic, and Asian/Pacific Islander patients with AMI were more commonly uninsured or publicly insured (Medicare or Medicaid) and lived in lower-income communities than White patients (**Table 3**). White patients had the highest prevalence of chronic ischemic heart disease (76.8%) and smoking (47.1%). COVID-19 infection disproportionately affected members of racial and ethnic minority groups, with the highest prevalence occurring in Hispanic and Asian/Pacific Islander patients. Black patients had the highest mean Charlson Comorbidity Index score (3.9), with a higher prevalence of heart failure, prior stroke, chronic kidney disease, and obesity.

Black, Hispanic, and Asian/Pacific Islander racial and ethnic minority patients with AMI had higher unadjusted mortality in the hospital during the early COVID-19 pandemic (2020) than White patients. On Model-1 adjusted analysis, only Asian/Pacific Islander patients had statistically significant higher odds of in-hospital mortality [aOR 1.13 (1.03-1.25); P < 0.01] than White patients. However, in Model-2 analysis, which excluded COVID-19 infection, Black, Hispanic, and Asian/Pacific Islander patients with AMI had higher odds of mortality than White patients. In addition, these racial and ethnic groups also had lower odds of revascularization and coronary angiography, along with longer lengths of stay and higher total hospitalization costs, compared with White patients (**Table 4** and **Figure 3**).

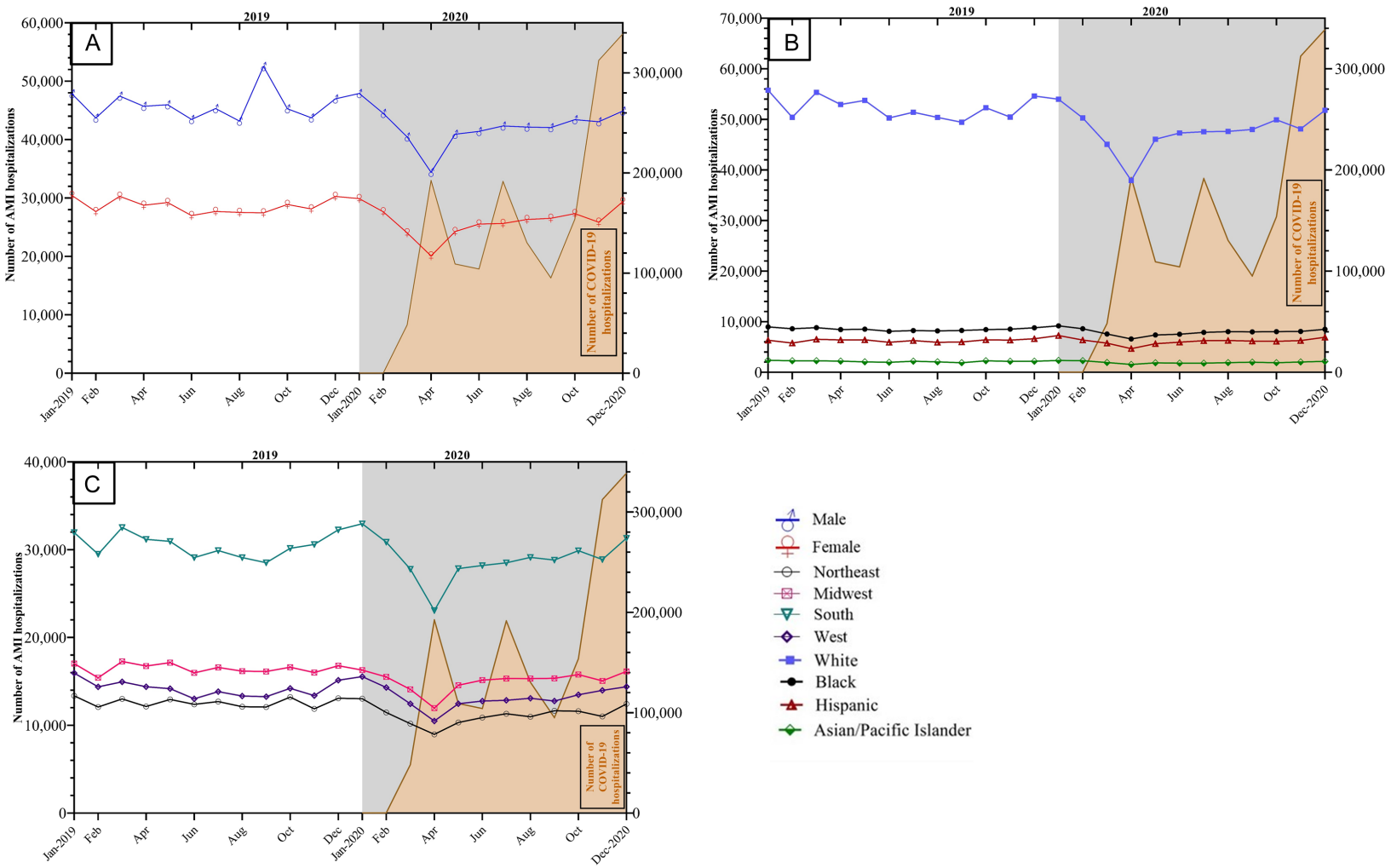

Figure 1. Trends of acute myocardial infarction hospitalizations categorized by sex, race and ethnicity, and hospital region.

Table 1. Baseline characteristics of acute myocardial infarction hospitalizations in 2020, stratified by sex

Variable	Male (n = 508,104) (61.9%)	Female (n = 312,789) (38.1%)	*p*-value
Age (years) (mean ± SD)	66.2 ± 13.1	70.2 ± 13.4	< 0.01
18-49	10.6	7.7	
50-64	33.7	24.4	
65-74	27.3	26.3	
> 75	28.3	41.4	
Race or Ethnicity (%)			< 0.01
White	72.5	71.2	
Black	10.7	14.1	
Hispanic	9.6	8.7	
Asian or Pacific Islander	< 5	< 5	
Other/Multiple Races	< 5	< 5	
Primary payer insurance (%)			
Medicare	56.3	69.3	
Medicaid	10.6	9.7	
Private	27.6	17.8	
Uninsured	5.4	3.2	
Hospital region (%)			< 0.01
Northeast	16.3	16.4	
Midwest	21.7	22.4	
South	42	42.8	
West	19.9	18.3	
Hospital teaching status (%)			< 0.01
Rural	7.4	9.1	
Urban non-teaching	18.9	19.1	
Urban teaching	73.6	71.8	
Median household income by ZIP code, percentile (%)			< 0.01
76th-100th	18.6	16.2	
51st-75th	22.7	21.5	
26th-50th	28.3	28.7	
0-25th	30.4	33.4	
Charlson Comorbidity Index score (%)			< 0.01
1	20	15.1	
2	22.4	21.3	
≥ 3	57.5	63.6	
Charlson Comorbidity Index score (mean ± SD)	3.4 ± 2.1	3.6 ± 2.1	< 0.01
Comorbidities* (%)			
Hypertension	79.1	80.2	< 0.01
Diabetes mellitus	42.1	43.7	< 0.01
Chronic ischemic heart disease	78.8	68.8	< 0.01
Obesity	21.4	23.5	< 0.01
Atrial fibrillation/flutter	22	21.9	0.88
COPD	17.3	21.3	< 0.01
Heart failure	40.3	44.3	< 0.01
Prior stroke	9.8	12.1	< 0.01
CKD	25.6	26.7	< 0.01

ESRD	5.6	6.1	< 0.01
Peripheral vascular disease	25.3	22.5	< 0.01
Anemia	26.4	31.3	< 0.01
Smoker	49.1	37.8	0.78
Alcohol dependence	5	1.6	< 0.01
COVID-19	3.9	3.9	0.97

COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; ESRD = end-stage renal disease. *ICD-10-CM codes were used to identify comorbidities, which are reported in Supplementary Table 1.

Table 2. Outcomes of acute myocardial infarction hospitalizations by sex

Outcomes	Male	Female	Unadjusted OR	*p*-value	Adjusted OR	*p*-value
AMI mortality (n) (%)	44,664 (8.8%)	31,154 (9.9%)	1.14 (1.10-1.18)	< 0.01	0.89 (0.85-0.92)	< 0.01
STEMI	13,584 (10.1%)	9,004 (14.4%)	1.49 (1.40-1.59)	< 0.01	1.08 (1.03-1.16)	0.03
NSTEMI	31,304 (8.3%)	22,284 (8.8%)	1.07 (1.02-1.11)	< 0.01	0.84 (0.80-0.88)	< 0.01
Revascularization (n) (%)	259,954 (51.1%)	115,809 (37.1%)	0.56 (0.54-0.57)	< 0.01	0.68 (0.66-0.69)	< 0.01
Coronary angiography (n) (%)	308,909 (60.8%)	163,109 (52.1%)	0.70 (0.68-0.71)	< 0.01	0.93 (0.91-0.95)	< 0.01
Length of stay (days ± SD)	5.4 ± 7.4	5.5 ± 7.1	0.10 (0.02-0.17)	< 0.01	-0.40	< 0.01
Total hospitalization costs (USD, $)	28,513 ± 35,143	24,831 ± 33,926	-3,682	< 0.01	-3,757	< 0.01

AMI = Acute myocardial infarction; STEMI = ST elevation myocardial infarction; NSTEMI = Non-ST elevation myocardial infarction. Odds ratio (or) mean difference for females compared to males. Variables used for adjusted analysis in Model-1 include age, race/ethnicity, hospital region, household income by ZIP code, Charlson comorbidity index score, hypertension, diabetes mellitus, chronic ischemic heart disease, COPD, obesity, atrial fibrillation/flutter, history of prior stroke, anemia, CKD/ESRD, smoking status, peripheral vascular disease, and COVID infection.

Regional disparities in baseline characteristics and outcomes of AMI

Hospitals in Southern states had the highest AMI-related hospitalizations in 2020, with more than one-thirds (42.3%) of total US AMI hospitalizations, followed by hospitals in the Midwest (21.9%), West (19.3%) and Northeast (16.4%) (**Figure 1C**). Southern and Western region hospitals in the United States shared the highest in-hospital mortality rates (10.3%) in 2020, followed by Northeast (9.7%) and Midwest (8.3%) region hospitals (**Table 5**). Additionally, in our adjusted Model-1 analysis, in the AMI patient population, Northeast hospitals had higher odds of mortality [aOR 1.11 (1.03-1.19); P < 0.01] and lower odds of revascularization [aOR 0.81 (0.74-0.88); P < 0.01] and coronary angiography [aOR 0.75 (0.68-0.83); P < 0.01], and a longer length of stay than Midwest hospitals (**Table 6** and **Figure 4**). Western hospitals had the highest total hospitalization costs (aMD 7,141 USD; P < 0.01) compared with Midwest hospitals.

Discussion

Our study using a large sample of inpatient hospitalizations in the United States highlights disparities in AMI care and outcomes during the early COVID-19 pandemic phase in 2020. First, we showed that racial and ethnic minority groups, including Black (African American), Hispanic, and Asian/Pacific Islander patients with AMI, had higher in-hospital mortality, lower receipt of invasive strategies i.e., coronary angiography and revascularization (PCI/CABG), and longer length of stay compared with White AMI patients. However, only the Asian/Pacific Islander group was found to have higher adjusted odds of mortality compared with White patients. Second, the adjusted odds of in-hospital mortality were lower for female patients than for male patients. Similarly, the adjusted odds of receiving an intervention, mean length of stay, and total hospitalization costs were lower for females throughout the study period. Third, Northeast and Western region hospitals had higher odds of in-hospital mortality, lower odds of revascularization, and higher hospitalization costs than those in the Midwest (**Figure 5**).

The COVID-19 pandemic has introduced significant challenges to healthcare systems worldwide, with potential implications for the management and outcomes of acute myocardial infarction (AMI) patients. Several studies have shed light on the multifaceted relationship between COVID-19 and AMI outcomes, high-

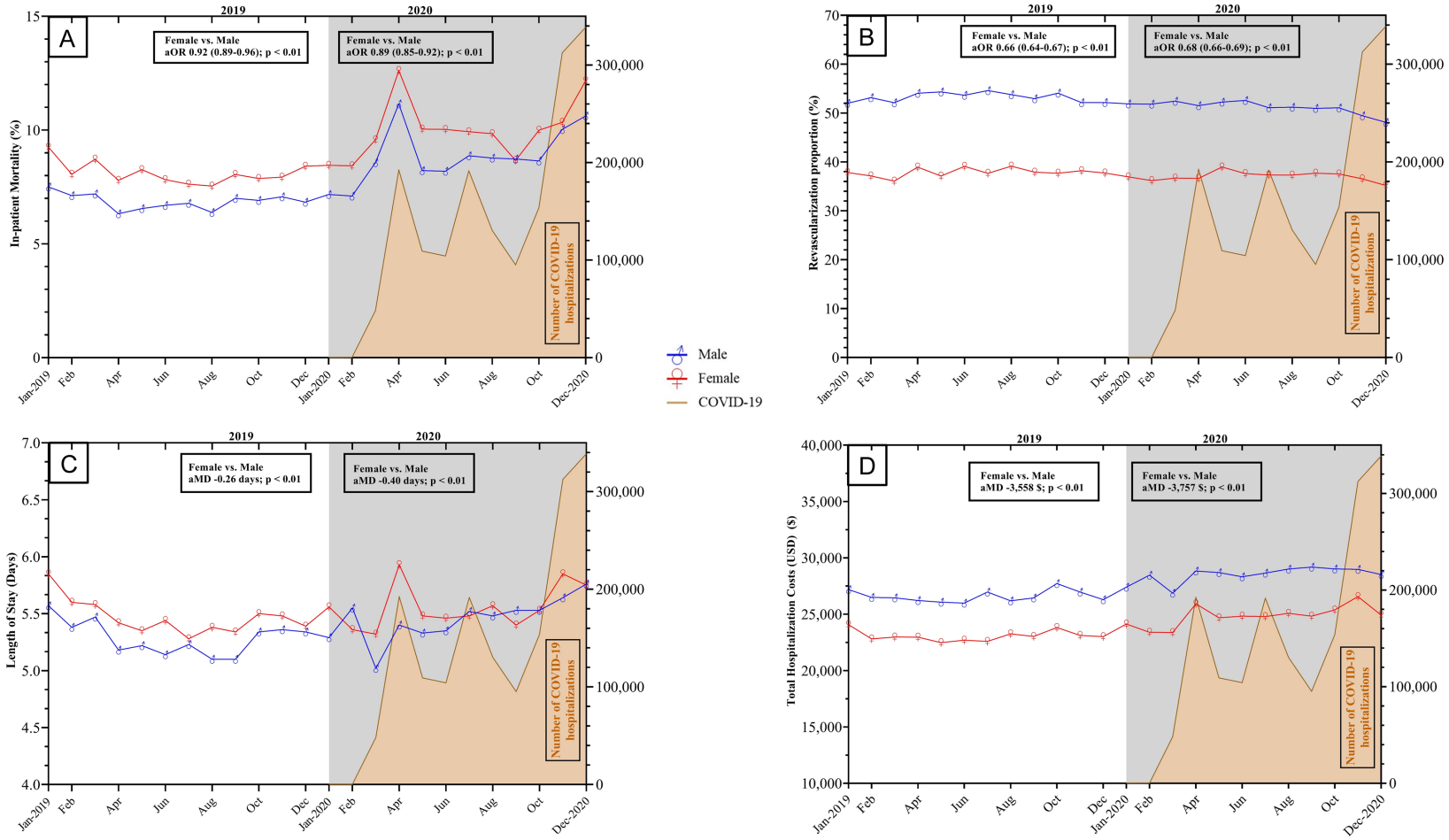

Figure 2. Sex differences in outcomes of acute myocardial infarction hospitalizations in 2020 and 2019.

Table 3. Baseline characteristics of acute myocardial infarction hospitalizations in 2020, stratified by race and ethnicity

Variable	White (n = 574,045) (72.1%)	Black (n = 95,560) (11.9%)	Hispanic (n = 73,824) (9.3%)	Asian/ Pacific Islander (n = 23,564) (2.9%)	*p*-value
Age (years) (mean ± SD)	69 ± 12.9	63.5 ± 13.9	65.2 ± 13.9	67.3 ± 14	< 0.01
18-49	7.6	16.1	13.4	11.4	
50-64	28.4	35.7	34.3	29.7	
65-74	27.6	25.3	24.5	25.2	
> 75	36.3	22.7	27.6	33.7	
Female (%)	37.7	44.6	36.1	34.5	
Primary payer insurance (%)					< 0.01
Medicare	34.9	54.6	51.7	51.8	
Medicaid	7.4	17.4	18.5	14.4	
Private	23.9	21.3	21.9	30.4	
Uninsured	3.7	6.6	7.7	3.4	
Hospital region (%)					< 0.01
Northeast	17.1	13.3	14.1	14.1	
Midwest	24.7	18.8	6.4	9.8	
South	41.6	57.8	41.6	17.5	
West	16.4	10.1	38	58.7	
Hospital teaching status (%)					< 0.01
Rural	9.6	5.5	1.8	1.6	
Urban non-teaching	19.5	15.3	20.4	20.7	
Urban teaching	70.9	79.1	77.7	77.6	
Median household income by ZIP code, percentile (%)					< 0.01
76th-100th	18.6	9.4	12.5	11.2	
51st-75th	23.5	14.6	21.4	20.1	
26th-50th	30.1	22.7	27.2	27.1	
0-25th	27.7	53.3	38.8	41.4	
Charlson Comorbidity Index score (%)					< 0.01
1	19.1	14.1	16.1	16	
2	22.4	18.6	22.4	20.4	
≥ 3	58.5	67.3	61.5	63.5	
Charlson Comorbidity Index score (mean ± SD)	3.4 ± 2.1	3.9 ± 2.2	3.7 ± 2.2	3.8 ± 2.2	< 0.01
Comorbidities* (%)					
Hypertension	78.6	84.6	81.1	80.5	< 0.01
Diabetes mellitus	39.3	48.2	56.6	54.2	< 0.01
Chronic ischemic heart disease	76.8	67.5	71.4	72.9	< 0.01
Obesity	22.3	24.3	23.2	11.1	< 0.01
Atrial fibrillation/flutter	23.9	15.9	17.5	20.2	< 0.01
COPD	20.9	16.8	10.8	8.9	< 0.01
Heart failure	40.8	47.3	43.2	43.5	< 0.01
Prior stroke	10.2	14.4	10.1	10.6	< 0.01
CKD	24.3	33.6	29.6	34.1	< 0.01
ESRD	3.7	11.9	11.4	12.5	< 0.01
Peripheral vascular disease	24.7	24.5	24.3	19.9	< 0.01
Anemia	26.2	34.6	33.2	37.1	< 0.01
Smoker	47.1	44.4	33.5	29.9	< 0.01
Alcohol dependence	3.6	4.7	3.5	1.4	< 0.01
COVID-19	2.9	5.7	8.5	5.4	< 0.01

COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; ESRD = end-stage renal disease. *ICD-10-CM codes were used to identify the comorbidities, which are reported in Supplementary Table 1.

Table 4. Outcomes of acute myocardial infarction hospitalizations by race and ethnicity

	White	Black	Hispanic	Black vs. White (aOR or MD)	Hispanic vs. White (aOR or MD)	Asian/Pacific Islander vs. White
AMI mortality (n) (%)	49,744 (8.6%)	9,199 (9.6%)	8,019 (10.8%)	0.98 (0.92-1.04); P = 0.63	1.03 (0.96-1.11); P = 0.32	1.13 (1.03-1.25); P < 0.01
STEMI	14,974 (10.7%)	2,475 (13.5%)	2,284 (13.5%)	1.17 (1.04-1.24); P = 0.01	1.09 (0.96-1.24); P = 0.18	1.21 (1.01-1.45); P = 0.03
NSTEMI	35,044 (8.1%)	6,744 (8.7%)	5,759 (10.1%)	0.95 (0.88-1.02); P = 0.17	1.01 (0.93-1.10); P = 0.69	1.13 (1.02-1.27); P = 0.04
Revascularization (n) (%)	274,479 (47.8%)	34,149 (35.7%)	30,425 (41.2%)	0.65 (0.62-0.68); P < 0.01	0.78 (0.73-0.83); P < 0.01	0.86 (0.79-0.93); P < 0.01
Coronary angiography (n) (%)	304,319 (59.3%)	48,619 (50.8%)	39,359 (53.3%)	0.77 (0.73-0.82); P < 0.01	0.84 (0.78-0.91); P < 0.01	0.80 (0.73-0.88); P < 0.01
Length of stay (days ± SD)	5.2 ± 6.5	6.3 ± 9.1	6.1 ± 8.3	0.29 (0.13-0.45); P < 0.01	0.24 (0.08-0.40); P < 0.01	0.39 (0.10-0.67); P < 0.01
Total hospitalization costs (USD, $)	25,991 ± 30,989	26,450 ± 41,133	30,721 ± 40,146	-1,319; P < 0.01	1,805; P < 0.01	6,772; P < 0.01

AMI = Acute myocardial infarction; STEMI = ST elevation myocardial infarction; NSTEMI = Non-ST elevation myocardial infarction. Odds ratio (or) mean difference for Black/Hispanic/Asian patients compared with White patients. Variables used for adjusted analysis in Model-1 include age, sex, hospital region, household income by Zip code, Charlson comorbidity index score, hypertension, diabetes mellitus, chronic ischemic heart disease, COPD, obesity, atrial fibrillation/flutter, history of prior stroke, anemia, CKD/ESRD, smoking status, peripheral vascular disease, and COVID infection.

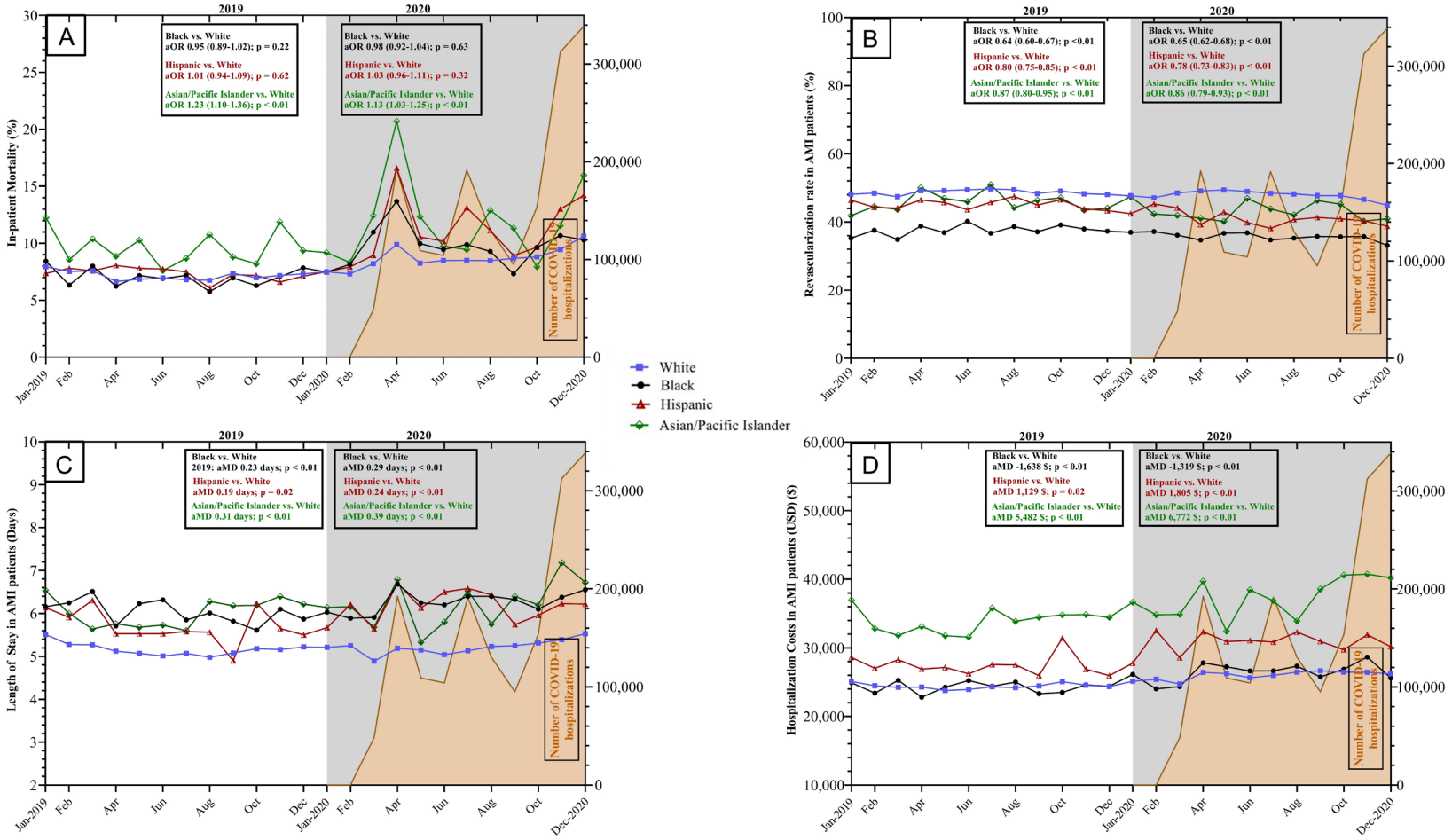

Figure 3. Racial and ethnic differences in outcomes of acute myocardial infarction hospitalizations in 2020 and 2019.

Table 5. Baseline characteristics of acute myocardial infarction hospitalizations in 2020 by hospital region

Variable	Northeast (n = 134,674) (16.4%)	Midwest (180,500) (21.9%)	South (347,250) (42.3%)	West (158,494) (19.3%)	*p*-value
Age (years) (mean ± SD)	68.7 ± 13.3	68.1 ± 13.4	67.1 ± 13.3	68 ± 13.4	< 0.01
18-49	8.2	9.2	10.3	9.1	
50-64	29.1	29.7	31.2	29.5	
65-74	26.7	27.1	26.8	27.3	
> 75	35.9	33.9	31.6	34.1	
Female (%)	38.2	38.8	38.5	36.2	< 0.01
Race or Ethnicity (%)					< 0.01
White	74.4	83	70.3	61.3	
Black	9.6	10.5	16.2	6.2	
Hispanic	7.8	< 5	9.1	18.2	
Asian or Pacific Islander	< 5	< 5	< 5	9.0	
Other/Multiple Races	5.4	< 5	< 5	< 5	
Primary payer insurance (%)					< 0.01
Medicare	61.3	64	60.5	60.1	
Medicaid	11.5	9.5	7.8	15.2	
Private	25.3	23.1	24.2	22.6	
Uninsured	< 5	3.4	7.3	< 5	
Hospital teaching status (%)					< 0.01
Rural	5.7	11.8	9.2	3.5	
Urban non-teaching	9.1	14.3	22.5	24.9	
Urban teaching	58.2	73.8	68.4	71.5	
Median household income by ZIP code, percentile (%)					< 0.01
76th-100th	31.3	13.1	10.7	27.1	
51st-75th	26.4	23.6	17.2	28.1	
26th-50th	24.5	34.5	28.2	25.3	
0-25th	17.7	28.8	43.8	19.5	
Charlson Comorbidity Index score (%)					< 0.01
1	19.5	17.7	17.8	18.1	
2	23	21	22.2	21.9	
≥ 3	57.4	61.2	59.9	60.1	
Charlson Comorbidity Index score (mean ± SD)	3.4 ± 2.1	3.6 ± 2.2	3.5 ± 2.1	3.5 ± 2.2	0.01
Comorbidities* (%)					
Hypertension	77.2	80.4	80.7	77.8	< 0.01
Diabetes mellitus	41.1	41.7	43.7	42.9	< 0.01
Chronic ischemic heart disease	73.4	78.1	75.2	72.7	< 0.01
Obesity	19.9	25.2	22.5	20.3	< 0.01
Atrial fibrillation/flutter	21.8	23.3	21.1	22.5	< 0.01
COPD	16.8	21.3	20	15.2	< 0.01
Heart failure	39.6	42.4	42.1	42.7	< 0.01
Prior stroke	9.1	11.7	10.8	10.5	< 0.01
CKD	24.3	27.8	25.1	27.6	< 0.01
ESRD	4.9	5	5.58	7.3	< 0.01
Peripheral vascular disease	22.5	26.1	24.3	23.6	< 0.01
Anemia	25.5	29.8	28.4	28.6	< 0.01
Smoker	43.5	51.2	44.3	39.7	< 0.01
Alcohol dependence	3.5	3.8	3.7	3.8	< 0.01
COVID-19	4.1	3.8	3.9	4.1	0.71

COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; ESRD = end-stage renal disease. Data with lesser values were reported as "< 5%" to ensure compliance with HCUP's requirements. *ICD-10-CM codes were used to identify the comorbidities, which are reported in Supplementary Table 1.

Table 6. Outcomes of acute myocardial infarction hospitalizations by geographic region

Outcomes	Northeast	Midwest	South	West	Northeast vs. Midwest	South vs. Midwest	West vs. Midwest (aOR or MD)
AMI mortality (n) (%)	13,184 (9.7%)	15,110 (8.3%)	31,100 (10.3%)	16,424 (10.3%)	1.12 (1.04-1.20); P < 0.01	1.04 (0.98-1.10); P = 0.19	1.13 (1.05-1.21); P < 0.01
STEMI	3,889 (11.8%)	4,525 (10.3%)	9,205 (11.4%)	4,969 (12.7%)	1.08 (0.96-1.22); P = 0.16	1.15 (1.04-1.27); P < 0.01	1.19 (1.06-1.34); P < 0.01
NSTEMI	9,329 (9.1%)	10,655 (7.8%)	22,090 (8.2%)	11,514 (9.6%)	1.14 (1.05-1.24); P < 0.01	1.02 (0.95-1.09); P = 0.52	1.12 (1.03-1.21); P < 0.01
Revascularization (n) (%)	59,584 (44.2%)	88,205 (48.8%)	157,340 (45.3%)	70,634 (44.5%)	0.81 (0.74-0.88); P < 0.01	0.86 (0.80-0.92); P < 0.01	0.88 (0.82-0.95); P < 0.01
Coronary angiography (n) (%)	75,159 (55.8%)	111,295 (61.6%)	196,300 (56.5%)	89,269 (56.3%)	0.75 (0.68-0.83); P < 0.01	0.77 (0.71-0.83); P < 0.01	0.84 (0.77-0.91); P < 0.01
Length of stay (days ± SD)	5.8 ± 8.1	5.2 ± 6.1	5.5 ± 7.1	5.4 ± 7.9	0.75; P < 0.01	0.23; P < 0.01	-0.07; P = 0.42
Total hospitalization costs (USD, $)	29,045 ± 38,113	25,809 ± 28,489	23,851 ± 23,851	34,173 ± 34,173	3,040; P < 0.01	-2,085; P < 0.01	7,141; P < 0.01

AMI = Acute myocardial infarction; STEMI = ST elevation myocardial infarction; NSTEMI = Non-ST elevation myocardial infarction. Odds ratio (or) mean difference for Northeast/South/West hospital regions compared with Midwest. Variables used for adjusted analysis in Model-1 included age, sex, race/ethnicity, household income by Zip code, Charlson comorbidity index score, hypertension, diabetes, chronic ischemic heart disease, COPD, obesity, atrial fibrillation/flutter, history of prior stroke, anemia, CKD/ESRD, smoking status, peripheral vascular disease, and COVID infection.

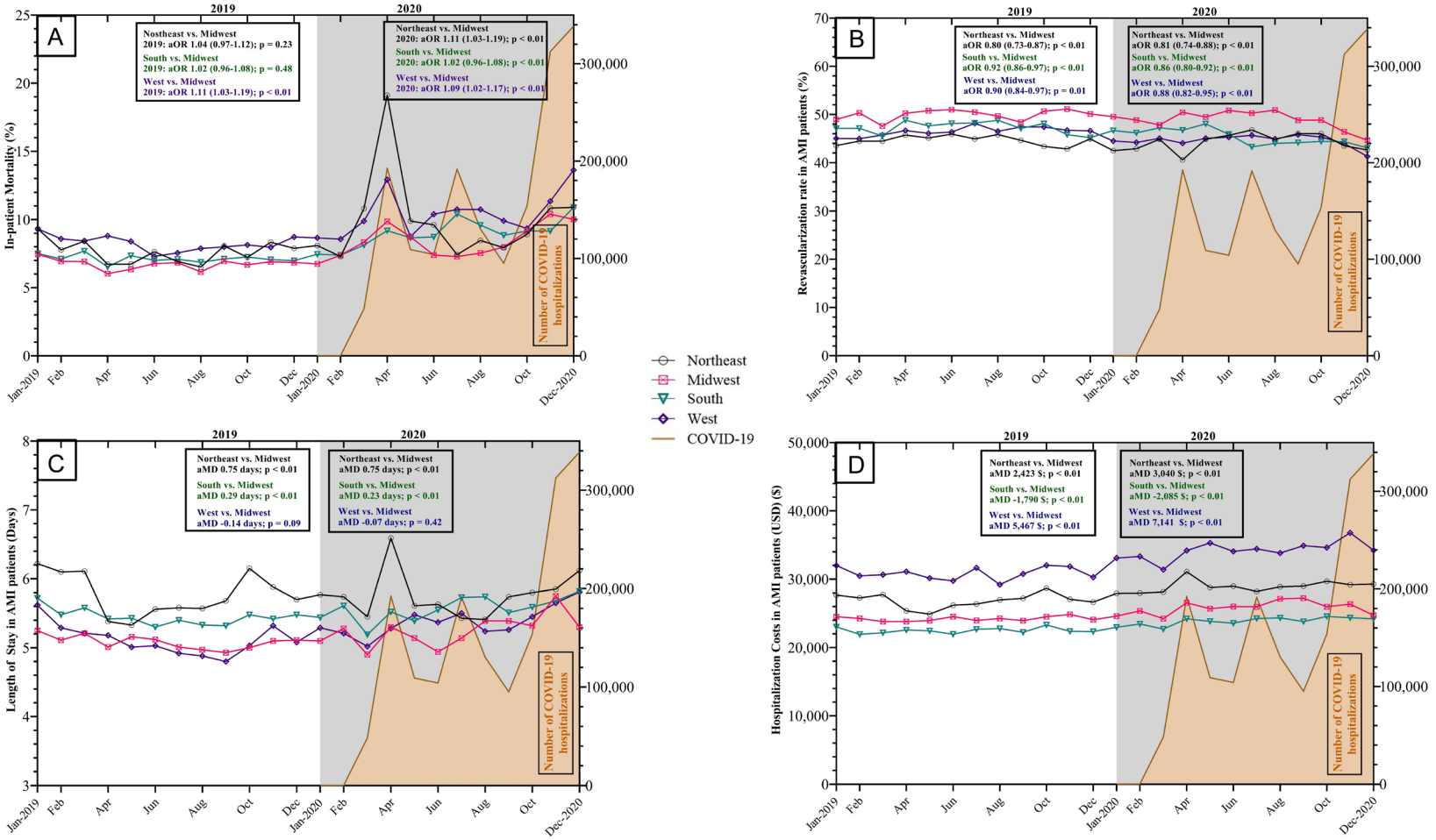

Figure 4. Regional differences in outcomes of acute myocardial infarction hospitalizations in 2020 and 2019.

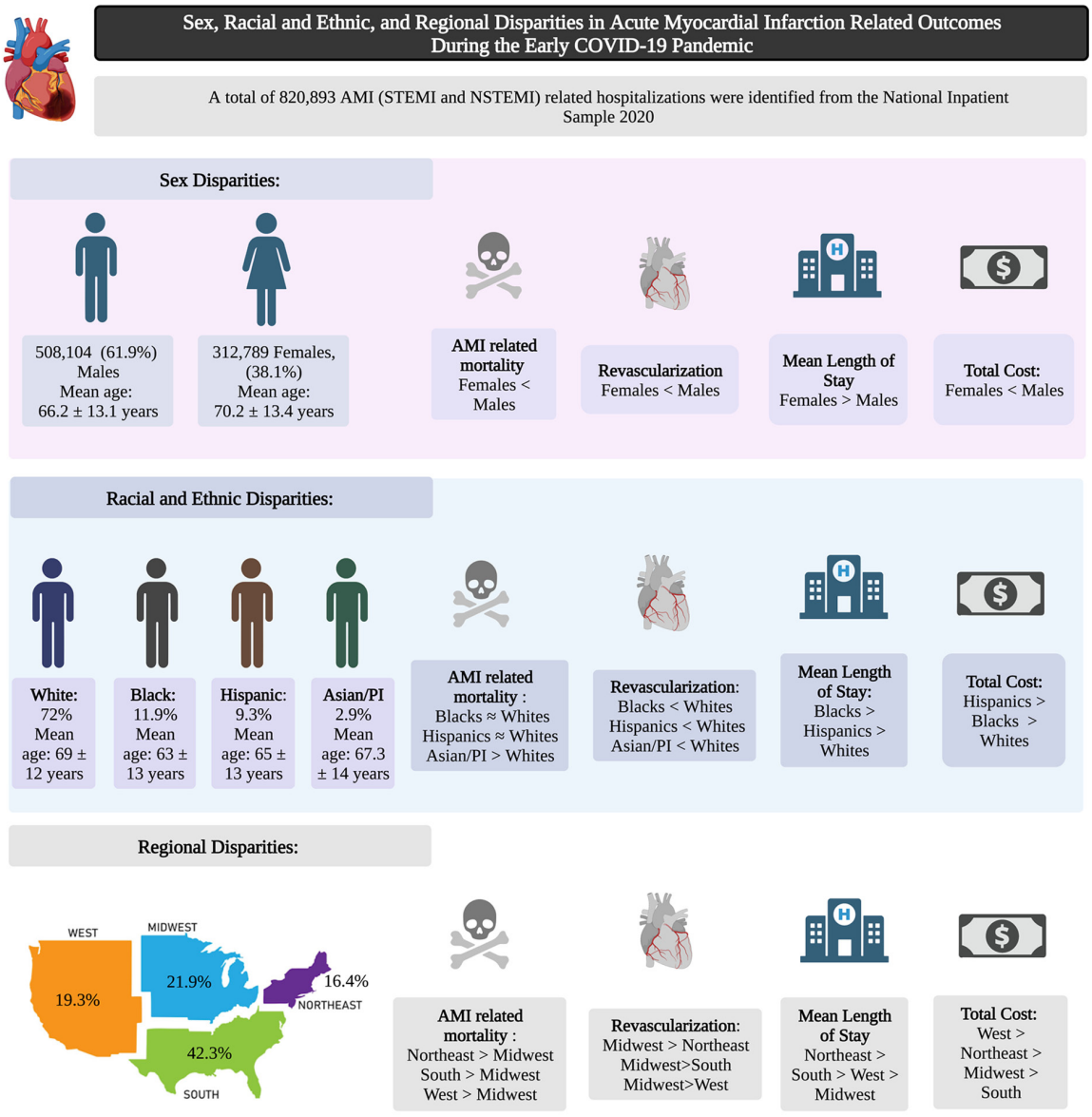

Figure 5. Sex, racial and ethnic, and regional disparities in acute myocardial infarction-related outcomes during the early COVID-19 pandemic.

lighting both direct and indirect effects. One notable finding is the observed decrease in hospital admissions for AMI during the pandemic. A study by Garcia et al. reported a 38% decline in STEMI activations during the peak of the pandemic, compared to the same period in the previous year [7]. This decline may be attributed to patient reluctance to seek medical care amid fears of contracting COVID-19 in healthcare settings [8]. The delay in seeking timely medical attention has significant implications for AMI outcomes. A systematic review by Mafham et al. found that delayed presentation to hospitals during the pandemic was associated with higher mortality rates among AMI patients [9]. Delays in reperfusion therapy, such as primary PCI, can lead to increased myocardial damage and worse clinical outcomes [10]. SARS-CoV-2 infection has been associated with myocardial injury, myocarditis, and thrombotic events, all of which can exacerbate AMI severity [11]. Additionally, the systemic inflammatory response induced by COVID-19 may destabilize atherosclerotic plaques, increasing the risk of plaque rupture and subsequent AMI [12].

COVID-19 adversely impacted the care of patients with AMI both directly and indirectly. For example, STEMI patients with COVID-19 infection had significantly higher in-hospital mortality than those without COVID-19 [8]. Moreover, there were excess deaths due to non-COVID causes, such as heart disease, during the COVID-19 pandemic [13, 14]. To the best of our knowledge, this is the largest study assessing the sex, ethnic and racial, and regional disparities of in-hospital mortality among AMI patients during the early COVID-19 pandemic in the United States. Overall, unadjusted in-hospital AMI mortality remained significantly higher for females than for males throughout the study period (9.9% vs. 8.8%). However, the adjusted analysis showed that females in the overall AMI group and NSTEMI group had lower odds of in-hospital mortality than males, except for the STEMI group, where mortality was higher than in males. The higher unadjusted mortality in females is likely driven by older age (41% of females were > 75 years old) and higher comorbidity burden. In addition, the proportion of revascularization in females presenting with AMI was substantially lower than in males (37% vs. 51.1%; $P < 0.01$). These sex-based differences existed in the pre-pandemic era (2019); however, comparing the respective aOR between 2019 and 2020 suggests that the degree of these differences was exacerbated in 2020, likely driven by the COVID-19 pandemic. Prior studies have reported that women are less likely than men to receive evidence-based medical care and have shown higher mortality rates after AMI, especially when requiring urgent revascularization [15]. Osman et al. reported that AMI cardiogenic shock-related mortality was higher in females (age 45-84 years) [16]. Our study showed that the odds of receiving intervention for females presenting with AMI was 32% less than in males. The finding of lower adjusted in-hospital mortality among females compared to males aligns with some previous studies that have reported similar trends [17]. This may reflect differences in baseline characteristics, response to treatment, or other factors that warrant further investigation. Using evidence-based treatments and avoiding delays in reperfusion among women may represent potential opportunities for mitigating these sex-based disparities in AMI-related outcomes.

Race is entirely a social construct rather than biological, and, as such, studying differences in outcomes by race or ethnicity is important to shed light on disparities due to bias, systemic constructs, or unequal access to healthcare. Several studies have reported that racial and ethnic minority groups showed concerning trends for morbidity and mortality during the COVID-19 pandemic in the United States [18-22]. We also noticed discouraging trends of higher unadjusted AMI-related mortality among Black, Hispanic, and Asian/Pacific Islander patients compared with the pre-COVID-19 phase. However, our adjusted analysis showed that Black and Hispanic AMI patients had similar odds of in-hospital mortality compared with White patients. This is consistent with studies that have shown improvements in the quality of AMI care over time and a reduction in disparities across racial and ethnic groups [23]. Interestingly, Black patients admitted for STEMI and Asian/Pacific Islander patients (admitted for both STEMI/NSTEMI) had higher adjusted odds of AMI-related hospital mortality than White patients. The exact etiology of these disparities is unknown but appears to be multifactorial. First, although Asian and Pacific Islander patients are considered among historically understudied US populations [24], the limited literature that is available indicates that this group has a higher burden of cardiovascular-related risk factors at baseline than other racial and ethnic groups [25]. Second, differences may exist in the quality of AMI care among racial and ethnic minority groups during hospitalization, which can impact outcomes. Indeed, the proportion of patients who received invasive interventions for AMI was lower for Black, Hispanic, and Asian/Pacific Islander AMI patients than for White patients. The available data in the literature have shown that racial and ethnic minority individuals are at a significant disadvantage in receiving guideline-mediated care and are more likely to experience delays in treating and managing AMI, a fact well known even before the COVID-19 pandemic [26-30]. Furthermore, Rashid et al. reported substantial delays in the receipt of reperfusion therapy for STEMI and NSTEMI among racial and ethnic minority groups in the United Kingdom during the pandemic [31]. Social determinants of health such as low socioeconomic status, lower education level, a lack of awareness and early recognition of AMI-related

symptoms, and lack of English language proficiency are known to negatively impact cardiovascular outcomes. In our study, minority racial and ethnic groups with AMI lived predominantly in low-income neighborhoods. The pandemic phase likely exacerbated economic disparities, with greater losses in earnings suffered by minority families and historically higher unemployment rates overall [32]. Factors unique to the pandemic period, such as delays in seeking early medical attention due to fear of contracting COVID-19 [21, 33-37] delays in access to care during the lockdown phase, delays in EMS response, and delays after a patient's arrival to the emergency room also likely affected AMI care. Nonetheless, acknowledging the direct impact of the COVID-19 pandemic on health systems nationwide, there was a disproportionate burden of AMI mortality in racial and ethnic minority groups. There is a need for a multilevel approach involving health systems, providers, patients, and policymakers to eradicate inequities and improve access to healthcare for minority racial and ethnic individuals. It is noteworthy that in our model that did not adjust for COVID-19 infection, Black and Hispanic patients had higher odds of mortality than White patients. This finding is likely driven by higher rates of COVID-19 infection in racial and ethnic minority individuals and the direct impact of COVID-19 infection on those with AMI, as shown in prior studies [13]. Black, Hispanic, and Asian/Pacific Islander patients have been consistently shown to experience worse outcomes and receive less aggressive treatment for AMI compared to White patients [38]. These disparities are multifactorial and are influenced by factors such as socioeconomic status, access to healthcare, cultural beliefs, and systemic racism within healthcare systems [39]. The disproportionate impact of COVID-19 on minority populations further exacerbates these disparities, as evidenced by the higher prevalence of COVID-19 infection and its association with worse outcomes among minority groups [40].

In addition, although the COVID-19 pandemic created nationwide disruptions, our study showed that the AMI-related magnitude of the pandemic was not distributed equally among regions. For example, the Midwest showed the lowest AMI-related mortality, the highest rate of coronary angiography and revascularization (PCI + CABG) use, and the lowest average hospital length of stay compared with the Northeast and West. On the other hand, the Northeast showed the lowest rate of revascularization and coronary angiography and the highest hospital length of stay. These differences could be because the Northeast was affected earliest by the pandemic. However, this is unlikely the sole determinant, as COVID-19 had spread rapidly to the entire country by the summer of 2020, with case fatality numbers peaked through fall and winter. Although healthcare systems across the United States faced an unprecedented scarcity of resources in the early pandemic period, our study indicates that an unequal allocation of resources and lack of adequate coping strategies may have played a significant role in these disparities. At least two large international studies have reported similar regional differences, pointing toward the volatile capacity of healthcare systems, and highlighting the importance of ensuring allocation of financial resources [41]. Our findings suggest a need for further research into this matter and highlight the importance of standardized regional and national strategies to mitigate healthcare inequities in the future. Previous studies have documented differences in AMI care and outcomes between regions, with factors such as hospital volume, availability of resources, and regional healthcare policies influencing these disparities [42]. The higher mortality rates and lower rates of revascularization and coronary angiography observed in certain regions may reflect disparities in access to timely and appropriate care, highlighting the need for targeted interventions to address regional variations in healthcare delivery.

Our study has certain limitations. First, as this is a retrospective observational study, the possibility of residual measured and unmeasured confounding cannot be ruled out. Second, because NIS is an administrative database, the accuracy and consistency of data depend heavily on the coders. The dataset is subject to errors in coding of diagnosis and procedure codes. Ostrominski et al. reported nonadherence to standard methodological practices and significant variation (up to 8.8%) in code selection in various studies using the NIS [43]. However, we adhered to the essential elements and methodological standards recommended by the HCUP [44]. Third, the NIS database does not allow differentiation between AMI present-

ing on admission or developing during hospitalization. Fourth, the dataset has no blood chemistry, electrocardiographic, echocardiographic, or coronary angiographic details. Last, it is also difficult to assess why revascularization was not undertaken in certain patients and circumstances as well as the reasons for opting for PCI vs. CABG. Despite these limitations, our study is one of the largest investigation providing insights into the sex, racial and ethnic disparities in the care of hospitalized AMI patients during the early COVID-19 pandemic.

Conclusion

Our study disclosed ethnic and racial, regional, and sex-based disparities in AMI-related mortality and use of invasive strategies during the early COVID-19 pandemic period. There was a high burden of in-hospital mortality due to AMI in minority racial and ethnic groups and females. Future pandemic preparedness strategies should address at-risk groups, and geographically overburdened healthcare systems to provide evidence-based, timely, and equitable AMI care that mitigates disparities.

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Disclosure of conflict of interest

Dr. Michos has served as a consultant for Amgen, Amarin, AstraZeneca, Bayer, Boehringer Ingelheim, Edwards Life Science, Esperion, Novartis, Novo Nordisk, and Pfizer.

Address correspondence to: Dr. Harshith Thyagaturu, Department of Cardiology, Heart and Vascular Institute, West Virginia University, Morgantown, WV, USA. Tel: 832-670-2276; E-mail: harshith.thyagaturu@hsc.wvu.edu

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Supplementary Table 1. ICD 10 codes for cohort identification and stratification with major baseline comorbidities

Variable	ICD-10 CM Codes
COVID 19	U00, U071, U49, U50, U85, J1282
ST-elevation myocardial infarction	I2.10x, I21.1x, I21.2x, I21.3
Non-ST elevation myocardial infarction	I21.4
Hypertension	I10, I11, I12, I13, I14, I15, I16
Diabetes mellitus	E08, E09, E10, E11, E13
History of CVA	I69.3, Z86.73
Atrial fibrillation/flutter	I48
Peripheral vascular disease	E08.5, E09.5, E10.5, E11.5, E13.5, I73, T82.856, Z98.62, Z95.820, I25.2, I25.83
Obstructive sleep apnea	G47.33
Coronary artery disease	I20, I22, I23, I24, I25
Chronic obstructive pulmonary disease	J41, J42, J43, J44
Obesity	E66, Z683, Z684
Chronic kidney disease ≥ stage 3	N183, N184, N185, E082, E132, I12, I13
End-stage renal disease	N186, Z992, Z4931, Z4901
Anemia	D50, D51, D52, D53, D55, D56, D57, D58, D59, D60, D61, D62, D63, D64, D46.0, D46.1, D46.2, D46.4, 099.0
Smoker	F17, Z87.891
Coronary angiography	B20.0, B201, B202, B203, B205, B206, B207, B208, B20F, B210, B211, B212, B213, B215, B216, B217, B218, B21F
Percutaneous coronary intervention	02703xx, 02713xx, 02723x, 02733xx, 02C03xx, 02C13x, 02C23x, 02C33x

Supplementary Table 2. Model 2 analysis (Did not adjust for COVID-19 infection) - Summary of sex, racial and ethnic, and racial disparities in mortality of AMI patients

	Male vs. Female	Black vs. White	Hispanic vs. White	Asian/Pacific Islander vs. White	Northeast vs. Midwest	South vs. Midwest	West vs. Midwest
AMI mortality (n) (%)	0.85 (0.82-0.89); P < 0.01	1.07 (1.01-1.14); P = 0.01	1.23 (1.14-1.31); P < 0.01	1.23 (1.11-1.35); P < 0.01	1.11 (1.03-1.19); P < 0.01	1.02 (0.96-1.08); P = 0.49	1.09 (1.02-1.17); P < 0.01
STEMI	1.05 (0.98-1.13); P = 0.15	1.26 (1.11-1.42); P < 0.01	1.25 (1.11-1.42); P < 0.01	1.26 (1.06-1.51); P < 0.01	1.07 (0.95-1.21); P = 0.21	1.12 (1.01-1.24); P = 0.02	1.17 (1.04-1.31); P < 0.01
NSTEMI	0.81 (0.77-0.84); P < 0.01	1.05 (0.97-1.13); P = 0.16	1.22 (0.13-1.32); P < 0.01	1.23 (1.09-1.39); P < 0.01	1.12 (1.03-1.22); P < 0.01	1.00 (0.93-1.07); P = 0.92	1.07 (0.99-1.17); P = 0.06

Variables used for adjusted analysis of Model 2 included age, sex (except for sex disparities analysis), hospital region (except for regional disparities analysis), household income by Zip code, Charlson comorbidity index score, hypertension, diabetes mellitus, chronic ischemic heart disease, COPD, obesity, atrial fibrillation/flutter, history of prior stroke, anemia, CKD/ESRD, smoking status, and peripheral vascular disease - did not adjust for COVID-19 infection.