

Original Research



# Trends and Outcomes of Type 2 Myocardial Infarction During the COVID-19 Pandemic in the United States

Harshith Thyagaturu , MD<sup>1</sup>, Nicholas Roma , MD<sup>2</sup>, Aakash Angirekula , BS<sup>3</sup>, Sittinun Thangjui , MD<sup>4</sup>, Alex Bolton , MD<sup>5</sup>, Karthik Gonuguntla , MD<sup>1</sup>, Yasar Sattar , MD<sup>1</sup>, Muchi Ditah Chobufo , MD<sup>1</sup>, Abhiram Challa , MD<sup>6</sup>, Neel Patel , MD<sup>7</sup>, Gayatri Bondi , MD<sup>8</sup>, and Sameer Raina , MD<sup>9</sup>

<sup>1</sup>Department of Cardiology, West Virginia University School of Medicine, Morgantown, WV, USA

<sup>2</sup>Department of Internal Medicine, St. Luke's University Health Network, Bethlehem, PA, USA

<sup>3</sup>University of Texas at Austin, Austin, TX, USA

<sup>4</sup>Department of Internal Medicine, Bassett Healthcare Network, Cooperstown, NY, USA

<sup>5</sup>University of Iowa College of Public Health, Iowa City, IA, USA

<sup>6</sup>Department of Medicine, University of Kansas School of Medicine, Wichita, KS, USA

<sup>7</sup>Department of Internal Medicine, New York Medical College/Landmark Medical Center, Woonsocket, RI, USA

<sup>8</sup>Department of Internal Medicine, Bassett Medical Center, Cooperstown, NY, USA

<sup>9</sup>Department of Cardiology, Stanford University School of Medicine, CA, USA



**Received:** Mar 13, 2023

**Revised:** Jun 22, 2023

**Accepted:** Jul 18, 2023

**Published online:** Sep 5, 2023

**Correspondence to**

**Nicholas Roma, MD**

Department of Internal Medicine, St. Luke's University Health Network, 801 Ostrum St. Bethlehem, PA 18015, USA.

Email: nroma127@gmail.com

Copyright © 2023. The Korean Society of Cardiology

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0>) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

**ORCID iDs**

Harshith Thyagaturu

<https://orcid.org/0000-0002-0457-5851>

Nicholas Roma

<https://orcid.org/0000-0002-7321-0100>

Aakash Angirekula

<https://orcid.org/0009-0004-0791-3336>

Sittinun Thangjui

<https://orcid.org/0000-0002-5846-4620>

Alex Bolton

<https://orcid.org/0000-0001-7965-1858>

## AUTHOR'S SUMMARY

This study describes the trends in type 2 myocardial infarctions (T2MIs) during the coronavirus disease 2019 (COVID-19) pandemic in the United States using the National Inpatient Sample (NIS) database. This correlation between COVID-19 and T2MI has been rarely studied and more so no concrete trends have been discovered until now. The trends found in this study include increasing trend of T2MI hospitalizations corresponded to the rise in COVID-19 hospitalizations with an increase in-hospital mortality and total cost of hospitalizations.

## ABSTRACT

**Background and Objectives:** There is limited data on the impact of type 2 myocardial infarction (T2MI) during the coronavirus disease 2019 (COVID-19) pandemic.

**Methods:** The National Inpatient Sample (NIS) database from January 2019 to December 2020 was queried to identify T2MI hospitalizations based on the appropriate International Classification of Disease, Tenth Revision-Clinical Modification codes. Monthly trends of COVID-19 and T2MI hospitalizations were evaluated using Joinpoint regression analysis. In addition, the multivariate logistic and linear regression analysis was used to compare in-hospital mortality, coronary angiography use, and resource utilization between 2019 and 2020.

**Results:** A total of 743,535 patients hospitalized with a diagnosis of T2MI were identified in the years 2019 (n=331,180) and 2020 (n=412,355). There was an increasing trend in T2MI hospitalizations throughout the study period corresponding to the increase in COVID-19 hospitalizations in 2020. The adjusted odds of in-hospital mortality associated with T2MI hospitalizations were significantly higher in 2020 compared with 2019 (11.1% vs. 8.1%: adjusted odds ratio, 1.19 [1.13–1.26]; p<0.01). In addition, T2MI hospitalizations were associated with lower odds of coronary angiography and higher total hospitalization charges,

Karthik Gonuguntla 


<https://orcid.org/0000-0002-5607-7993>

Yasar Sattar 

<https://orcid.org/0000-0002-1304-5748>

Muchi Ditah Chobufo 


<https://orcid.org/0000-0002-4490-5480>

Abhiram Challa 

<https://orcid.org/0000-0001-5686-8819>

Neel Patel 

<https://orcid.org/0009-0009-0122-1028>

Gayatri Bondi 

<https://orcid.org/0009-0002-6570-3535>

Sameer Raina 

<https://orcid.org/0000-0002-2998-8812>

#### Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

#### Conflict of Interest

The authors have no financial conflicts of interest.

#### Data Sharing Statement

The data generated in this study is available from the corresponding author upon reasonable request.

#### Author Contributions

Conceptualization: Thyagaturu H, Thangjui S, Bondi G; Data curation: Thyagaturu H, Thangjui S; Formal analysis: Thangjui S, Roma N; Investigation: Bolton A; Visualization: Bolton A; Writing - original draft: Thyagaturu H, Roma N, Gonuguntla K, Sattar Y, Ditah Chobufo M, Challa A, Raina S; Writing - review & editing: Roma N, Angirekula A, Bolton A, Gonuguntla K, Sattar Y, Ditah Chobufo M, Challa A, Patel N, Bondi G, Raina S.

with no difference in the length of stay in 2020 compared with 2019.

**Conclusions:** We found a significant increase in T2MI hospitalizations with higher in-hospital mortality, total hospitalization costs, and lower coronary angiography use during the early COVID-19 pandemic corresponding to the trends in the rise of COVID-19 hospitalizations. Further research into the factors associated with increased mortality can increase our preparedness for future pandemics.

**Keywords:** COVID-19; SARS-CoV-2; Myocardial infarction; Myocardial ischemia

## INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has overwhelmed the United States healthcare system, the effects of which will reverberate for years.<sup>1)</sup> While most cases presented as respiratory failure, cardiovascular complications were frequently encountered and contributed to the mortality and morbidity burden.<sup>2)</sup> Approximately 1 in 4 hospitalized COVID-19 patients had preexisting cardiovascular disease, and nearly half had a myocardial injury resulting in cardiac arrhythmias and dysfunction.<sup>3,4)</sup> Many of these hospitalized patients also had type 2 myocardial infarction (T2MI) as defined by the fourth universal definition of myocardial infarction (MI).<sup>5)</sup> Moreover, the cardiac biomarker elevation was frequently observed among patients with underlying cardiovascular disease, with levels shown to be directly predictive of worse outcomes.<sup>6,7)</sup> It is also well known that T2MI is associated with worse short and long-term outcomes.<sup>8-10)</sup> In addition, the association of COVID-19 with T2MI is known.<sup>11)</sup> However, the impact of the COVID-19 pandemic on the outcome of T2MI is unknown. In this context, we aimed to evaluate the burden of the first year of the COVID-19 pandemic on the incidence trends and in-hospital outcomes of T2MI in a large cohort using the National Inpatient Sample (NIS) database.

## METHODS

### Ethical statement

All data within the NIS is publicly available and de-identified. Therefore, Institutional Review Board approval was not required for our study.

### Data source

We conducted a retrospective cohort study using the NIS 2019 and 2020 databases. The NIS is the largest all-payer publicly available database developed through a Federal-State-Industry partnership for the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NIS database contains discharge weights designed to produce US national estimates of inpatient utilization, access, cost, quality, and outcomes. The database includes over 100 clinical and nonclinical data elements equating to up to 8 million unweighted hospital discharges, representing roughly 20% of hospital admissions across different hospital types and geographic regions. The database has been utilized to report the trends, inpatient outcomes, and associated procedural utilization of various diseases.

### Study population

Patients aged 18 years or older hospitalized with a diagnosis of T2MI between January 1st, 2019, to December 31st, 2020, were identified using the appropriate International Classification of

Disease, Tenth Revision (ICD-10)-Clinical Modification (CM) code (see **Supplementary Table 1** for all the ICD-10-CM and ICD-10-Procedure Coding System codes used in the study) in the primary and secondary diagnosis sections. We excluded patients with concurrent diagnoses of ST-elevation myocardial infarction (STEMI). We stratified patients according to the calendar year of hospitalization. We extracted patient-level baseline characteristics, including age, demographics, primary payer, hospital characteristics, comorbidities, and the Charlson comorbidity index (CCI) (surrogate index for comorbidity burden).

### Outcomes

The primary outcome was to assess the in-hospital mortality difference between 2020 and 2019. Secondary outcomes included identifying the common cause of death in patients with T2MI, differences in coronary angiography, length of stay, and total hospitalization charges between patients with T2MI in 2020 compared with 2019.

### Statistical analyses

The NIS database was downloaded from the HCUP central distributor after completing mandatory HCUP data use agreement training. We adhered to the methodological standard of HCUP and followed the checklist provided by the HCUP. Categorical variables were presented as frequency (%) and were compared using the chi-square test. Continuous variables were presented in weighted mean  $\pm$  standard deviation (SD) and were compared using the student's t-test if normally distributed. The median and interquartile range were used for non-normal distribution data and compared using the Mann-Whitney U test. Joinpoint regression analysis evaluated the monthly trends and surges of COVID-19 hospitalizations in 2020. To produce national estimates, Stata facilitates analysis by considering NIS's complex sampling design, including stratification, clustering, and weighting. For 2020 versus 2019 outcomes comparison, univariate logistic and linear regression were used to calculate the unadjusted odds ratio (OR) and mean difference, respectively. Subsequently, multivariate logistic and linear regression analyses were used to adjust for potential confounders and produce adjusted odds ratios (aORs). Multiple covariates were built into the model based on the association of the diagnosis reported in the literature. All p values were calculated based on 2-tailed tests, with 0.05 as a threshold for statistical significance. All statistical analyses were performed using the Stata software package, version 17.0 SE-Standard Edition (StataCorp, College Station, TX, USA).

## RESULTS

A total of 743,535 patients hospitalized with a concurrent diagnosis of T2MI were identified in the years 2019 (331,180 patients) and 2020 (412,355 patients). Detailed patient characteristics are shown in **Table 1**. Although statistically significant, the sex (female: 47.2% vs. 46%,  $p < 0.01$ ) and age (70.9 $\pm$ 14 vs. 70.4 $\pm$ 14.1,  $p = 0.02$ ) differences between 2019 and 2020 were very

**Table 1.** Baseline characteristics of type 2 myocardial infarction, National Inpatient Sample 2019-2020

Characteristics	2019 (n=331,180)	2020 (n=412,355)	p value
Mean age with SD (year)	70.9 $\pm$ 14	70.4 $\pm$ 14.1	0.02
18-49	8.2	8.9	
50-64	21.6	22.1	
65-74	24.6	25.1	
>75	45.4	43.8	
Female (%)	47.2	46	<0.01

(continued to the next page)

**Table 1.** (Continued) Baseline characteristics of type 2 myocardial infarction, National Inpatient Sample 2019-2020

Characteristics	2019 (n=331,180)	2020 (n=412,355)	p value
Weekend hospitalizations (%)	26.2	26.1	0.58
Insurance (%)			<0.01
Medicare	73.8	71.7	
Medicaid	10.7	11.6	
Private	12.6	13.7	
Uninsured	2.8	2.9	
Hospital bed size (%)			0.80
Small	20.6	21.5	
Medium	27.6	28.1	
Large	51.7	50.3	
Teaching/location (%)			0.91
Rural	8.5	8.2	
Urban non-teaching	15.5	15.9	
Urban teaching	76.1	75.8	
Zip income (%)			0.25
1	32.7	33.2	
2	26.6	28.1	
3	23.2	21.8	
4	17.5	16.9	
Disposition (%)			<0.01
Home	42.9	42.3	
Short term hospital	3.7	3.4	
SNF	30.8	28.4	
Home health care	20.9	23.7	
AMA	1.6	2.1	
Race (%)			0.02
White	69.8	66.7	
Blacks	16.2	17.4	
Hispanics	7.8	9.5	
Mean CCI	4.3	4.3	0.12
CCI score (%)			
1	7.7	8.2	
2	15.3	15.7	
≥3	76.9	76	
Comorbidities (%)			
Hypertension	70	69.6	0.30
Diabetes Mellitus	40.6	41.6	<0.01
Obesity	18.7	20.4	<0.01
Obstructive sleep apnea	10.2	9.6	0.01
Afib/flutter	30.2	30.3	0.88
Chronic pulmonary disease	15.4	15.7	0.46
CAD	96.2	98.7	<0.01
Heart failure	55.4	53.3	<0.01
Prior CVA	12.8	12.4	0.07
Renal failure	40.6	40.6	0.98
Liver disease	9.1	9.8	0.01
Lymphoma	1.4	1.4	0.63
Metastatic cancer	3.4	3.5	0.72
Solid tumor without metastases	6.3	6.2	0.28
Sepsis	26	29	<0.01
PVD	21.4	20.2	<0.01
Anemia	39.8	40.7	0.07
Smoker	39	36.5	<0.01
Pneumonia (Bacterial or viral)	65.1	67.2	<0.01
Respiratory failure	41.3	43.9	<0.01
COVID-19	0	10.1	N/A

Comorbidities were indexed via International Classification of Disease, Tenth Revision-Clinical Modification codes (**Supplementary Table 1**).

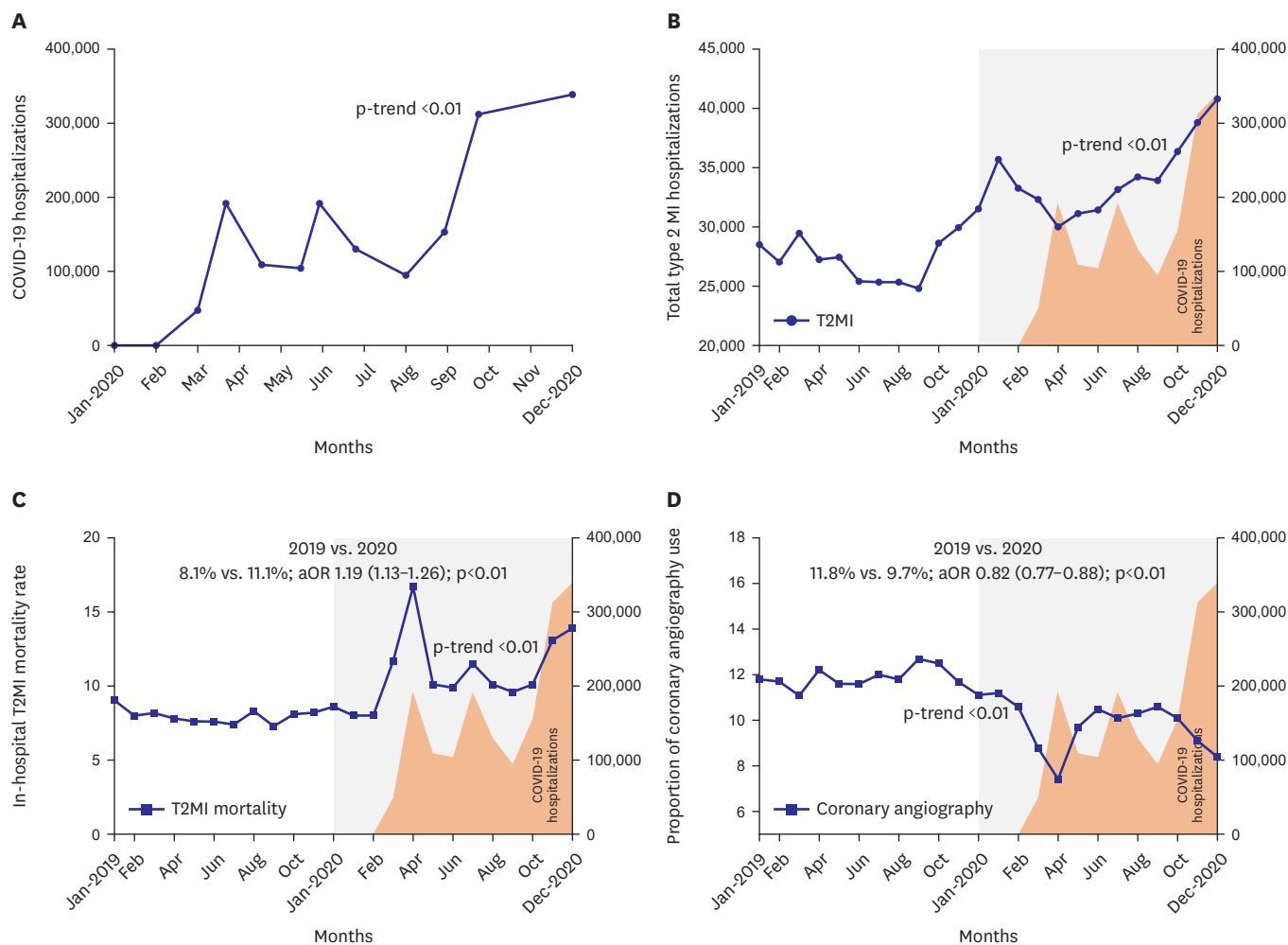
AMA = against medical advice; CAD = coronary artery disease; CCI = Charlson comorbidity index; COVID-19 = coronavirus disease 2019; CVA = cerebrovascular accident; N/A = not applicable; PVD = peripheral vascular disease; SD = standard deviation; SNF = skilled nursing facility.

minimal. In 2020, we had more African American patients (16.2% vs. 17.4%,  $p=0.02$ ) and Hispanic patients (7.8% vs. 9.5%,  $p=0.02$ ) compared with 2019. There were no significant differences in hospital type and size and mean household income determined by ZIP code between the calendar years. The CCI scores were similar in both 2019 and 2020 (CCI  $\geq 3$ , 76.9% vs 76%,  $p=0.12$ ). The year 2020 was associated with higher prevalence of diabetes mellitus (41.6% vs. 40.6%,  $p<0.01$ ), CAD (98.7% vs. 96.2%,  $p<0.01$ ), liver disease (9.8% vs. 9.1%,  $p=0.01$ ), sepsis (29% vs. 26%,  $p<0.01$ ), viral or bacterial pneumonia (67.2% vs. 65.1%,  $p<0.01$ ), respiratory failure (43.9% vs. 41.3%,  $p<0.01$ ), and COVID-19 (10.1% vs. 0%) compared with 2019. There was a small but statistically significant difference in discharge dispositions between the calendar years, with fewer patients going to skilled nursing facility (30.8% vs. 28.4%,  $p<0.01$ ) but more dispositions with home health care (20.9% vs. 23.7%) support in the year 2020 compared with 2019. The top 3 primary diagnoses associated with T2MI were similar in 2019 and 2020, including sepsis, hypertensive heart & chronic kidney disease, and hypertensive heart disease with heart failure. In 2020, COVID-19 was the fourth most common cause of admission associated with T2MI (**Supplementary Table 2**).

During the COVID-19 pandemic in 2020, there were a total of 1,676,695 COVID-19 hospitalizations identified in the dataset (**Supplementary Table 3**). Approximately half (805,110 or 48%) occurred during the final three months of 2020, and overall, there was an increasing trend of COVID-19 hospitalization as 2020 progressed (**Figure 1A**). Similarly, there was a rising trend of T2MI hospitalizations across the study period, with a visible peak seen in December 2020 as was seen for COVID-19 hospitalizations (**Figure 1B, Supplementary Tables 3 and 4**). Likewise, there were peaks in T2MI hospitalizations associated with COVID-19 diagnosis seen in April 2020 (6,025, or 20.8% of all T2MI hospitalizations), July 2020 (4,055 hospitalizations, or 12.2%) and December 2020 (8,580, or 21%). The incidence of T2MI in COVID-19 infection patients ranges from <1% to 20.8%, as shown in **Table 2**.

Overall, the increasing trend of T2MI hospitalizations was statistically significant by the Joinpoint regression analysis model with an average annual percent change (AAPC) of +1.8% over the study period and a corresponding  $p$ -value of 0.004. A graph of the Joinpoint model is provided in **Supplementary Figure 1**. The model demonstrates a significant decrease in T2MI hospitalizations from January to August 2019 (with an annual percent change [APC] of -2.1%,  $p=0.043$ ), as well as significant increases in T2MI hospitalizations from August 2019 to April 2020 (APC +6.4%,  $p<0.001$ ) and July to December 2020 (APC +4.8%,  $p<0.001$ ).

There were significantly higher odds of in-hospital mortality for T2MI hospitalizations in 2020 compared with 2019 (11.1% vs. 8.1%: aOR, 1.19 [1.13–1.26];  $p<0.01$ ), **Table 3** and **Figure 1C**. The top 3 causes of mortality in 2020 were sepsis, COVID-19, and heart failure. In 2019, the top 3 causes were sepsis, acute respiratory failure, and heart failure (**Table 4**). The monthly trend of inpatient mortality of patients with T2MI correlated with the higher incidence of COVID-19 infection of in-hospital mortality was seen again in April (5,010, or 16.7% of all T2MI hospitalizations) and December 2020 (5,665, or 13.9%) (**Supplementary Tables 3 and 5**). Coronary angiography for patients with associated diagnosis of T2MI were less commonly performed in 2020 compared with 2019 (11.8% vs. 9.7%: aOR, 0.82 [0.77–0.88];  $p<0.01$ ) (**Figure 1D, Supplementary Table 6**). The other outcomes of T2MI in 2020 were significantly different when compared with 2019, including the total hospitalization charges (adjusted mean difference, \$6,953;  $p=0.02$ ) and total hospitalization costs (adjusted mean difference, \$1,333;  $p<0.01$ ) (**Supplementary Table 7**). However, there was no statistically significant difference in the length of stay ( $7.7\pm 9.1$  vs.  $7.2\pm 8.3$  days: adjusted mean difference, 0.09 days;  $p=0.21$ ).



**Figure 1.** Various trends in COVID-19 hospitalizations and T2MI.

(A) Trends in COVID-19 hospitalizations in the year 2020. The trend of COVID-19 patient hospitalizations across 2020 by month with a p-trend <0.01. (B) Trends of T2MI hospitalizations in the background of COVID-19 hospitalizations. The patients admitted to the hospital with T2MI in 2019 and 2020 were displayed with COVID-19 hospitalizations in 2020. (C) Trends of in-hospital T2MI mortality rate in the background of COVID-19 hospitalizations. The trends in the mortality rate for patients admitted to the hospital with T2MI in 2019 and 2020 were displayed with the COVID-19 hospitalizations in 2020. The overall p-trend was <0.01. (D) Trends in coronary angiography use in T2MI patients in 2019 and 2020. The trends in the use of coronary angiography in patients admitted to the hospital with T2MI in 2019 and 2020 were displayed with the COVID-19 hospitalizations in 2020. The p-trend was <0.01. COVID-19 = coronavirus disease 2019; T2MI = type 2 myocardial infarction.

**Table 2.** COVID-19 hospitalizations with type 2 myocardial infarction in 2020, National Inpatient Sample

Month	Count	Proportions
January	<11	<1%
February	<11	<1%
March	1,615	5%
April	6,025	20.8%
May	2,925	9.4%
June	2,204	7.1%
July	4,055	12.2%
August	2,900	8.5%
September	2,075	6.1%
October	3,465	9.5%
November	7,784	20.1%
December	8,580	21%
Total	41,640	

COVID-19 = coronavirus disease 2019.

**Table 3.** Clinical and resource outcomes for T2MI hospitalizations, National Inpatient Sample 2019-2020

Outcomes	2019 (n=331,180)	2020 (n=412,355)	Unadjusted OR or mean difference	p value	Adjusted OR or mean difference <sup>†,‡</sup>	p value
In-hospital mortality	26,680 (8.1%)	45,740 (11.1%)	1.42 (1.35, 1.49)	<0.01	1.19 (1.13, 1.26)	<0.01
Coronary angiography	39,235 (11.8%)	40,189 (9.7%)	0.80 (0.75, 0.85)	<0.01	0.82 (0.77, 0.88)	<0.01
Length of stay (days)	7.2±8.3	7.7±9.1	0.54 (0.36, 0.75)	<0.01	0.09 (-0.05, 0.25)	0.21
Total hospitalization charges (\$)	94,019±151,173	107,460±170,478	13,440 (6,730, 20,151)	<0.01	6,953 (1,083, 12,823)	0.02

Values are presented as mean±standard deviation or number (%).

COVID-19 = coronavirus disease 2019; OR = odds ratio; T2MI = type 2 myocardial infarction

<sup>†</sup>OR or mean difference for T2MI patients in 2020 compared with 2019.

<sup>‡</sup>Variables used for adjusted analysis include age, gender, admission day, insurance status, median household income by zip code, hospital bed size, Charlson comorbidity index, COVID-19 infection, sepsis, respiratory failure, obesity, Atrial fibrillation/flutter, hypertension, diabetes mellitus, chronic obstructive pulmonary disease, coronary artery disease, prior stroke, chronic kidney disease, end-stage renal disease, peripheral vascular disease, anemia, smoking status.

**Table 4.** Five most common mortality cause (primary diagnosis) associated with type 2 myocardial infarction hospitalizations, National Inpatient Sample, 2019 & 2020

ICD-10-CM code	Diagnosis	Number and percentage of mortality
Year 2019 (n=26,680)		
A41.9, A41.51	Sepsis	9,140 (34.3%)
J96.01, J96.21	Acute respiratory failure with hypoxia	1,395 (5.4%)
I13.0	Hypertensive heart and CKD with HF	1,040 (3.9%)
Year 2020 (n=45,740)		
A41.9, A41.89	Sepsis	17,689 (38.7%)
U07.1	COVID-19	6,060 (13.2%)
I13.0	Hypertensive heart and CKD with HF	1,400 (3.1%)
J96.01	Acute respiratory failure with hypoxia	1,195 (2.6%)

CKD = chronic kidney disease; HF = heart failure; ICD-10-CM = International Classification of Disease, Tenth Revision-Clinical Modification.

## DISCUSSION

This is the first study to compare the outcome of patients with T2MI during the COVID-19 pandemic to those before the pandemic. First, COVID-19 was the second most common cause of admissions related to T2MI in 2020. Second, the majority of COVID-19-related hospitalizations in 2020 happened during the first 3 months after the beginning of the pandemic and was after that followed by a steady increase. Third, T2MI during hospital admission was associated with higher in-hospital mortality in 2020 compared with 2019. Fourth, patients with T2MI were less likely to receive coronary angiography in 2020, albeit with higher hospitalization costs when compared with 2019.

Troponin elevation above the 99th percentile of the upper reference limit has traditionally been the marker of myocardial injury.<sup>12)</sup> However, the underlying pathophysiological mechanisms contributing to ischemia are used to further classify in the most recent Fourth Universal definition of MI. Although myocardial injury is frequently observed among patients with COVID-19, identifying the ischemic component remains challenging.<sup>7)</sup> Thus, the incidence of T2MI among patients hospitalized with COVID-19 infection widely ranged from <1% to 21%.<sup>13)14)</sup> COVID-19 infection causes endothelial dysfunction, systemic inflammation, pro-thrombotic state, and hypoxia.<sup>5)15)</sup> These lead to an imbalance in oxygen demand and supply to the heart, causing T2MI. Moreover, we also noted an increase in the incidence of T2MI with the trend of the COVID-19 outbreak, as seen by the rise of COVID-19 hospitalizations from April through December 2020. Apart from the direct effect of the COVID-19 disease, the pandemic also indirectly affected the outcome of T2MI. This was evidenced by using COVID-19 infection as one factor to be adjusted in the multivariable regression analysis for the outcomes of T2MI patients. The T2MI patients in 2020 had worse outcomes than the pre-COVID-19 era,

with nearly 20% increased odds of inpatient death. A prior study by Kwok et al.,<sup>16)</sup> studying the impact of COVID-19 on STEMI, showed a higher incidence of mortality among these patients compared with those without concurrent infection. Moreover, it is well established that prognosis of T2MI is worse compared with T1MI.<sup>9)17)</sup> This is probably the reason for the higher mortality rates among COVID-19 patients with T2MI observed in our study. Several factors have been proposed, including patient and healthcare-related factors.<sup>18)</sup> The primary reason for patient-related factors was the fear of obtaining the COVID-19 infection leading to avoidance and reluctance to seek healthcare.<sup>16)19)20)</sup> Healthcare-related factors include resource constraints in the pandemic setting, including a shortage of medications, medical equipment, and healthcare providers. Besides the resource's restriction, COVID-19-related symptoms can mimic myocardial infarction, especially shortness of breath, which could lead to misdiagnosis or delayed treatment.<sup>3)</sup>

We also observed a decline in the use of coronary angiography during our study period. This was also observed in prior studies that showed a lower rate of coronary angiography and myocardial revascularization in patients with T2MI during this period.<sup>15)</sup> Moreover, a study by Kwok et al.,<sup>16)</sup> observed a decline in the utilization of primary percutaneous coronary intervention (PCI) for STEMI following the lockdown in England, along with an increase in door-to-balloon times. However, whether this cutback was due to a lack of resources or a postponement of intervention in acutely ill patients is unclear. Thus, all these factors contributed to moral distress amongst healthcare workers, resulting in occupational burnout and post-traumatic stress disorder, ultimately affecting healthcare.<sup>21)</sup>

Furthermore, we found significantly higher hospital charges and hospitalization costs in 2020 compared with 2019. These findings were adjusted for COVID-19 infection, and the result suggested that the pandemic also indirectly affected these outcomes, like the inpatient-mortality outcome. The major contributors to these findings are age, comorbidities, Medicare insurance, the requirement of supplemental oxygen, including mechanical ventilation and extracorporeal membrane oxygenation, and patients in the Northeast region. In contrast, teaching status and hospital size have little impact on the costs and length of stay.<sup>22)</sup>

We acknowledge three main limitations in this study. First, the NIS is an administrative data based on ICD-10 coding, which did not include essential clinical information like symptoms, laboratory tests, imaging, and medication prescriptions. This leads to heavily rely on the accuracy of the input data which could cause misclassification of non-STEMI patients as T2MI. However, this ICD-10 coding method for identification of T2MI patients has been used in the previous studies.<sup>23-25)</sup> In our study, any concurrent diagnosis of STEMI and non-STEMI reported in the same T2MI patient was excluded from the study, which was a small proportion (<1%) of patient population. Secondly, our study includes only hospitalized patients. Therefore, our results do not reflect all patients with T2MI patients. Third, given the nature of retrospective studies, there remains a potential for bias due to unmeasurable confounding factors, despite adjustment for baseline comorbidities.

In summary, our study demonstrated that the rise in COVID-19 hospitalizations was in conjunction with trends in the increase of T2MI and its associated mortality. In addition, we found that T2MI in 2020 was associated with higher in-hospital mortality, lower use of coronary angiography, and higher total hospitalization charges compared to 2019. Further research into the factors associated with increased mortality can increase our preparedness for future pandemics.



## SUPPLEMENTARY MATERIALS

### Supplementary Table 1

ICD-10 codes for cohort identification and stratification with major baseline comorbidities

[Click here to view](#)

### Supplementary Table 2

Three most common cause (primary diagnosis) associated with type 2 myocardial infarction hospitalizations, National Inpatient Sample, 2019 & 2020

[Click here to view](#)

### Supplementary Table 3

COVID-19 hospitalizations in 2020, National Inpatient Sample

[Click here to view](#)

### Supplementary Table 4

Type 2 myocardial infarction hospitalizations in 2019 and 2020, National Inpatient Sample 2019-2020

[Click here to view](#)

### Supplementary Table 5

In-hospital mortality in type 2 myocardial infarction patients, National Inpatient Sample, 2019-2020

[Click here to view](#)

### Supplementary Table 6

Coronary angiography in type 2 myocardial infarction patients, National Inpatient Sample, 2019-2020

[Click here to view](#)

### Supplementary Table 7

Resource outcomes for type 2 myocardial infarction patients, National Inpatient Sample 2019-2020

[Click here to view](#)

### Supplementary Figure 1

Jointpoint analysis of type 2 myocardial infarction in-patient stays, National Inpatient Sample 2019-2020.

[Click here to view](#)

## REFERENCES

1. Cuadros DF, Branscum AJ, Mukandavire Z, Miller FD, MacKinnon N. Dynamics of the COVID-19 epidemic in urban and rural areas in the United States. *Ann Epidemiol* 2021;59:16-20.  
[PUBMED](#) | [CROSSREF](#)
2. Long B, Brady WJ, Koefman A, Gottlieb M. Cardiovascular complications in COVID-19. *Am J Emerg Med* 2020;38:1504-7.  
[PUBMED](#) | [CROSSREF](#)
3. Clerkin KJ, Fried JA, Raikhelkar J, et al. COVID-19 and cardiovascular disease. *Circulation* 2020;141:1648-55.  
[PUBMED](#) | [CROSSREF](#)
4. Di Fusco M, Shea KM, Lin J, et al. Health outcomes and economic burden of hospitalized COVID-19 patients in the United States. *J Med Econ* 2021;24:308-17.  
[PUBMED](#) | [CROSSREF](#)
5. Talanas G, Dossi F, Parodi G. Type 2 myocardial infarction in patients with coronavirus disease 2019. *J Cardiovasc Med (Hagerstown)* 2021;22:603-5.  
[PUBMED](#) | [CROSSREF](#)
6. Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol* 2020;5:802-10.  
[PUBMED](#) | [CROSSREF](#)
7. Lala A, Johnson KW, Januzzi JL, et al. Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. *J Am Coll Cardiol* 2020;76:533-46.  
[PUBMED](#) | [CROSSREF](#)
8. Saaby L, Poulsen TS, Diederichsen AC, et al. Mortality rate in type 2 myocardial infarction: observations from an unselected hospital cohort. *Am J Med* 2014;127:295-302.  
[PUBMED](#) | [CROSSREF](#)
9. Chapman AR, Shah AS, Lee KK, et al. Long-term outcomes in patients with type 2 myocardial infarction and myocardial injury. *Circulation* 2018;137:1236-45.  
[PUBMED](#) | [CROSSREF](#)
10. White K, Kinarivala M, Scott I. Diagnostic features, management and prognosis of type 2 myocardial infarction compared to type 1 myocardial infarction: a systematic review and meta-analysis. *BMJ Open* 2022;12:e055755.  
[PUBMED](#) | [CROSSREF](#)
11. Sattar Y, Taha A, Patel N, et al. Cardiovascular outcomes of type 2 myocardial infarction among COVID-19 patients: a propensity matched national study. *Expert Rev Cardiovasc Ther* 2023;21:365-71.  
[PUBMED](#) | [CROSSREF](#)
12. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth Universal Definition of Myocardial Infarction (2018). *Circulation* 2018;138:e618-51.  
[PUBMED](#) | [CROSSREF](#)
13. Weber B, Siddiqi H, Zhou G, et al. Relationship between myocardial injury during index hospitalization for SARS-CoV-2 infection and longer-term outcomes. *J Am Heart Assoc* 2022;11:e022010.  
[PUBMED](#) | [CROSSREF](#)
14. Sandoval Y, Januzzi JL Jr, Jaffe AS. Cardiac troponin for assessment of myocardial injury in COVID-19: JACC review topic of the week. *J Am Coll Cardiol* 2020;76:1244-58.  
[PUBMED](#) | [CROSSREF](#)
15. Elyaspour Z, Zibaenezhad MJ, Razmkhah M, Razeghian-Jahromi I. Is it all about endothelial dysfunction and thrombosis formation? The secret of COVID-19. *Clin Appl Thromb Hemost* 2021;27:10760296211042940.  
[PUBMED](#) | [CROSSREF](#)
16. Kwok CS, Gale CP, Kinnaird T, et al. Impact of COVID-19 on percutaneous coronary intervention for ST-elevation myocardial infarction. *Heart* 2020;106:1805-11.  
[PUBMED](#) | [CROSSREF](#)
17. DeFilippis AP, Chapman AR, Mills NL, et al. Assessment and treatment of patients with type 2 myocardial infarction and acute nonischemic myocardial injury. *Circulation* 2019;140:1661-78.  
[PUBMED](#) | [CROSSREF](#)
18. Fox ER, Stolbach AI, Mazer-Amirshahi M. The landscape of prescription drug shortages during the COVID-19 pandemic. *J Med Toxicol* 2020;16:311-3.  
[PUBMED](#) | [CROSSREF](#)
19. De Luca G, Verdoia M, Cercek M, et al. Impact of COVID-19 pandemic on mechanical reperfusion for patients with STEMI. *J Am Coll Cardiol* 2020;76:2321-30.  
[PUBMED](#) | [CROSSREF](#)

20. Sun C, Dyer S, Salvia J, Segal L, Levi R. Worse cardiac arrest outcomes during the COVID-19 pandemic in boston can be attributed to patient reluctance to seek care. *Health Aff (Millwood)* 2021;40:886-95.  
[PUBMED](#) | [CROSSREF](#)
21. Raudenská J, Steinerová V, Javůrková A, et al. Occupational burnout syndrome and post-traumatic stress among healthcare professionals during the novel coronavirus disease 2019 (COVID-19) pandemic. *Best Pract Res Clin Anaesthesiol* 2020;34:553-60.  
[PUBMED](#) | [CROSSREF](#)
22. Ohsfeldt RL, Choong CK, Mc Collam PL, Abedtash H, Kelton KA, Burge R. Inpatient hospital costs for COVID-19 patients in the United States. *Adv Ther* 2021;38:557-95.  
[PUBMED](#) | [CROSSREF](#)
23. McCarthy CP, Kolte D, Kennedy KF, Vaduganathan M, Wasfy JH, Januzzi JL Jr. Patient characteristics and clinical outcomes of type 1 versus type 2 myocardial infarction. *J Am Coll Cardiol* 2021;77:848-57.  
[PUBMED](#) | [CROSSREF](#)
24. McCarthy CP, Murphy S, Cohen JA, et al. Underutilization of cardiac rehabilitation for type 2 myocardial infarction. *J Am Coll Cardiol* 2019;73:2005-7.  
[PUBMED](#) | [CROSSREF](#)
25. Nazir S, Minhas AM, Kamat IS, et al. Patient characteristics and outcomes of type 2 myocardial infarction during heart failure hospitalizations in the United States. *Am J Med* 2021;134:1371-1379.e2.  
[PUBMED](#) | [CROSSREF](#)