hearts

MDPI

Article

Prevalence, Predictors, and Outcomes of Myocardial Injury in Hospitalized COVID-19 Patients—An Observational Retrospective Study

Ghanshyam Patel [1,*], Jeffrey Smith [2], Luqman Baloch [1], Mario Affinati [1], Advait Vasavada [3], Shilpa Reddy [4], Shikha Jain [5], Gashaw Hassen [6,7], Michael Araya [8] and Shrestha Adak [9]

1 Mercyhealth Internal Medicine Residency, Javon Bea Hospital, Rockford, IL 61114, USA; lbaloch@mhemail.org (L.B.); maffinati@mhemail.org (M.A.)
2 Department of Medicine and Medical Specialties, University of Illinois College of Medicine, Rockford, IL 61107, USA; jsmith59@uic.edu
3 Department of Internal Medicine, MP Shah Medical College, Jamnagar, Gujarat 361008, India; advait2163@gmail.com
4 Department of Internal Medicine, Marian University, Indianapolis, IN 46222, USA; reddsp@gmail.com
5 Department of Internal Medicine, MVJ Medical College & Research Hospital, Hoskote, Karnataka 562114, India; shikha.jain1885@gmail.com
6 Department of Internal Medicine, Addis Ababa University, Addis Ababa P.O. Box 9086, Ethiopia; dr.gashaw@yahoo.com
7 Department of Internal Medicine, University of Parma, 43121 Parma, Italy
8 Department of Internal Medicine, Northside Gwinnett Hospital, Lawrenceville, GA 30046, USA; findmichael@yahoo.com
9 Department of Internal Medicine, Medical College and Hospital, Kolkata, West Bengal 700073, India; dr.shrestha.adak@gmail.com
* Correspondence: gpatel@mhemail.org

Abstract: COVID-19 mainly causes pulmonary manifestation; nonetheless, its systemic inflammatory response involves multiple organs, including the heart. We aimed to evaluate the prevalence, predictors, and outcomes of myocardial injury in hospitalized patients with SARS-CoV-2 infection. Methods and Results: We performed an observational retrospective analysis on patients hospitalized with COVID-19 in a moderate-sized community hospital system. Myocardial injury was defined as highly sensitive troponin T levels in the 99th percentile above the normal upper limit for the respective biological sex. Multivariable logistic regression models were fitted to assess the association between the myocardial-injury and the no-myocardial-injury groups for primary and secondary outcomes. A total of 1632 (49.3% male, 41.7% aged 60–79 years) patients with COVID-19 were included, out of which 312 (19.1%) had a myocardial injury. Patients with myocardial injury were older (36.9% > 80 years) and had higher cardiovascular-related comorbidities than those without. The prevalence of cardiovascular risk factors (78.5% vs. 52.0%) and cardiovascular diseases (78.2% vs. 56.1%) was much higher in the myocardial-injury group. Older age (50–64 years vs. <49 years; OR, 3.67 [1.99–6.74]), Angiotensin Receptor Blockers (ARBs) (OR, 1.44 [1.01–2.05]), Beta-blockers (OR, 2.37 [1.80–3.13]), and cardiovascular comorbidities (OR, 1.49 [1.09–2.05]) were strong predictors of cardiac injury after multivariable adjustment. Myocardial injury was strongly associated with ICU admission (adjusted OR, 1.68 [1.29–2.19]) and longer length of hospital stay (median days, 5 (3, 9) vs. 4 (2, 7)). The results do not show a significant difference in the use of mechanical ventilation (OR, 1.29 [0.87–1.89]) or in-hospital mortality (OR, 1.37 [0.98–1.91]) with respect to myocardial injury. Conclusion: This multicenter retrospective study of nearly 1600 patients revealed the following findings: Myocardial injury was observed in 1 out of 5 patients hospitalized with COVID-19 but was more often clinically insignificant. Patients of age > 65 had very high odds of having elevated troponin levels after adjusting for sex and other illnesses. Pre-existing cardiac diseases and risk factors were robust predictors of cardiac injury after adjusting for age and sex. In the adjusted model, myocardial injury was not associated with the requirement of mechanical ventilation or change in in-hospital mortality.

Citation: Patel, G.; Smith, J.; Baloch, L.; Affinati, M.; Vasavada, A.; Reddy, S.; Jain, S.; Hassen, G.; Araya, M.; Adak, S. Prevalence, Predictors, and Outcomes of Myocardial Injury in Hospitalized COVID-19 Patients—An Observational Retrospective Study. *Hearts* **2022**, *3*, 66–75. https://doi.org/10.3390/hearts3030009

Academic Editors: Lukas J. Motloch, Anna-Maria Dieplinger and Rudin Pistulli

Received: 1 June 2022
Accepted: 6 July 2022
Published: 8 July 2022

Keywords: COVID-19; SARS-CoV-2 infection; cardiovascular injury; myocardial injury; cardiac injury

1. Introduction

Myocardial injury associated with severe acute respiratory syndrome coronavirus 2 infection was initially observed among hospitalized patients in China [1]. Later studies documented elevated troponin levels defined as cardiac injury in COVID-19 compared with similar conditions such as influenza [2]. Multiple studies demonstrated the varied degree of prevalence among these populations, ranging from 20% to 40% [3–5]. Uncertainty remains regarding the variable risk for myocardial injury among patients depending on their comorbidities, predictors of cardiac injury, and overall clinical outcomes in patients hospitalized with COVID-19 who experienced a cardiac injury.

COVID-19 is mainly a respiratory disease; however, systemic inflammation and micro thrombosis can lead to multiorgan failure, often including cardiac manifestations [6]. A varying degree of cardiac injuries were noted in patients diagnosed with COVID-19. It was speculated that patients with previously known cardiac diseases or risk factors had a higher prevalence of cardiac injury compared to patients without cardiac disease; nevertheless, myocardial injury among patients without pre-existing cardiac conditions had worse outcomes overall [7]. Wei et al. identified multiple mechanisms of myocardial injury in COVID-19, including the direct virulence of SARS-CoV-2 through ACE-2, exaggerated inflammatory reaction, micro thrombosis and endothelial injury, and hypoxic cardiac injury [8,9].

We conducted a retrospective analysis to determine whether an initial strategy to measure troponin level can predict in-hospital length of stay, ICU admission, and in-hospital mortality among hospitalized patients with COVID-19. In this study, we observed hospitalized COVID-19 patients with myocardial injury defined as elevated troponin levels in a considerable national representative sample. Based upon the current literature, we hypothesized that male sex, elder age, cardiovascular comorbidities, and cardiac-related medicine use are risk factors for cardiac injury among hospitalized COVID-19 patients. We also evaluated the impact of the myocardial injury on the risks of prolonged length of hospital stay, ICU admission, and in-hospital mortality during COVID-19 admission.

2. Methods

2.1. Study Design and Population

We performed an observational retrospective study on a large series of patients from 25 cities comprising Mercyhealth System in northern Illinois and southern Wisconsin, including 6 main hospitals: Mercyhealth, in Riverside, Rockford; Mercyhealth, in Rockton, Rockford; Mercyhealth, in Harvard; Mercyhealth, in Walworth; Mercyhealth, in Janesville; Van Matre, in Rockford. We included all patients diagnosed with a laboratory-confirmed SARS-CoV-2 infection who were 18 years or older regardless of their demographics, comorbidities, and socio-economic status between 1 January 2020, and 1 December 2021. The Mercy Health Corporation Institutional Review Board approved this research study under a regulatory protocol allowing the analysis of patient-level data to be conducted.

2.2. Data Collection

Data were collected from the electronic medical record (EMR) system from central Mercyhealth (Rockford, IL, USA). The main variables collected included patient's demographic characteristics (age, sex, race, and ethnicity), disease diagnoses based on ICD 10 codes, laboratory measurements, previous comorbidities (diabetes, hypertension, atherosclerotic disorders, heart failure, arrhythmic disorders), procedures performed, and outcome as in deceased at discharge, ICU admission anytime during their stay at the hospital, the status of mechanical ventilation, and length of stay at the hospital. The main laboratory measurement of Troponin T (Tn T) was assessed, wherein the 99th percentiles of the normal

upper limits for males and females were 22 ng/mL and 14 ng/mL, respectively. Further details on the normal reference range of laboratory measurements are provided in the table.

2.3. Outcome Measures

The primary outcome was myocardial injury defined as a Tn T value above the 99th percentile normal upper limit, all-cause mortality evaluated at discharge, ICU admission, the requirement of mechanical ventilation, and length of stay. Patients who were discharged from the hospital were assumed to be alive. The primary outcome was stratified based on the myocardial injury and no-myocardial-injury arms. Patients with one of any cardiovascular diseases were included in the cardiovascular disease patient group. Cardiovascular disease was defined as atherosclerotic diseases, previous myocardial infarction, heart failure, arrhythmia, or peripheral arterial disease. Patients were also further stratified by risk for cardiac injury with hypertension, diabetes mellitus, unstable angina, or any combination of the three, and placed in the cardiovascular risk factor group. The secondary outcomes included respiratory organ support with mechanical ventilation, ICU admission anytime during their hospitalization, and length of hospital stay.

2.4. Statistical Analysis

Descriptive analyses were performed by Tn T levels stratified into positive and negative. Here, negative means the value falls below the 99th percentile of the normal upper limit for the general population based on their reported biological sex. We used the troponin measurements available anytime during their stay at the hospital. We evaluated demographic and baseline characteristics, medical history, and outcomes among patients in the myocardial-injury group vs. no-myocardial-injury group. The categorical variables were reported as the total count and percentage of the patients with their *p*-value based on the chi-squared (χ^2) test. The continuous variables were reported as median and interquartile range or mean $\pm$ standard deviation as appropriate and compared with a *t*-test or Mann–Whitney *u*-test. To assess the effects of troponin levels on outcomes, we calculated the odd ratio with a 95% confidence interval. Logistic regression analysis was performed to identify the predictor of primary and secondary endpoints. The odds ratio was noted between the troponin-positive group and the troponin-negative group. The primary endpoint was the odds of all-cause mortality between the two groups during hospitalization. Secondary endpoints were ICU admission, mechanical ventilation requirement, and length of stay at the hospital. These endpoints were all reported in odds. The analyses were adjusted for the following covariates: age, sex, and comorbidities as per requirement. We utilized IBM SPSS statistics software version 22 for the statistical analyses. Statistical analyses were set with an alpha of 5%, and all hypothesis tests were two-sided.

3. Result

3.1. Baseline Characteristics of Hospitalized COVID-19 Patients

A total of 16,350 patients were diagnosed with COVID-19 infection between January 2020 and November 2021 throughout the Mercyhealth system. In total, 1632 out of 16,350 (10%) patients were hospitalized due to SARS-CoV-2 infection. Table 1 summarizes the demographic and baseline characteristic of the patients hospitalized with COVID-19 stratified by myocardial injury. Of 1632 hospitalized patients with COVID-19, 312 (19.1%) had laboratory-confirmed Tn T positivity for myocardial injury. Patients with myocardial injury were 50.6% male, with a mean age of 74 $\pm$ 13 years; in total, 144 (46.2%) were managed in the ICU, and 71 (22.8%) died. The median days of hospitalization were 5, ranging from 3 to 9 for the 25–75% interquartiles. Patients with COVID-19 and myocardial injury were, on average, significantly older than those with COVID-19 without myocardial injury. Most of the myocardial injuries had occurred in those aged over 60 years. Meanwhile, 35.6% of myocardial injuries had occurred in patients aged over 80 years of age. The predominant racial group in our dataset was white, comprising 79.5% and being equally distributed in both groups. When looking at ethnicity, myocardial injuries were more

prevalent in the non-Hispanic group than in the Hispanic group, showing incidences of 20.1% and 12.4%, respectively. The use of ACE inhibitors, ARBs, beta-blockers, anticoagulants, and statins was collectively more prevalent among myocardial-injury patients. The myocardial-injury and no-myocardial-injury groups had patients with similar baseline BMIs with most of the population being in the overweight (25–29.9) category. Interestingly, the healthy (18.5–24.9) BMI population had 24.2% (67/277) of Tn T-positive patients compared with 18.6% (160/861) and 17.3% (78/449) among the overweight and obese populations, respectively. D-dimer levels were checked in a total of 903 (55.3%) patients; out of those, 245 patients had levels higher than 800 ng/mL, with equal distribution in both groups.

Table 1. Demographic and clinical characteristics of hospitalized COVID-19 patients at baseline stratified by myocardial injury.

Characteristics		Hospitalized with COVID-19 Infection	Myocardial-Injury Group	No-Myocardial-Injury Group	*p*-Value
		Count (%)	Count (%)	Count (%)	
	Total	1632	312 (19.1)	1320 (80.9)	
Age	Median (IQ)	65 (5177)	74.5 (6584)	62 (4774)	<0.05
	Mean (SD)	63 (19)	74 (13)	60 (19)	<0.05
	18–39	224 (13.7)	3 (1.0)	221 (16.7)	<0.01
	40–59	404 (24.8)	42 (13.4)	362 (27.4)	
	60–79	681 (41.7)	152 (48.7)	529 (40.0)	
	>80	323 (19.8)	115 (36.9)	208 (15.7)	
Sex	Male	804 (49.3)	158 (50.6)	646 (48.9)	0.589
	Female	828 (50.7)	154 (49.4)	674 (51.1)	
Race	White	1297 (79.5)	261 (83.7)	1036 (78.5)	0.134
	Black or African American	206 (12.6)	39 (12.5)	167 (12.7)	
	Asian	10 (0.6)	0	10 (0.8)	
	Multiracial	56 (3.4)	6 (1.9)	50 (3.8)	
	American Indian or Alaskan Native	34 (2.1)	4 (1.3)	30 (2.3)	
Ethnicity	Non-Hispanic	1422 (87.1)	286 (91.7)	1136 (86.1)	0.066
Drugs	ACE Inhibitor	292 (17.9)	71 (22.8)	221 (16.7)	0.013
	ARBs	188 (11.5)	56 (17.9)	132 (10.0)	<0.01
	Statin	569 (34.9)	152 (48.7)	417 (31.6)	<0.01
	Beta-blocker	675 (41.4)	208 (66.7)	467 (35.4)	<0.01
	Anticoagulants	91 (5.6)	31 (9.9)	60 (4.5)	<0.01
	VKA inhibitor	72 (4.4)	27 (8.7)	45 (3.4)	<0.01
Fever		561 (34.4)	114 (36.5)	447 (33.9)	0.371
Smoking		219 (13.4)	48 (15.4)	171 (13.0)	0.257
BMI	Below 18.5	24 (1.5)	5 (1.6)	19 (1.4)	0.139
	18.5–24.9	277 (17.0)	67 (21.5)	210 (15.9)	
	25–29.9	861 (52.8)	160 (51.3)	701 (53.1)	
	Above 30	449 (27.5)	78 (25.0)	371 (28.1)	
D-dimer Quantitative	<400.00	506 (31.0)	94 (30.1)	412 (31.2)	0.770
	Low level 400–800	152 (9.3)	31 (9.9)	121 (9.2)	
	High level > 800	245 (15.0)	52 (16.7)	193 (14.6)	
Cardiovascular risk factors		932 (57.1)	245 (78.5)	687 (52.0)	<0.05
Cardiovascular disease		984 (60.3)	244 (78.2)	740 (56.1)	<0.05
Neither		533 (32.7)	48 (15.4)	485 (36.7)	<0.05

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; VKA, vitamin K antagonist. Reference range D-dimer Quantitative < 400 ng/mL. Cardiovascular risk factors: hypertension, diabetes mellitus, unstable angina. Cardiovascular diseases: atherosclerotic diseases, previous myocardial infarction, heart failure, arrhythmia, peripheral arterial disease.

The use of hypertensive, cholesterol-lowering, cardioprotective, and anti-coagulant medications was significantly higher in the myocardial-injury stratum, with the highest difference being noted in beta-blocker use (66.7% vs. 35.4%). The prevalence of a fever or a history of smoking was equally distributed between the myocardial-injury and no-myocardial-injury group. Patients in the myocardial-injury group generally had a higher prevalence of coexisting illness than those without myocardial injury. The prevalence of cardiovascular risk factors for myocardial injury (hypertension and/or diabetes and/or unstable angina) and one or more cardiovascular diseases were higher in the myocardial-injury group than in the no-myocardial-injury group.

3.2. Myocardial-Injury Predictors

3.2.1. Sex and Age

We observed a proportion of males among COVID-19 patients with myocardial injury similar to that of those without myocardial injury (50.6% vs. 48.9%), but having male sex was not significantly associated with myocardial injury in the age- and comorbidity-adjusted model (OR, 1.04 [0.80–1.34]). We noted higher odds of myocardial injury among age groups 50–64 years and older than 65 years in both the unadjusted and adjusted models. The interpretation of these results in the younger age groups was limited by the lower proportion of hospitalization among the young population less than 49 years of age. All results are summarized in Table 2 with unadjusted and adjusted models.

Table 2. Predictors of myocardial injury obtained from univariate and multivariate analyses.

Characteristics	Crude Odds Ratio (95% Credible Interval)	*p*-Value	Adjusted Odds Ratio (95% Credible Interval)	*p*-Value
Age group		<0.05		<0.05
<49 years			Reference Category	
50–64 years	4.43 (2.44–8.08)		3.67 (1.99–6.74)	
>65 years	10.10 (5.80–17.58)		7.62 (4.29–13.54)	
Male sex	1.07 (0.83–1.37)	0.589	1.04 (0.80–1.34)	0.791
Fever	1.12 (0.87–1.45)	0.371	1.15 (0.88–1.52)	0.308
Smoking	1.22 (0.86–1.72)	0.257	0.99 (0.69–1.44)	0.994
Body mass index > 30	0.913 (0.71–1.17)	0.472	1.28 (0.97–1.68)	0.081
Drugs				
ACE inhibitor	1.46 (1.08–1.98)	<0.05	1.20 (0.87–1.65)	0.260
ARBs	1.96 (1.40–2.76)	<0.05	1.44 (1.01–2.05)	<0.05
Beta-blockers	3.65 (2.81–4.74)	<0.05	2.37 (1.80–3.13)	<0.05
Anticoagulant	2.32 (1.47–3.64)	<0.05	1.43 (0.89–2.29)	0.136
VKA	2.68 (1.64–4.39)	<0.05	1.43 (0.85–2.41)	0.173
Statin	2.06 (1.60–2.64)	<0.05	1.30 (0.99–1.70)	0.052
D-dimer > 400	1.15 (0.829–1.60)	0.400	1.15 (0.81–1.61)	0.444
Cardiovascular risk factor group	3.37 (2.52–4.51)	<0.05	1.98 (1.45–2.70)	<0.05
Cardiovascular Disease group	2.81 (2.11–3.76)	<0.05	1.49 (1.09–2.05)	<0.05
Neither	0.31 (0.27–0.43)	<0.05	0.60 (0.42–0.85)	<0.05

The odds ratios after adjustment for age, sex, and comorbidities. The multivariable logistic regression model fitted to establish the adjustment.

3.2.2. Patient-Level Characteristics

In the unadjusted and multivariate-adjusted models, fever and smoking were not significantly associated with increased odds of myocardial injury (ORs, 1.15 [0.88–1.52] and 0.99 [0.69–1.44], respectively). As we observed in our descriptive analysis, obesity did not show an increased risk of myocardial injury. After adjusting for age, sex, and comorbidities, obesity was not associated with a higher odd (OR, 1.28 [0.97–1.68]) of myocardial injury. In the adjusted model having a D-dimer level $\geq$ 400 ng/mL, it was not statistically associated with myocardial injury (OR 1.15 [0.81–1.61]).

3.2.3. Comorbidities and Medications

In the unadjusted and adjusted models for age, sex, and comorbidities, ARB and beta-blocker uses were significantly associated with increased odds of myocardial injury (ORs, 1.44 [1.01–2.05] and 2.37 [1.80–3.13] respectively). Having cardiovascular risk factors (defined as hypertension, diabetes mellitus, and/or unstable angina) and cardiovascular diseases (defined as coronary artery disease, arrhythmia, heart failure, and/or peripheral arterial disease) trended towards a positive association with myocardial injury (adjusted ORs, 1.98 [1.45–2.70] and 1.49 [1.09–2.05] respectively). Patients with neither cardiac risk factors nor cardiac diseases had significantly lower odds of having higher troponin levels according to the univariate and multivariate logistic regressions (ORs, 0.31 [0.27–0.43] and 0.60 [0.42–0.85], respectively).

3.3. Outcome Measures

The length of hospital stay, ICU admission rates, and in-hospital mortality were higher among myocardial-injury patients than no-myocardial-injury patients according to the univariate analyses (median length of stay, 5 (3–9) days for the myocardial-injury group and 4 (2–7) days for the no-myocardial-injury group; ICU admission, 46.2% vs. 31.4%; mortality, 22.8% vs. 11.6%; Table 3). The survival analysis showed a clear difference in the Kaplan–Meier plot based on the univariate analysis (Figure 1 shows the survival analysis results stratified by myocardial injury based on the univariate analysis).

Table 3. Outcomes from univariate and multivariate logistic regressions for length of hospital stay (LOS), ICU admission, the requirement of mechanical ventilation, and mortality stratified by cardiovascular comorbidities.

Variable	Myocardial-Injury Group	No-Myocardial-Injury Group	Crude Odds Ratio (95% CI)	*p*-Value	Adjusted Odds Ratio (95% CI)	*p*-Value
LOS median (interquartile range)	5 (3, 9)	4 (2, 7)				<0.05
ICU admission	144/312 (46.2)	415/1320 (31.4)	1.87 (1.45–2.40)	<0.05	1.68 (1.29–2.19)	<0.05
Mechanical ventilation	42/312 (13.5)	146/1320 (11.1)	1.25 (0.87–1.81)	0.233	1.29 (0.87–1.89)	0.202
Mortality	71/312 (22.8)	153/1320 (11.6)	2.25 (1.64–3.08)	<0.05	1.37 (0.98–1.91)	0.068
Cardiovascular risk factor group	56/245 (22.9)	105/687 (15.3)	1.64 (1.14–2.36)	<0.05	1.30 (0.89–1.90)	0.180
Cardiovascular disease group	55/244 (22.5)	113/740 (15.3)	1.62 (1.13–2.32)	<0.05	1.28 (0.88–1.87)	0.205
Neither	12/48 (25.0)	29/485 (6.0)	5.24 (2.47–11.13)	<0.05	2.02 (0.89–4.62)	0.095

The odds ratios after adjustment for age, sex, and comorbidities. The multivariable logistic regression model fitted to establish the adjustment.

Higher Tn T levels were not associated with the use of mechanical ventilation among hospitalized COVID-19 patients (unadjusted OR, 1.25 [0.87–1.81]; adjusted OR, 1.29 [0.87–1.89]). In the univariate and multivariate analysis among COVID-19 patients, a higher level of troponin was positively associated with ICU admission (ORs, unadjusted 1.87 [1.45–2.40] and adjusted 1.68 [1.29–2.19] respectively). In the univariate analysis, having cardiac injury was associated with higher in-hospital mortality, showing an OR of 2.25 [1.64–3.08]. However, in the logistic regression adjusted for age, sex, and comorbidities, the myocardial injury did not show a statistically significant difference in in-hospital mortality (OR, 1.37 [0.98–1.91]; Table 3).

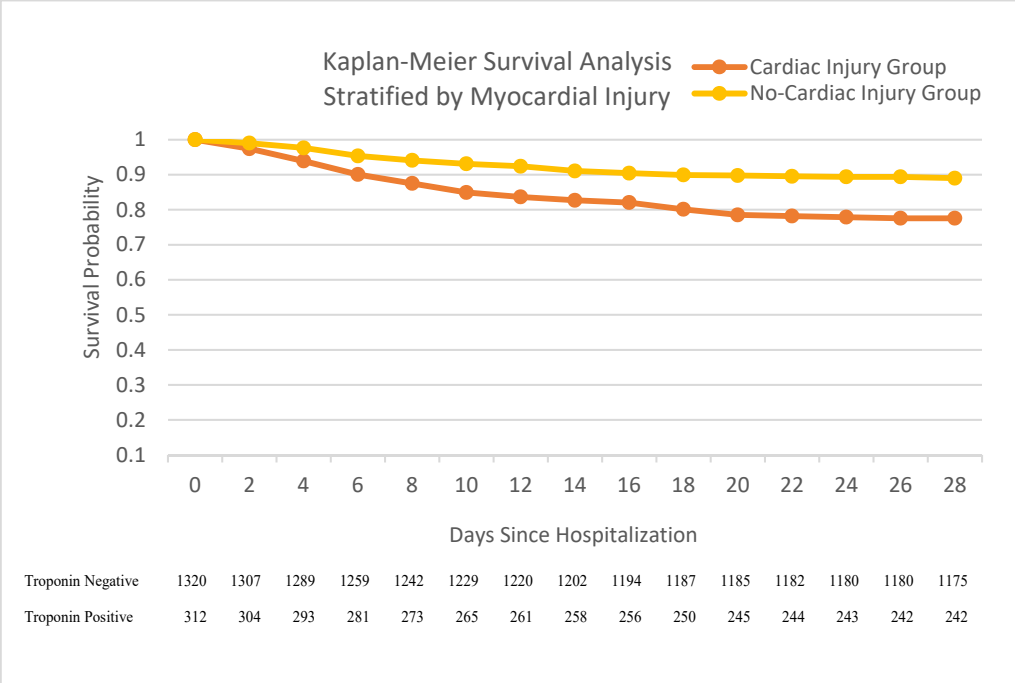

Figure 1. Kaplan–Meier survival analysis stratified by myocardial injury based on the univariate analysis.

4. Discussion

In this study, we present the characteristics of hospitalized COVID-19 patients with myocardial injury from southern Wisconsin and northern Illinois. We noted that COVID-19 patients with myocardial injury were more likely to be older patients with a higher prevalence of hypertension, diabetes mellitus, coronary artery disease, heart failure, and arrhythmia. We found that older age was strongly associated with higher odds of myocardial injury; after adjusting for comorbidities and sex, age groups > 65 years and 50–64 years had a higher risk of myocardial injury in all our models. Although these findings must be interpreted with caution due to the potential for selection bias, given the small sample of younger individuals in our study, they are consistent, given the generally higher prevalence of atherosclerotic risk factors with the increase in age. Given the gender disparities in preexisting cardiac diseases and outcomes, we sought to investigate potential disparities in cardiac injury by sex and race. Although we had a greater white population in our study, in the adjusted model we did not find any disparities by race. Even though there was a predilection for cardiac disease among males, we did not find any dissimilarities in terms of myocardial injury between males and females.

The SARS-CoV-2 virus attaches to the ACE2 receptor, which is expressed by cardiomyocytes and is likely associated with cardiac injury [10]. We found higher use of ACE-inhibitors, ARBs, statins, and/or beta-blockers in the myocardial-injury group. However, according to the multivariate logistic regression, ARB and beta-blocker use could predict the likelihood of myocardial injury. Of all patients with cardiac medications, beta-blocker users were at the greatest risk of cardiac injury. We did not find a protective association between statin use and myocardial injury, as opposed to Reynold et al. and Lala et al. [11,12]. Although a high BMI is generally associated with a higher prevalence of hypertension and metabolic syndrome, in our population, there were no differences in the troponin strata.

In this large retrospective study, more than half of the patients hospitalized with COVID-19 had underlying cardiac risk factors or diseases. Patients in the myocardial-injury group were generally older and had a higher prevalence of coexisting illnesses than those in the no-myocardial-injury group. It has been shown that patients with a history of cardiac injury and pre-existing cardiac conditions have a poorer outcome once

hospitalized with COVID-19 [13]. The absolute differences in predicting myocardial injury were more apparent in the cardiovascular-risk-factor group versus the no-risk-factor group, even after adjusting the model for age and sex (78.5% vs. 52.0%; OR, 1.98 [1.45–2.70]). Similarly, a retrospective study involving hospitalized patients with COVID-19 demonstrated that cardiovascular diseases were more prevalent in patients with higher troponin concentrations [11]. In contrast to our findings, a cohort study in a multicenter setting showed that preexisting cardiac conditions had no relations with cardiac injury according to a multivariate logistic regression [14]. It is possible that previous cardiac conditions cannot influence a patient's current myocardial injury in patients with younger age despite having severe infection with COVID-19. It is also possible that differences in the patient's age along with other comorbidities may have contributed to these findings. Moreover, SARS-CoV-2 infection incites a profound inflammatory response that may cause tissue injury, leading to myocardial damage [15].

In hospitalized patients with COVID-19, myocardial injury decreased the probabilities of survival until hospital discharge with a higher need for ICU admission as compared with no-myocardial-injury patients [16]. Checking troponin levels was useful among older individuals regardless of their cardiac-related comorbidities [17]. Increased length of hospital stay (median days, 5 [3–9] vs. 4 [2–7]) and ICU admission (46.2% vs. 31.4%) occurred more frequently in the myocardial-injury group. Based on these findings, for every 100 hospitalized patients, patients with higher troponin levels would be anticipated to result in 15 additional ICU admissions until hospital discharge with an overall increased length of stay. Among patients hospitalized with COVID-19, an initial strategy to check troponin levels regardless of their age, sex, and illness severity may help stratify the patient's use of the ICU until hospital discharge.

In our analysis after multivariable adjustment, we did not find a significant association between myocardial injury and in-hospital mortality. Our finding that myocardial injury was not a predictor of in-hospital mortality suggests that the higher mortality among these populations may be driven by COVID-19-associated illness severity rather than the cardiac injury itself. Our analysis also suggests that ICU admission was significantly associated with higher troponin levels. Although we did not observe any association with mortality among these populations, further measures are needed to define the burden of morbidity from concomitant COVID-19 and myocardial injury.

In our retrospective analysis, we used an unadjusted analysis and logistic regression model adjusted for multiple variables that allowed us to simultaneously compare myocardial-injury predictors and in-hospital mortality accurately. Multivariate logistic regression allowed us to reach the conclusion more accurately and mitigate the influence of other confounders. The nature of retrospective design may have led to an imbalance in baseline characteristics and selection bias between cases and controls; the logistic regression models were, therefore, adjusted for age, sex, and comorbidities. Therefore, crude odds ratio and adjusted odds ratio were calculated. The potential for information and selection biases could not be excluded from the outcomes of in-hospital mortality or ICU admission. Along with these factors, the absence of information verification provided by EMR to chart review may have contributed to increased confounding bias. Furthermore, elevated troponin can also be seen in subclinical pulmonary embolism, which could not be ruled out. In addition, myocardial injury was not confirmed by abnormal electrocardiogram or echocardiogram. The CT value calculated via SARS-CoV-2 RT PCR could have given an in-depth insight into the viral load's impact on cardiovascular injury, but the CT value was not available to be reported. Thus, it was not possible to fully assess the generalizability of our findings. In addition, in our data, 80% of the population was white, which could be a limiting factor for our study to be generalized. We reported findings by race, sex, and ethnicity in this dataset from self-reported clinical records. Given that this study was based on hospitalized patients, it lacks generalizability to non-hospitalized patients.

5. Conclusions

This study aimed to evaluate the disease course and outcome in hospitalized COVID-19 patients with and without myocardial injury. We aimed to assess predictive risk factors for cardiac injury. The association between prior cardiac diseases and cardiac risk factors was found to be a strong predictor of higher troponin levels. Myocardial injury was more strongly associated with ICU admission. Though in-hospital mortality was initially thought to be higher among myocardial-injury patients (22.8% vs. 11.6%), when adjusted for comorbidities we could not find a statistically significant difference in in-hospital mortality. Importantly, apart from ICU admission and length of hospital stay, none of the other outcomes were associated with myocardial injury. Therefore, further research is needed to understand whether all patients with myocardial injury should be defined as a group at risk, certainly when viewed in the context of other demographic factors such as age, sex, and concomitant illnesses, as these appear to contribute to COVID-19 outcome to a much larger extent than cardiac injury itself.

Author Contributions: Conceptualization, G.P., J.S., L.B. and M.A. (Mario Affinati); Writing, G.P., A.V., S.R., S.J., G.H., M.A. (Michael Araya) and S.A.; Data analysis, G.P., A.V., S.R., S.J., G.H., M.A. (Michael Araya) and S.A.; Intellectual content, G.P.; Critical feedback and editing, J.S., L.B. and M.A. (Mario Affinati). All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: IRB approval was obtained from Mercyhealth Corporation and University of Illinois college of Medicine, Rockford. IRB (FWA00005607) (IRB000000616) Project# 1755831-1; Reference# 21030.

Informed Consent Statement: Though this article does not contain any studies with the direct involvement of human participants or animals performed by any of the authors, the ethical standards of the institutional and/or national research committee were in accordance with the 1975 Helsinki Declaration.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Fu, L.; Li, X.Y.; Fei, J.; Xiang, Y.; Xiang, H.X.; Li, M.D.; Liu, F.F.; Li, Y.; Zhao, H.; Xu, D.X. Myocardial injury at early stage and its association with the risk of death in COVID-19 patients: A hospital-based retrospective cohort study. *Front. Cardiovasc. Med.* **2020**, *7*, 590688. [CrossRef] [PubMed]
2. Abbasi, J. Researchers Investigate What COVID-19 Does to the Heart. *JAMA* **2021**, *325*, 808. [CrossRef] [PubMed]
3. Myocardial Injury in Patients Hospitalized with COVID-19—American College of Cardiology. Available online: https://www.acc.org/latest-in-cardiology/journal-scans/2020/07/27/15/17/prevalence-and-impact-of-myocardial-injury (accessed on 17 January 2022).
4. Fu, L.; Liu, X.; Su, Y.; Ma, J.; Hong, K. Prevalence and impact of cardiac injury on COVID-19: A systematic review and meta-analysis. *Clin. Cardiol.* **2020**, *44*, 276–283. [CrossRef] [PubMed]
5. Maino, A.; Di Stasio, E.; Grimaldi, M.C.; Cappannoli, L.; Rocco, E.; Vergallo, R.; Biscetti, F.; Baroni, S.; Urbani, A.; Landolfi, R.; et al. Prevalence and characteristics of myocardial injury during COVID-19 pandemic: A new role for high-sensitive troponin. *Int. J. Cardiol.* **2021**, *338*, 278–285. [CrossRef]
6. Mokhtari, T.; Hassani, F.; Ghaffari, N.; Ebrahimi, B.; Yarahmadi, A.; Hassanzadeh, G. COVID-19 and multiorgan failure: A narrative review on potential mechanisms. *Histochem. J.* **2020**, *51*, 613–628. [CrossRef]
7. Long, J.; Luo, Y.; Wei, Y.; Xie, C.; Yuan, J. The effect of cardiovascular disease and acute cardiac injury on fatal COVID-19: A meta-analysis. *Am. J. Emerg. Med.* **2021**, *48*, 128–139. [CrossRef] [PubMed]
8. Wei, Z.; Geng, Y.; Huang, J.; Qian, H. Pathogenesis and management of myocardial injury in coronavirus disease 2019. *Eur. J. Heart Fail.* **2020**, *22*, 1994–2006. [CrossRef] [PubMed]
9. Patel, G.; Affinati, M.; Smith, J.; Baloch, L.; Aqeel, A. Mechanisms of cardiovascular injuries in SARS-CoV-2 infection. *Int. J. Cardiol. Cardiovasc. Dis.* **2022**, *2*, 1–5. Available online: https://probiologists.com/Article/Mechanisms-of-cardiovascular-injuries-in-SARS-CoV-2-infection (accessed on 1 June 2022).

10. Nicin, L.; Abplanalp, W.T.; Mellentin, H.; Kattih, B.; Tombor, L.; John, D.; Schmitto, J.D.; Heineke, J.; Emrich, F.; Arsalan, M.; et al. Cell type-specific expression of the putative SARS-CoV-2 receptor ACE2 in human hearts. *Eur. Heart J.* **2020**, *41*, 1804–1806. [CrossRef] [PubMed]
11. Reynolds, H.R.; Adhikari, S.; Pulgarin, C.; Troxel, A.B.; Iturrate, E.; Johnson, S.B.; Hausvater, A.; Newman, J.D.; Berger, J.S.; Bangalore, S.; et al. Renin–angiotensin–aldosterone system inhibitors and risk of COVID-19. *N. Engl. J. Med.* **2020**, *382*, 2441–2448. [CrossRef] [PubMed]
12. Lala, A.; Johnson, K.W.; Januzzi, J.L.; Russak, A.J.; Paranjpe, I.; Richter, F.; Zhao, S.; Somani, S.; Van Vleck, T.; Vaid, A.; et al. Prevalence and Impact of Myocardial Injury in Patients Hospitalized With COVID-19 Infection. *J. Am. Coll. Cardiol.* **2020**, *76*, 533–546. [CrossRef] [PubMed]
13. Guo, T.; Fan, Y.; Chen, M.; Wu, X.; Zhang, L.; He, T.; Wang, H.; Wan, J.; Wang, X.; Lu, Z. Cardiovascular Implications of Fatal Outcomes of Patients with Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol.* **2020**, *5*, 811–818. [CrossRef] [PubMed]
14. The CAPACITY-COVID Collaborative Consortium and LEOSS Study Group; Linschoten, M.; Uijl, A.; Schut, A.; Jakob, C.E.M.; Romão, L.R.; Bell, R.M.; McFarlane, E.; Stecher, M.; Zondag, A.G.M.; et al. Clinical presentation, disease course, and outcome of COVID-19 in hospitalized patients with and without pre-existing cardiac disease: A cohort study across 18 countries. *Eur. Heart J.* **2021**, *43*, 1104–1120. [CrossRef]
15. Ferro, M.D.; Bussani, R.; Paldino, A.; Nuzzi, V.; Collesi, C.; Zentilin, L.; Schneider, E.; Correa, R.; Silvestri, F.; Zacchigna, S.; et al. SARS-CoV-2, myocardial injury and inflammation: Insights from a large clinical and autopsy study. *Clin. Res. Cardiol.* **2021**, *110*, 1822–1831. [CrossRef] [PubMed]
16. Qian, H.; Gao, P.; Tian, R.; Yang, X.; Guo, F.; Li, T.; Liu, Z.; Wang, J.; Zhou, X.; Qin, Y.; et al. Myocardial Injury on Admission as a Risk in Critically Ill COVID-19 Patients: A Retrospective in-ICU Study. *J. Cardiothorac. Vasc. Anesth.* **2021**, *35*, 846–853. [CrossRef] [PubMed]
17. de Guadiana-Romualdo, L.G.; Morell-García, D.; Rodríguez-Fraga, O.; Morales-Indiano, C.; Jiménez, A.M.L.P.; Revilla, J.I.G.; Urrechaga, E.; Álamo, J.M.; Holgado, A.M.H.; Lorenzo-Lozano, M.D.C.; et al. Cardiac troponin and COVID-19 severity: Results from BIOCOVID study. *Eur. J. Clin. Investig.* **2021**, *51*, e13532. [CrossRef] [PubMed]