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Original Article

Cardiac Muscle Injury and Echocardiographic Plus Electrocardiographic Findings in Patients With 2019 Novel Coronavirus (COVID-19): A Retrospective Cohort Study

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ABSTRACT

Background: Myocardial injury has been described in coronavirus-2019 (COVID-19). Few studies have reported cardiovascular imaging data with transthoracic echocardiography (TTE) and electrocardiography (ECG) findings in COVID-19 patients, and their correlation with mortality.

Methods: We conducted a retrospective cohort study that included COVID-19 patients from March 2020 through February 2021 who had TTE and ECG during hospital admission. Myocardial injury was defined by an elevated high-sensitivity troponin T level > 20 ng/L. Bivariate analysis was used to compare patients with myocardial injury and those without. Multivariate logistic regression analysis was performed

RÉSUMÉ

Contexte : Des atteintes myocardiques ont été décrites en présence d'une infection par le coronavirus 2019 (COVID-19). Quelques études ont rapporté des données d'imagerie cardiovasculaire obtenues par échocardiographie transthoracique (ETT) et électrocardiographie (ECG) chez des patients atteints de la COVID-19, et leur corrélation avec la mortalité.

Méthodologie : Nous avons mené une étude de cohorte rétrospective comprenant des patients atteints de la COVID-19 entre mars 2020 et février 2021 qui ont été soumis à une ETT ou à une ECG pendant leur hospitalisation. L'atteinte myocardique était définie comme un taux élevé de troponine T de haute sensibilité > 20 ng/L. Une analyse à

The 2019 novel coronavirus (COVID-19) has caused a pandemic throughout the world. The most common symptoms are fever, cough, myalgia, fatigue, headache, dyspnea, sore throat, vomiting, and diarrhea. Patients can present with end-stage organ failure, such as acute respiratory distress syndrome (ARDS), shock, and acute kidney injury, which can lead to hospitalization and death.[1] Myocardial involvement is common in patients hospitalized with COVID-19, and it is associated with worse outcomes. Yet, why myocardial injury occurs in some patients and not in others is still unclear. Various mechanisms and theories have been considered to explain this injury. These explanations include cytokine-mediated damage, oxygen supply–demand imbalance, ischemic injury from microvascular thrombi formation, and

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to identify the variables associated with mortality.

Results: A total of 438 patients were included. The mean age was 62.1 ± 14.9 years, and 58.9% were male. A total of 149 patients died, with a mortality rate of 34%. A total of 260 patients (59.4%) had myocardial injury. The average left ventricular ejection fraction was 59.8% ± 11.2%, with 30 patients (6.8%) having an ejection fraction of < 40%. Patients with myocardial injury had higher mortality than those without ($P < 0.05$, χ^2 test). A multiple regression analysis model indicated that age, race and/or ethnicity, the development of acute respiratory distress syndrome, shock, the need for vasopressors, mechanical ventilation, and hemodialysis were the variables significantly associated with mortality.

Conclusion: COVID-19 patients with myocardial injury had higher mortality than those without. Age, race and/or ethnicity, acute respiratory distress syndrome, shock, the need for vasopressors, mechanical ventilation, and hemodialysis were the clinical variables associated with mortality. The TEE and ECG variables studied were not significantly associated with mortality.

deux variables a été utilisée pour comparer les patients présentant une atteinte myocardique et ceux qui n'en présentaient pas. Une analyse de régression logistique à multiples variables a été menée pour définir les variables qui étaient associées à la mortalité.

Résultats : L'étude comptait un total de 438 patients. L'âge moyen était de 62,1 ± 14,9 ans; 58,9 % étaient des hommes. Un total de 149 patients sont décédés, soit un taux de mortalité de 34 %. Un total de 260 patients (59,4 %) présentaient une atteinte myocardique. La fraction d'éjection ventriculaire gauche moyenne était de 59,8 % ± 11,2 %, alors que 30 patients (6,8 %) affichaient une fraction d'éjection inférieure à 40 %. Le taux de mortalité était plus élevé chez les patients qui présentaient une atteinte myocardique que chez ceux qui n'en présentaient pas ($p < 0,05$, test χ^2). Selon un modèle d'analyse de régression multiple, l'âge, la race et/ou l'ethnicité, l'apparition du syndrome de détresse respiratoire aiguë, l'état de choc, le besoin de vasopresseurs, la ventilation artificielle et l'hémodialyse étaient les variables fortement liées à la mortalité.

Conclusion : Parmi les patients atteints de la COVID-19, la mortalité était plus élevée chez ceux qui présentaient une atteinte myocardique que chez ceux qui n'en présentaient pas. L'âge, la race et/ou l'ethnicité, le syndrome de détresse respiratoire aiguë, l'état de choc, le besoin de vasopresseurs, la ventilation artificielle et l'hémodialyse étaient les variables cliniques liées à la mortalité. Les variables d'ETT et d'ECG étudiées n'avaient pas de lien important avec la mortalité.

direct viral invasion of the myocardium.[2-4] Given that few magnetic resonance imaging studies have been done in these patients, owing to COVID-19 exposure restrictions, biomarker evidence of troponin-level elevation has been used as a sign of cardiac involvement.[5-7] Few studies have reported cardiovascular imaging data, such as transthoracic echocardiography (TTE) and electrocardiography (ECG) findings, in patients with COVID-19.[8] Our study highlights the association between myocardial injury in COVID-19 patients and mortality. Also, the study investigated the correlation between cardiovascular imaging, such as ECG and TTE, and myocardial injury in COVID-19 patients. In addition, the study analyzed the significant clinical variables associated with mortality in these patients.

Methods

Study site

A single-centre retrospective cohort study was conducted by investigators at Texas Tech University Health Sciences Center on patients hospitalized in its affiliated hospital, University Medical Center (UMC) in Lubbock, Texas, which serves a large population in West Texas, New Mexico, and Oklahoma.

Ethics statement

The study was approved by the institution's institutional review board (IRB#: L21-149).

Subjects

We included adult patients (aged > 21 years) admitted between March 1, 2020 and February 28, 2021 who were diagnosed with COVID-19 and had a TTE and an ECG done during their hospital admission. Data were collected retrospectively from the medical records. We excluded vulnerable patients, such as children, prisoners, and pregnant women.

Design

A retrospective cohort study was conducted on patients hospitalized at University Medical Center in Lubbock, Texas. After subjects were identified, their records were retrieved from electronic medical records. We included more than 56 variables, including baseline demographics, chronic medical problems, relevant baseline biochemical markers on admission and the peak levels during hospitalization, the complications that developed during hospital admission that might affect mortality, and the TTE and ECG findings during the hospital admission. We measured the left ventricular ejection fraction via 2D TTE by the modified Simpson method, always using ultrasound-enhancing contrast. The data collected were revalidated by another independent researcher.

Analysis

We defined COVID-19 patients with myocardial injury as those with increased high-sensitivity cardiac troponin T (hs-cTnT) levels, > 20 ng/L, which is above the upper reference limit for the assay. We used the peak value of hs-cTnT measured during hospital admission. Conversely, those without myocardial injury were defined as those with an hs-cTnT level of < 20 ng/L. Although the definitive diagnosis of myocarditis and/or myocardial injury requires magnetic resonance imaging, this imaging was not feasible in most cases, owing to COVID-19 pandemic restrictions; hence, we considered an elevated level of hs-cTnT to be a sign of myocardial injury.

We compared the 2 groups regarding their baseline demographics, relevant biochemical markers on admission and the peak level during hospitalization, complications during hospital admission, TTE, and ECG. Histograms and box plots were used to assess the normality of data distribution. Categorical variables are presented as numbers and percentages; continuous variables are presented as medians and interquartile ranges or means and standard deviations.

We used the Statistical Package for Social Sciences (SPSS, version 25, IBM, Armonk, NY) for data analysis. A P value $<$ 0.05 was considered statistically significant. Bivariate analysis was used to study the differences between patients with myocardial injury and those without myocardial injury, regarding all variables. A χ^2 test was used for categorical variables, and a Student t test was used for continuous variables after histograms and box plots showed normally distributed data.

Multivariate logistic regression analysis was performed to identify the significant variables associated with mortality and identify potential confounders. Clinically significant variables based on previous literature review and a significant P value in the bivariate analysis were included in the multivariate analysis. The primary outcome was in-hospital mortality for the multivariate analysis. Results of the logistic regression models are reported as odds ratios (ORs) and their corresponding 95% confidence intervals (CIs).

Time-to-event analysis was carried out using the Kaplan-Meier curve, with censoring performed at either discharge date or death.

Results

Baseline characteristics

We included 438 patients who had COVID-19 and had a TTE done during their hospital admission. The mean age was 62.1 ± 14.9 years. Of 438 subjects, 258 (58.9%) were male. Most of our patients were Hispanic (n = 180; 41.1%) or White (n = 170; 38.4%; Table 1).

Table 1. Baseline demographics, including chronic medical problems

Characteristic	Value
Age, y, mean (SD)	62.1 (14.9)
Gender	
Female	180 (41.1)
Male	258 (58.9)
Race	
Hispanic/Latino	180 (41.1)
White	170 (38.4)
Other/refused to reveal	67 (15.3)
African American	21 (4.8)
BMI, kg/m^2, mean (SD)	32.6 (9.1)
< 25	75 (17.1)
25−30	115 (26.6)
30−35	117 (26.6)
35−40	63 (14.5)
≥ 40	68 (15.2)
Diabetes	231 (52.7)
Hypertension	298 (68.0)
Congestive heart failure	56 (12.8)
Coronary artery disease	101 (23.1)
CABG	18 (17.8)
CABG stent	4 (4.0)
Just medical treatment	52 (51.5)
Stent	27 (26.7)
COPD or asthma	66 (15.1)
Cancer	21 (4.8)
Immunosuppressive drugs	41 (9.4)
CKD creatinine > 1.5 mg/d or CL Cr < 60 mL/min	78 (17.8)

Values are n (%), unless otherwise indicated.

BMI, body mass index; CABG, coronary artery bypass grafting; CKD, chronic kidney disease; CL Cr, creatinine clearance; COPD, chronic obstructive pulmonary disease; SD, standard deviation.

Biochemical markers

Relevant biochemical markers, including N-terminal pro-brain natriuretic peptide (NT-proBNP) if available, on admission and during hospitalization, are reported in Table 2. These values are reported as the median and interquartile range (IQR) because they were skewed. The median hs-cTnT value was 30.95 ng/L, and the IQR was 100 ng/L. The median NT-proBNP value was 1016.5 pg/mL, and the IQR was 4330 pg/mL.

Complications developed during hospital admission

Of 438 patients, 361 patients (82.4%) required oxygen supplementation during hospitalization, 303 (67.8%) developed ARDS, and 165 (37.7%) required mechanical ventilation. The majority of patients (82.4%) received corticosteroids, and no patients received tocilizumab. The mortality rate was 34% in hospitalized patients who had a TTE scan. Thirteen patients underwent cardiac catheterization, usually after the isolation restrictions were removed (Table 3).

TTE and ECG findings

Of 438 patients, myocardial injury occurred in 260 patients (59.4%). Of 438 patients, 392 (89.5%) were in sinus rhythm, 59 (13.5%) had ST changes, and 8 (1.83%) had ST-elevation (Table 4). Twelve patients had myocardial infarction diagnosed based on chest pain, troponin increase, and TTE showing wall-motion abnormalities. The average left ventricular ejection fraction was 59.8% ± 11.2%. Thirty patients (6.8 %) had an ejection fraction of < 40%, and 32 (7.3%) had an ejection fraction between 40% and 50%. Tricuspid annular plane systolic excursion (TAPSE) was < 1.7 cm in 33 patients (7.5%). Left ventricular diastolic dysfunction was

Table 2. Biochemical markers on admission and during hospitalization

Lab test results	Median	IQR
Peak NT-proBNP, pg/mL	1016.5	4330
Baseline Troponin, ng/L	18.25	33
Peak Troponin, ng/L)	30.95	100
Baseline ESR, mm/h	53	41
Peak ESR, mm/h	74.5	55
Baseline CRP, mg/dL)	11.5	14
Peak CRP, mg/dL	14.15	20
Baseline D-dimer, ng/mL	1159	1415
Peak D-dimer, ng/mL	2543	10,409

Interquartile range (IQR) is quartile 3−quartile 1.

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; NT-proBNP, N-terminal pro-brain natriuretic peptide.

Table 3. Complications, investigations, and treatment during hospital admission

Complications	n (%)
PE on admission	17 (3.9)
Duplex lower extremity showing DVT	6 (1.4)
ARDS	303 (67.8)
ARDS degree	
Mild ARDS	31 (9.3)
Moderate ARDS	102 (34)
Severe ARDS	170 (56.7)
Deceased	149 (34)
Investigations	
Cardiac catheterization during hospitalization	13 (3)
Treatment	
Mechanical ventilation	165 (37.7)
CRRT/hemodialysis	43 (9.8)
Vasopressors	138 (31.5)
Anticoagulation	418 (95.4)
Corticosteroids	361(82.4)

Acute respiratory distress syndrome (ARDS) was defined as follows: partial pressure of oxygen in the arterial blood, in mm Hg—mild = 200−300; moderate = 100−200; severe = < 100,

CRRT, continuous renal replacement therapy; DVT, deep venous thrombosis; PE, pulmonary emboli.

reported in 89 patients (20.3%), but it could not be assessed in 42 patients (9.6%), owing to body habitus. Moderate-to-severe aortic regurgitation was reported in 7 patients (1.6%), and moderate-to-severe mitral regurgitation in 15 patients (3.4%). Pericardial effusion developed in 54 patients (12.3%; Table 4).

Comparison of patients with vs without myocardial injury

Bivariate analysis showed significant differences between the 2 groups in age, race, body mass index (BMI), diabetes, hypertension, congestive heart failure, coronary artery disease (CAD), and chronic kidney disease, with significant $P < 0.05$ (Table 5). Bivariate analysis showed significant differences between the 2 groups in peak NT-proBNP level, baseline troponin level, peak erythrocyte sedimentation rate level, baseline and peak C-reactive protein levels, and baseline and peak D-dimer levels ($P < 0.05$), with those in the myocardial injury group having higher values (Table 6). Bivariate analysis showed a significant difference between the 2 groups in mortality, the need for mechanical ventilation, the development of ARDS, vasopressor requirement, hemodialysis, and cardiac catheterization during hospital admission ($P < 0.05$ for all comparisons), with those in the myocardial injury group more likely to develop these complications (Table 7). The log-rank test was used to compare the mortality rate between the 2 groups and showed a significant difference, as displayed in the Kaplan-Meier curve, with the myocardial injury population associated with worse survival (Fig. 1). The administration of corticosteroids was not significantly different between the 2 groups. The bivariate analysis revealed that patients with myocardial injury had significantly higher rates of ST changes, T wave changes, diastolic dysfunction, right ventricular dysfunction, and left ventricular wall motion abnormalities. In addition, they had significantly lower left ventricular ejection fraction and higher pulmonary artery systolic pressure ($P < 0.05$; Table 8).

Table 4. Transthoracic echocardiography and electrocardiographic (ECG) findings during hospital admission

ECG and echocardiography	Value
Sinus rhythm	392 (89.5)
Atrial flutter or fibrillation	46(10.5)
ST changes	59 (13.5)
Nature of ST changes	
Nonspecific changes	40 (67.8)
ST depression	11 (18.6)
ST elevation	8 (13.6)
T wave changes	114 (26.0)
Myocardial infarction	12 (2.7)
LVEF, %, mean (SD)	59.8 (11.2)
< 40	30 (6.8)
40−50	32 (7.3)
> 50	376 (85.8)
TAPSE, cm, mean (SD)	2.3 (1.7)
< 1.7	33 (7.5)
≥ 1.7	405 (92.5)
Diastolic dysfunction	
Yes	89 (20.3)
No	307 (70.1)
Cannot be assessed	42 (9.6)
Grade of diastolic dysfunction	
1	72 (80.9)
2	15 (16.9)
3	2 (2.2)
Right ventricular dysfunction	25 (36.0)
Pulmonary artery systolic pressure, mm Hg, mean (SD)	25.2 (13.7)
M−S aortic stenosis	0 (0)
M−S aortic regurgitation	7 (1.6)
M−S mitral regurgitation	15 (3.4)
M−S mitral stenosis	0 (0)
LV wall-motion abnormality	43 (9.8)
Apical	7 (16.3)
Basal	1 (2.3)
Global	28 (65.1)
Mid-septal	2 (4.7)
Other	5 (11.6)
Pericardial effusion	54 (12.3)
Trivial	9 (16.7)
Small	41 (75.9)
Moderate	4 (7.4)

Values are n (%), unless otherwise indicated.

LV, left ventricular; LVEF, left ventricular ejection fraction; M−S, moderate-to-severe; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion.

Determinants of mortality

A multivariate regression analysis model was conducted to identify the significant variables associated with mortality and identify potential confounding factors. Age, race and/or ethnicity, the development of ARDS, shock, the need for vasopressors, mechanical ventilation, and the need for hemodialysis were the significant variables associated with mortality, after adjusting for other variables (Table 9).

Discussion

In this retrospective study, we studied the association between myocardial injury in COVID-19 patients and mortality. Also, we analyzed the correlation between cardiovascular imaging, such as ECG and TTE, and myocardial injury in

Table 5. Bivariate analysis of baseline demographics in patients with myocardial injury, compared to patients without myocardial injury

	Total	Troponin Level			
		< 20	≥ 20		
Characteristic	n (%)	178 (40.6)	260 (59.4)	OR (95% CI)	*P*
Age, y, Mean (SD)	62.1 (14.9)	56.5 (14.7)	66 (13.7)	1.047	< 0.001*
Gender					
Male	258	97	161	1.36	0.121
Female	180	81	99	ref	
Race					
White	170	55	115	1.045	0.025*
Hispanic and/or Latino	180	88	92	0.523	
Other or refuse to reveal	66	28	39	0.696	
African American	21	7	14	ref	
BMI, Kg/m^2, Mean (SD)	32.6 (9.1)	33.9 (9.6)	31.7 (8.7)	0.974	0.015*
< 25	75	19	56	ref	0.02*
25−<30	115	48	67	0.474	
30−<35	117	49	68	0.471	
35−<40	63	26	37	0.483	
≥ 40	68	36	32	0.302	
Diabetes					
Yes	231	80	151	1.7	0.007*
No	207	98	109	ref	
Hypertension					
Yes	298	104	194	2.1	< 0.001*
No	140	74	66	ref	
Congestive heart failure					
Yes	56	14	42	2.25	0.012*
No	382	164	218	ref	
Coronary artery disease					
Yes	101	29	72	1.97	0.006*
No	337	149	188	ref	
COPD or asthma					
Yes	66	24	42	1.24	0.443
No	372	154	218	ref	
Cancer					
Yes	21	10	11	0.74	0.506
No	417	168	249	ref	
Immunosuppressive drugs					
Yes	41	14	27	1.36	
No	397	164	233	ref	0.375
Chronic kidney disease					
Yes	78	7	71	9.17	< 0.001*
No	360	171	189	ref	

Values are n, unless otherwise indicated.

BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio; ref, reference comparison; SD, standard deviation.

* $P < 0.05$.

these patients. In addition, we investigated the clinical variables associated with mortality. Since the pandemic began, reports have described the association between COVID-19 and possible myocarditis indicated by increased troponin levels.[9,10] However, few reports have studied the association between COVID-19 and cardiac imaging. Our cohort had an

Table 6. Bivariate analysis of biochemical markers in patients with myocardial injury compared to patients without injury

Biochemical marker	Total	Troponin level			
		< 20	≥ 20		
Value	Median	178 (40.6%)	260 (59.4%)	OR (95% CI)	*P*
Peak NT-ProBNP, pg/mL	1016.5	318	2140	1	0.001*
Baseline troponin, ng/L	18.25	9	34	1.3	< 0.001*
Peak troponin, ng/L	30.95	10.8	78.15	1.02	0.470
Baseline ESR, mm/h	53	51	54	1.01	0.005*
Baseline CRP, mg/dL	11.5	8.5	11.6	1.02	0.02*
Peak CRP, mg/dL	14.15	11.2	17.5	1.02	0.019*
Baseline D-dimer, ng/mL	1159	855	1404	1	0.008*
Peak D-Dimer, ng/mL	2543	1266	4537	1	< 0.001*

CI, confidence interval; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; OR, odds ratio; NT-proBNP, N-terminal pro-brain natriuretic peptide.

* $P < 0.05$.

Table 7. Bivariate analysis of complications, investigations, and treatment in patients with myocardial injury compared to patients without injury

		Troponin level			
		< 20	≥ 20		
Measure	Total	178 (40.6%)	260 (59.4%)	OR (95% CI)	*P*
Complications					
PE on admission					
Yes	17	5	12	1.67	0.341
No	421	173	248	ref	
Duplex lower extremity showing DVT					
Yes	6	3	3	0.67	0.640
No	432	175	257	ref	
ARDS					
Yes	303	105	198	2.22	< 0.001*
No	135	73	62	ref	
ARDS degree†					
Mild, 200−300	31	18	13	ref	0.012*
Moderate, 100−<200	102	42	60	3.8	
Severe, < 100	170	45	125	1.9	
Deceased					
Yes	149	23	126	6.32	< 0.001*
No	289	155	134	ref	
Investigation					
Cardiac catheterization during hospitalization					
Yes	13	1	12	8.54	0.04*
No	425	177	248	ref	
Treatment					
Mechanical ventilation					
Yes	165	31	134	5.05	< 0.001*
No	273	147	126	ref	
Hemodialysis/CRRT					
Yes	43	1	42	34.48	0.001*
No	395	177	218	ref	
Vasopressor					
Yes	138	23	115	5.34	< 0.001*
No	300	155	145	ref	
Anticoagulation					
Yes	418	168	250	0.68	0.383
No	20	10	10	ref	
Corticosteroid					
Yes	361	142	219	1.35	0.23
No	77	36	41	ref	

Values are n, unless otherwise indicated.

ARDS, acute respiratory distress syndrome; CI, confidence interval; CCRT, continuous renal replacement therapy; DVT, deep venous thrombosis; OR, odds ratio; PE, pulmonary emboli; ref, reference

* $P < 0.05$.

† Partial pressure of oxygen in the arterial blood (PaO_2), mm Hg.

overall mortality of 34% with an incidence of myocardial injury of 59.4%, similar to results of other published studies on this topic.[8,11] Our results showed that those with myocardial injury likely had reduced ejection fraction, diastolic dysfunction, right ventricle dysfunction, elevated right ventricular systolic pressure, and wall-motion abnormalities. Bivariate analysis indicated a significant difference between patients with vs without myocardial injury in ST changes, T wave changes, left ventricular ejection fraction, diastolic dysfunction, right ventricular dysfunction, mean pulmonary artery systolic pressure, and left ventricular wall-motion abnormality, with worse hemodynamic parameters in the patients with elevated troponin levels. However, based on the multiple regression analysis model, echocardiographic changes were not among the variables associated with mortality, in contrast to some published data that showed an association with mortality.[8] Our results indicate that age, race and/or ethnicity, the development of ARDS, shock, the need for vasopressors, mechanical ventilation, and hemodialysis were the significant variables associated with mortality. These results suggest that multi-organ dysfunction and/or failure had the most significant effect on mortality, and that echocardiographic findings and ECG changes were more likely confounding factors rather than independent predictors. However, the presence of myocardial injury and/or myocardial dysfunction on ECG and/or TTE still requires attention in managing these patients.

Other studies have also evaluated cardiac injury in patients with COVID-19 infection. Giustino et al. reported that echocardiographic findings had an important association with mortality. That study included only patients with severe ARDS; our study was not limited to this subgroup of patients.[8] However, our study population did have severe clinical illness, often required oxygen, and had a higher mortality

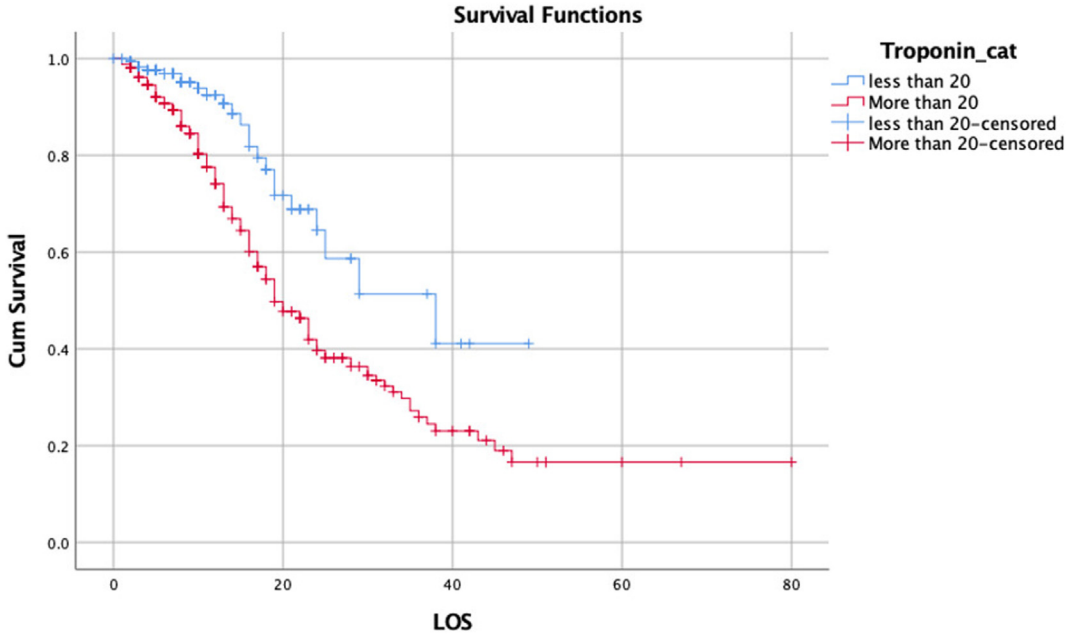

Figure 1. Kaplan-Meier curve showing a significant difference between myocardial injury vs no myocardial injury and mortality, with the myocardial injury population associated with worse survival. The **vertical lines** indicate censored. Cum, cumulative; LOS, length of stay; Troponin_cat, troponin level category.

rate. Another study by Jain et al. also investigated the echocardiographic findings in patients with COVID-19. Their study included only 72 patients and did not analyze the echocardiographic findings in relation to myocardial injury, or their correlation with mortality. Also, their cohort included a higher percentage of patients (34.7%) with an ejection fraction $\leq$ 50%.[12]

Several studies have investigated myocarditis using cardiovascular magnetic resonance imaging (CMR). Esposito et al. included 10 patients, and CMR in all of them showed diffuse intense myocardial edema. All the patients were discharged home with no deaths.[6] Galea et al. studied 27 patients and reported that 74% of patients had tissue signal abnormalities, such as late gadolinium enhancement (n = 12) or pericardial enhancement (n = 2). These CMR studies were done approximately 20 days after the COVID-19 diagnosis.[7] Their data did not include mortality outcomes or prognostic indicators in their patients; 26 of 27 patients had mild disease. Our study did not include CMR during the hospital admission, but an important point to stress is that this troponin increase above the normal level provides a practical indicator of myocardial injury and a factor to consider regarding the possible need for additional testing.

Our results demonstrated that 12.3% of the patients had pericardial effusions. These pericardial effusions were moderate in 4 patients, small in 41 patients, and trivial in 9 patients. The pathogenesis underlying the development of these effusions is uncertain; the results in this study are similar to results published by Giustino et al.[8] More studies with CMR in COVID-19 patients with pericardial effusion could help explain why the effusion occurs in some patients and not others, to identify potential underlying mechanisms. In addition, long-term follow-up of patients with pericardial effusions should provide information about their clinical importance.

An elevated troponin level is a useful guide for myocardial injury, but it is not specific for myocarditis. The difference in interpretation of the 2 terms in COVID-19 patients has created some confusion. A study done by Halushka et al. showed that myocarditis is rare in COVID-19 autopsies in postmortem hearts.[13] Their literature review included 277 autopsies from 22 separate publications on COVID-19-positive patients. The data showed that 20 hearts (7.2%) had myocarditis. However, closer examination of the report details revealed that most cases were not functionally important, and the true prevalence of myocarditis was likely much lower (< 2%).[13] At least one acute, potentially COVID-19-related cardiovascular histopathologic finding, such as macro or microvascular thrombi, inflammation, or intraluminal megakaryocytes, was reported in 47.8% of cases.[13] However, the studies have significant differences in the reporting of histopathologic findings, suggesting differences in analysis and reporting and the need for more consistent reporting.[13] Hence, we have used the term myocardial injury or troponin level elevation, rather than myocarditis, in this report. Indeed, troponin level elevation may help identify patients with worse clinical outcomes. An elevated troponin level presents a clinical dilemma in patients who develop acute coronary syndrome during a COVID-19 infection, as the troponin level alone cannot be used as a guide. Therefore, doctors should use the constellation of chest pain, a troponin increase, and TTE showing wall-motion abnormalities to consult cardiologists regarding acute coronary syndrome.

COVID-19 is a systemic disease with organ dysfunction secondary to both infection and inflammation. Myocardial injury seems to correlate with the severity of the clinical

Table 8. Bivariate analysis of echocardiographic and electrocardiographic findings in patients with myocardial injury compared to patients without injury

		Troponin level			
		< 20	≥ 20		
Measure	Total	178 (40.6%)	260 (59.4%)	OR (95% CI)	*P*
Sinus rhythm					
Yes	392	163	229	0.68	0.243
No	46	15	31	ref	
Atrial flutter and/or fibrillation					
Yes	44	14	30	1.52	0.212
No	394	164	230	ref	
ST changes					
Yes	59	15	44	2.22	0.012*
No	379	163	215	ref	
T wave changes					
Yes	114	29	85	2.49	< 0.001*
No	324	149	175	ref	
Nature of ST changes					
Nonspecific	40	7	33	2.82	0.118
ST depression	11	5	6	0.729	
ST elevation	8	3	5	ref	
LVEF, %, mean (SD)	59.8 (11.2)	61.23 (8.4)	58.8 (12.6)	0.980	0.028*
< 40	30	4	26		
40–50	32	10	22		
> 50	376	164	212		
TAPSE, cm, mean (SD)	2.3 (1.7)	2.37 (1.34)	2.31 (1.93)	0.981	
< 1.7	33	6	27	ref	0.009*
≥ 1.7	405	172	233	0.301	
Diastolic dysfunction					
Yes	89	27	62	0.620	0.032*
No	307	137	170	1.148	
Cannot be assessed	42	14	28	ref	
Right ventricular dysfunction					
Yes	33	6	27	3.32	0.009*
No	405	172	233	ref	
RVSP, Mm Hg, mean (SD)	25.2 (13.7)	22.6 (12.5)	26.9 (14.2)	1.025	0.009*
PASP ≤ 25 mm Hg	328	145	183	ref	0.009*
PASP > 25 Mm Hg	110	33	77	1.85	
Moderate-to-severe aortic regurgitation					
Yes	7	4	3	0.51	0.379
No	431	174	257	ref	
Moderate-to-severe mitral regurgitation					
Yes	15	7	8	0.77	0.629
No	423	171	252	ref	
LV wall-motion abnormality					
Yes	43	7	36	3.92	0.001*
No	395	171	224	ref	
If yes					
Apical	7	1	6	ref	0.06
Basal	1	0	1	4.5	
Global	28	4	24	1.2E+9	
Mid-septal	2	1	1	4.5	
Other	5	1	4	3.1	

Values are n, unless otherwise indicated.

LV, left ventricle; LVEF, left ventricular ejection fraction; PASP, pulmonary arterial systolic pressure; ref, reference comparison; RVSP, right ventricular systolic pressure; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion.

* $P < 0.05$.

manifestations of COVID-19, but the degree of injury likely varies from patient to patient. Although the exact cause of myocardial injury is not completely understood, various mechanisms have been suggested. These include cytokine-mediated myocardial damage, oxygen supply–demand imbalance, microvascular and macrovascular thrombosis, endothelial damage, and direct viral invasion of the myocardium. This virus enters human cells by attaching to the angiotensin-converting enzyme 2 receptor (ACE2) found in multiple tissues, including cardiovascular, renal, and lung tissues.[14,15] Viral RNA enters the cell nucleus for replication after penetration and causes apoptosis, which could explain the troponin level elevation. However, immunologic responses in humans vary, which explains the diverse clinical presentations, with greater cytokine levels being present in the plasma in severe cases.[14,15]

Table 9. Multivariate regression analysis with mortality as outcome

Characteristic	Intercept	SE	Wald	P	OR
Age	0.057	0.012	23.327	< 0.001*	0.945
BMI group (> 40)					
< 25	−0.106	0.529	0.04	0.842	0.9
25−<30	0.823	0.486	2.863	0.091	2.277
30−<35	0.473	0.468	1.02	0.312	1.604
35−<40	0.57	0.519	1.207	0.272	1.769
Race and/or ethnicity (African American)			8.968	0.062	
Hispanic and/or Latino	−1.992	0.901	4.886	0.027*	0.136
Other or refused to reveal	21.621	42.969	0	1	24
White	0.486	0.327	2.213	0.137	1.626
Diabetes	0.248	0.301	0.68	0.41	1.282
Hypertension	−0.3	0.33	0.83	0.362	0.741
Congestive heart failure	−0.029	0.451	0.004	0.948	0.971
Chronic kidney disease	−0.736	0.378	3.785	0.052	0.479
Mechanical ventilation	−1.083	0.366	8.738	0.003*	0.339
Vasopressor	−1.298	0.349	13.848	< 0.001*	0.273
ARDS	−1.82	0.445	16.755	< 0.001*	0.162
Right ventricular function	−0.765	0.544	1.979	0.159	0.465
LV wall-motion abnormality	0.238	0.495	0.23	0.631	1.268
Hemodialysis	−1.368	0.513	7.097	0.008*	0.255
Constant	1.996	1.451	1.891	0.169	7.358

ARDS, acute respiratory distress syndrome; BMI, body mass index; LV, left ventricle; LVEF, left ventricular ejection fraction; OR, odds ratio.
* $P < 0.05$.

Several factors contribute to the strength of the study; these include the number of patients compared to that in other published studies, the inclusion of more than 56 variables in the data collection, and adjustment for most factors that might explain the difference in mortality between those with vs without myocardial injury. In addition, our data were validated by 2 independent researchers. However, our study did have several limitations. First, it is a single-centre, retrospective study that may have missing data or unrecognized confounders. Second, no guidelines were used to determine whether TTE was ordered on our patients; some patients may have had TTE ordered as a routine test upon medical intensive care unit admission. Third, no long-term follow-up data are available for our patients with myocardial injury. Some patients with baseline CAD and congestive heart failure likely were admitted for the first time to our hospital during their COVID-19 infections; hence, the reported TTE was the only one available, and the exact number of patients with previous ECG and/or TTE changes cannot be determined. However, adjusting for the comorbidity variables in the multivariate analysis should minimize possible confounding or bias in these results. In addition, the majority of the patients in this study had preserved ejection fraction and only grade-1 diastolic dysfunction. Finally, information about the time when peak biomarkers occurred and their exact correlation with the troponin level was not collected.

Conclusions

COVID-19 patients with myocardial injury tend to have a higher mortality rate than those without myocardial injury. Age, race and/or ethnicity, the development of ARDS, shock, the need for vasopressors, mechanical ventilation, and the need for hemodialysis were significantly associated with mortality in this cohort of patients with COVID-19. The TTE and ECG variables studied did not appear to be associated with mortality. More studies need to compare echocardiographic findings during COVID-19 infection with baseline TTE before infection, especially in patients with CAD and congestive heart failure, and they need to evaluate cardiac complications in long-term COVID-19 patients. CMR imaging studies might provide the best answers.

Ethics Statement

The study was approved by the institution's Institutional Review Board (IRB #: L21-149).

Patient Consent

The authors confirm that patient consent is not applicable to this article. This is a retrospective cohort study using de-identified data; therefore, the IRB did not require consent from the patient.

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