Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Cardiothoracic and Vascular Anesthesia 35 (2021) 3581–3593

Contents lists available at ScienceDirect

Journal of Cardiothoracic and Vascular Anesthesia

journal homepage: www.jcvaonline.com

Original Article

Outcomes and Risk Factors for Cardiovascular Events in Hospitalized COVID-19 Patients

Qian Xu, MS[*], Harideep Samanapally, MBBS[†], Pavani Nathala, MBBS[†], Vidyulata Salunkhe, MBBS, MPH[†], Stephen Furmanek, MS[†], Meredith N. Cahill, BA[†,‡], Trevor McGuffin, BSN[§], Tahboub Mohammad, MD[†], Bradford Marsili, DO[¶], Jessica Petrey, MLS[#], Ruth Carrico, PhD[†], Julio Ramirez, MD[†], Ozan Akca, MD[¶], Sean P. Clifford, MD[¶], Siddharth Pahwa, MD[‖], Lynn Roser, PhD[§], Maiying Kong, PhD[*], Jiapeng Huang, MD, PhD[†,¶,‖,**,1], the Center of Excellence for Research in Infectious Diseases (CERID) Coronavirus Study Group on behalf of the COVID-19 CardioVascular Research Group (COVID-CVRG)

[*]*Department of Bioinformatics and Biostatistics, School of Public Health and Information Sciences, University of Louisville, Louisville, KY*
[†]*Division of Infectious Diseases, Center of Excellence for Research in Infectious Diseases (CERID), University of Louisville, Louisville, KY*
[‡]*School of Medicine, University of Louisville, Louisville, KY*
[§]*School of Nursing, University of Louisville, Louisville, KY*
[¶]*Department of Anesthesiology & Perioperative Medicine, University of Louisville, Louisville, KY*
[#]*Kornhauser Health Sciences Library, University of Louisville, Louisville, KY*
[‖]*Department of Cardiovascular & Thoracic Surgery, University of Louisville, Louisville, KY*
[**]*Center for Integrative Environmental Health Sciences, University of Louisville, Louisville, KY*

Research reported in this publication was supported by the National Center For Advancing Translational Sciences of the National Institutes of Health under Award Number U18TR003787. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Jiapeng Huang is supported by NIH P30 (P30ES030283) grant. Jiapeng Huang is supported by Gilead Sciences COMMIT COVID-19 RFP Program grant (Gilead IN-US-983-6063). Jiapeng Huang is supported National Center for Advancing Translational Sciences grant 1U18TR003787-01.

L. Roser, M. Kong, and J. Huang contributed equally to this work. Q. Xu, H. Samanapally, P. Nathala, and V. Salunkhe contributed equally and are co-First Authors. J. Petrey, R. Carrico, J. Ramirez, O. Akca, S.P. Clifford, L. Roser, M. Kong, and J. Huang are Senior Authors.

Author contributions: Qian Xu: study design, statistical analysis, manuscript preparation. Harideep Samanapally, Pavani Nathala, Vidyulata Salunkhe: study design, data collection, manuscript preparation. Stephen Furmanek: study design, statistical analysis, manuscript preparation. Meredith N. Cahill, Trevor McGuffin, Tahboub Mohammad: study design, data collection. Bradford Marsili: study design, manuscript preparation. Jessica Petrey: literature review, study design, manuscript preparation. Ruth Carrico, Julio Ramirez, Ozan Akca, Sean P. Clifford, Siddharth Pahwa, Lynn Roser, Maiying Kong, Jiapeng Huang: Study design, data analysis, manuscript preparation. Data collection was performed by the Center of Excellence for Research in Infectious Diseases (CERID) group at the University of Louisville Division of Infectious Diseases. Statistical analysis and draft writing were performed by Qian Xu under the leadership of Maiying Kong. All authors have read and approved the manuscript.

[1]*Address correspondence to* Jiapeng Huang, Department of Anesthesiology & Perioperative Medicine, University of Louisville, 530 South Jackson Street, Louisville, KY 40202.

E-mail address: jiapeng.huang@louisville.edu (J. Huang).

https://doi.org/10.1053/j.jvca.2021.03.035

Objective: To analyze outcomes and risk factors of cardiovascular events in a metropolitan coronavirus disease 2019 (COVID-19) database, and to perform a subgroup analysis in African American populations to determine whether outcomes and risk factors are influenced by race.
Design: Retrospective cohort analysis from March 9, 2020 to June 20, 2020.
Setting: Population-based study in Louisville, KY, USA.
Participants: Seven hundred adult inpatients hospitalized with COVID-19.
Interventions: N/A.
Measurements and Main Results: This cohort consisted of 126 patients (18%) with cardiovascular events and 574 patients without cardiovascular events. Patients with cardiovascular events had a much higher mortality rate than those without cardiovascular events (45.2% *v* 8.7%, $p < 0.001$). There was no difference between African American and white patients regarding mortality (43.9% *v* 46.3%, $p = 1$) and length of stay for survivors (11 days *v* 9.5 days, $p = 0.301$). Multiple logistics regression analysis suggested that male, race, lower $SaO2/F_IO2$, higher serum potassium, lower serum albumin, and number of cardiovascular comorbidities were highly associated with the occurrence of cardiovascular events in COVID-19 patients. Lower serum albumin and neoplastic and/or immune-compromised diseases were highly associated with cardiovascular events for African American COVID-19 patients. $SaO2/F_IO2$ ratio and cardiovascular comorbidity count were significantly associated with cardiovascular events in white patients.
Conclusions: Cardiovascular events were prevalent and associated with worse outcomes in hospitalized patients with COVID-19. Outcomes of cardiovascular events in African American and white COVID-19 patients were similar after propensity score matching analysis. There were common and unique risk factors for cardiovascular events in African American COVID-19 patients when compared with white patients.

Key Words: COVID-19; SARS-CoV-2; cardiovascular; outcome; risk factors; coronavirus

THE FIRST case of severe acute respiratory syndrome-related coronavirus-2 (SARS-CoV-2) was reported in Wuhan, China in December 2019, and coronavirus disease 2019 (COVID-19) was declared a global pandemic by the World Health Organization on March 12, 2020.[1] This disease has resulted in substantial morbidity and mortality across the world.[2] Currently, there are numerous aspects relating to the pathogenesis and clinical course of COIVD-19 infection that remain unclear, as patients may be asymptomatic or have severe clinical manifestations of the disease. While SARS-CoV-2 primarily affects the lungs, it also is known to have significant effects on other organ systems, including the cardiovascular (CV) system; however, knowledge of the CV pathophysiology remains limited.[3,4] Many recent studies reported a higher prevalence of pre-existing CV diseases was associated with worse outcomes and increased risk of death among COVID-19 patients.[5,6,7] Currently, there are not enough data on detailed risk factor analysis in COVID-19 patients who suffered a new clinically diagnosed CV event.[5,8-12]

In addition, minority ethnic groups are reported to experience a higher burden of severe COVID-19 than white individuals, but there is uncertainty about the underlying factors and where risk lies during the disease trajectory. African American individuals have higher circulating biomarkers of systemic inflammation and myocyte injury, and subclinical CV disease occurs at a young age. Thus, African American individuals may be particularly vulnerable to the untoward effects of COVID-19.[13] Previous studies adjusted for clinical and demographic factors but involved aggregate analyses over large geographic regions and did not control for the wide local variations in ethnic composition and socio-demographic factors within such regions. A recent study found a strong association between African American or mixed ethnicity and an increased risk of admission for COVID-19. Neither African American nor mixed ethnicity was independently associated with increased in-hospital mortality risk, but a higher in-hospital mortality risk was estimated for Asian patients.[14] The authors have established a large COVID-19 database in a United States metropolitan city in a midwestern state that took into account the local population and individual-level comorbidities.[15] In this study, the primary objectives were to analyze outcomes and risk factors of CV events in a metropolitan COVID-19 database. The secondary objectives were to perform a subgroup analysis in African American populations to determine whether outcomes and risk factors were influenced by race.

Methods

Study Design

This retrospective cohort study was undertaken by the COVID-19 CardioVascular Research Group, at the University of Louisville Center of Excellence for Research in Infectious Diseases (CERID), to examine clinical, demographic, and laboratory predictors of CV events and clinical outcomes among hospitalized COVID-19 patients in Louisville, KY, hospitals. This study used data from electronic medical records (EMRs) of patients diagnosed with COVID-19, as identified by the CERID team.[16]

Human Subjects Protection

The University of Louisville Institutional Review Board (IRB) approved the CERID COVID-19 Cardiovascular Study, conducted at participating hospitals (IRB# 20-0257). In addition, the respective IRBs of the individual hospitals approved the conduct of these studies at their institutions. All studies were exempt from ascertaining informed consent. Information from the patients' EMR was entered into a secure health

insurance portability and accountability act-compliant REDCAP database. Standard data security procedures were utilized and approved by the respective IRBs to safeguard patients' private healthcare information.

Study Setting and Subjects

Patients in the CERID COVID-19 Cardiovascular Study were hospitalized at nine different hospitals within the Louisville metropolitan area including: one academic medical/trauma center; one large tertiary care and/or transplant hospital; three large (>400 beds) tertiary care community hospitals; three moderately- sized (<400 beds) tertiary care community hospitals; and one community women's hospital with delivery services.

Data used in this study consisted of 700 adult inpatients hospitalized with COVID-19 from March 9, 2020, to June 20, 2020. Inclusion criteria for this study included all adult hospitalized inpatients (equal to or older than 18 years old) with a diagnosis of COVID-19 as defined by evidence of a positive Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) on the first or the repeat test and/or ground glass opacities on chest computerized tomography (CT). This study excluded any COVID-19 patient who was not admitted as a hospital inpatient.

Data Collection

Standard testing was performed in the clinical laboratory of each participating facility. A certified laboratory at each facility performed the RT-PCR testing. Confirmation of positive or suspected positive COVID-19 patients was determined by daily EMR screenings or reports delivered by the participating facilities. Before July 2020, either positive RT-PCR tests or bilateral ground glass opacities on CT scans was considered positive for COVID-19. Out of the 700 hospitalized COVID-19 patients in the authors' database, 17 had CT-only inclusion criteria. Clinical diagnoses of COVID-19 were made independently by individual physicians at each site. Due to the limited availability of COVID-19 RT-PCR testing in Louisville, KY during early 2020, the 17 cases of CT diagnosis for COVID-19 were included with realized limitations. After July 2020, all cases were confirmed by positive RT-PCR results. Data collected consisted of COVID-19 test results; past medical and social history; current medications; signs and symptoms of illness; physical examination; laboratory, radiologic, and microbiologic findings; management and therapies; in-hospital complications; and the clinical course and outcomes of each patient. A comprehensive data abstraction instrument was developed by epidemiologists, physicians, nurses, biostatisticians, and students who were members of the CERID work group. Specially trained data abstractors utilized the data abstraction instrument to extrapolate data from the EMR of each patient. Each data point and variable was investigated in depth by the data abstractors to ensure consistency.

Table 1
Demographic and Comorbidities of COVID-19 patients With and Without Cardiovascular Events (N = 700)

Variables	Cases Without CV Events (n = 574)	Cases With CV Events (n = 126)	p Value
Age, mean ± SD	57.8 ± 19.37	66.8 ± 15.2	<0.001
Sex, n (%)			
Female	330 (57.5)	54 (42.9)	0.004
Male	244 (42.5)	72 (57.1)	
Race, n (%)			
Hispanic	77 (13.4)	4 (3.2)	<0.001
Non-Hispanic African American	179 (31.2)	41 (32.5)	
Non-Hispanic White	267 (46.5)	76 (60.3)	
Non-Hispanic other	51 (8.9)	5 (4.0)	
Body Mass Index, mean ± SD	31 ± 8.85	31.6 ± 7.81	0.270
Comorbidities, n (%)			
Pulmonary comorbidity	256 (44.6)	80 (63.5)	<0.001
Cardiovascular comorbidity	338 (58.9)	104 (82.5)	<0.001
Renal disease	86 (15.0)	39 (31.0)	<0.001
Diabetes	164 (28.6)	60 (47.6)	<0.001
Neoplastic/immune compromised diseases	47 (8.2)	20 (15.9)	0.013

Abbreviation: CV, cardiovascular.

Variables

Demographic Variables

Demographic data collected included patients' age, sex, height, weight, and race. Race and ethnicity were combined into the following categories: Hispanic; Non-Hispanic White; Non-Hispanic Black; Non-Hispanic others (Table 1).

Comorbidity Variables

Data on pre-existing comorbidities were collected from the EMR and included diabetes, renal disease, liver disease, pulmonary disease, neoplastic or immune compromising diseases, and pre-existing CV disease. Data on comorbidities were utilized to evaluate the influence of these disease states on clinical outcomes of patients with COVID-19 (Table 1).

Clinical and Laboratory Variables

Clinical and laboratory data were collected within 48 hours of admission or during intensive care unit (ICU) admission and included body mass index, oxygen saturation/fraction of inspired oxygen ($SpO2/F_IO2$) ratio, partial pressure of oxygen/fraction of inspired oxygen ($PaO2/F_IO2$) ratio, arterial blood gases when available, hemoglobin, hematocrit, platelets, white blood cell (WBC) count, neutrophil count, complete metabolic profile, bicarbonate level, serum potassium, serum blood urea nitrogen, serum creatinine, serum albumin, serum bilirubin, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, activated prothrombin time, activated partial thromboplastin time, international normalized ratio measurement, troponin, ferritin, procalcitonin, domain-dimer level,

Table 2
Admission Clinical and Laboratory Biomarkers of COVID-19 Patients With and Without Cardiovascular Events (N = 700)

Variables	Cases Without CV Events (n = 574) Mean ± SD	Cases With CV Events (n = 126) Mean ± SD	p Value
AST/ALT ratio	1.5 ± 0.77	1.7 ± 0.83	0.003
Neutrophil-lymphocyte ratio	6.4 ± 7.69	9 ± 10.74	<0.001
SaO2/F_IO2 ratio	382.1 ± 105.22	282.4 ± 136.89	<0.001
WBC, 10^3/mm^3	7.4 ± 4.43	8.6 ± 5.72	0.026
Neutrophil, %	71.5 ± 13.53	75.4 ± 14.24	0.002
Lymphocyte, %	18.5 ± 10.75	15.2 ± 10.53	0.001
Neutrophil, 10^3/mm^3	7.8 ± 13.03	8 ± 9.63	0.013
Lymphocyte, 10^3/mm^3	1.7 ± 3.3	1.5 ± 2.92	0.001
Serum potassium, mmol/L	3.8 ± 0.62	4.1 ± 0.73	<0.001
Glucose, mg/dL	145.7 ± 80.01	165.3 ± 91.96	0.001
BUN, mg/dL	21 ± 18.28	32.5 ± 24.82	<0.001
Creatinine, mg/dL	1.4 ± 1.8	1.7 ± 1.26	<0.001
Albumin, g/dL	3.6 ± 0.63	3.3 ± 0.68	0.001
Bilirubin, mg/dL	1 ± 4.05	1.1 ± 3.14	0.002
AST, units/L	55.7 ± 64.38	83.6 ± 168.01	0.033
INR	1.3 ± 0.8	1.4 ± 0.95	0.009
Procalcitonin, ng/mL	2.3 ± 22.06	2.2 ± 6.15	<0.001
D-dimer, μg/mL fibrinogen equivalent units	1729.9 ± 4686.23	4741.5 ± 13169.36	<0.001
Interleukin-6, pg/mL	95.7 ± 131.58	190.8 ± 266.21	0.001
CRP, mg/L	40.2 ± 95.65	53.2 ± 72.17	0.001
ABG F_IO2, %	49.5 ± 30.54	60.5 ± 33.08	0.016
BNP, pg/mL	1098.6 ± 9406.06	823.5 ± 1072.37	<0.001
NT-proBNP, pg/ml	3374.8 ± 17423.69	6168.1 ± 15115.23	<0.001

Abbreviations: ABG, arterial blood gas; ALT, alanine transaminase; AST, aspartate transaminase; BNP, Brain-type natriuretic peptide; BUN, blood urea nitrogen; CRP, C-reactive protein; CV, cardiovascular; D-dimer, domain-dimer; F_IO2, fraction of inspired oxygen; INR, international normalized ratio; NT-proBNP, N-terminal pro hormone brain-type natriuretic peptide; SaO2, saturation of oxygen in arterial blood; WBC, white blood cell count.

B-type natriuretic peptide and N-terminal pro b-type natriuretic peptide, interleukin-6, C-reactive protein, and erythrocyte sedimentation rate (Table 2). Please note that many patients did not have arterial blood gas samples during admission, and PaO2 was not available. However, almost all patients had SpO2 and were used to calculate SaO2/F_IO2 ratio.

Outcome Variables

In this study, the primary outcome variable of interest was CV events. The authors defined CV events as those events that occurred after admission to the hospital and included individual and composite CV events. The endpoints used in the analysis were diagnosed heart failure, cardiogenic shock, acute myocardial infarction, cardiomyopathy, myocarditis, cardiac arrhythmias (including tachycardia, bradycardia, supraventricular tachycardia, atrial tachycardia, and bundle-branch blocks), cerebrovascular events, pulmonary embolism, pulmonary edema, deep vein thrombosis (DVT), and cardiac arrest. Clinical diagnoses of CV events were made independently by individual physicians at each site. Research staff only retrieved the diagnosis through chart reviews and documentation but did not make any new diagnosis. The authors realized the limitations of potentially different diagnostic criteria used among providers, yet presented real-world situations, and future attempts will be made to use more uniform diagnostic criteria by the research team. The secondary endpoints included mortality, length of stay (LOS) for survivors, and days to mortality for non-survivors. LOS for survivors was defined as the time between the date of admission and the date of discharge from the hospital in days. Days to mortality for non-survivors were defined as the time between the date of admission and the time of death in days. The authors also examined ICU admission, invasive mechanical ventilation (defined as requiring endotracheal intubation), septic shock, disseminated intravascular coagulation (DIC) and acute respiratory distress syndrome (ARDS) to assess clinical severities among COVID-19 patients.

Data Analysis

Continuous measurements were summarized by mean and standard deviation, and categorical variables were summarized by counts and percentages. Comparison between the groups (eg, patients without CV events versus patients with CV events) was performed using the Mann-Whitney U test for continuous variables and the Chi-square test.

Subgroup analyses for African American and white patients were performed to examine the risk factors of CV events for each sub-population using the Mann-Whitney U test and the Chi-square test as appropriate (see the columns under “African American Patients” and “White Patients”). In addition, the authors compared the variables between African American and white patients who did not have CV events (see the column “p values without CV”), as well as those who had CV events (see the column “p values with CV”). Furthermore, the

authors compared mortality, LOS for survivors, and days to mortality for non-survivors between African American and white patients who had CV events, using the propensity score matching techniques, with control of the patients' demographic information and comorbidities, and the results were reported.

Pearson's correlation coefficients were used to evaluate the correlation among different variables. Multiple logistics regression analyses were conducted to examine which variables (ie, laboratory data, demographic data, and comorbidities) predict CV events for the entire cohort, African American-only patients, and white-only patients, respectively. Multiple logistics regression analyses included the variables that were predictive for CV events in bivariate analyses and were not highly correlated. The Kaplan-Meier estimator was conducted to compare the survivals between patients with and without CV events for the entire cohort, African American-only patients, and white-only patients, respectively. A p value of <0.05 was considered statistically significant. The statistical analyses were carried out using the statistics software R version 4.0.2 (R Foundation).

Results

Clinical Outcomes for the Entire Cohort

The present sample population consisted of 126 patients with CV events and 574 patients without CV events. Among the 126 CV-event patients, 26 (20.6%) patients had heart failure, 20 (15.8%) had cardiac arrest, 15 (11.9%) had cardiogenic shock, 13 (10.3%) had acute myocardial infarction, 13 (10.3%) had pulmonary edema, 53 (42.1%) had new serious arrhythmia, 20 (15.8%) had acute worsening of long-term arrhythmia, seven (5.6%) had cerebrovascular accidents, nine (7.1%) had pulmonary embolism, two (1.6%) had myocarditis, and seven (5.6%) had DVT. Among the 126 CV event patients, 78 (61.9%) patients had one CV event, 40 (31.7%) patients had two CV events, eight (6.4%) patients had more than two CV events. The incidence of CV events in the authors' COVID-19 database was 18%. Patients with CV events had a much higher mortality rate than those without CV events (45.2% *v* 8.7%). The Kaplan-Meier curves and the log-rank test revealed the survival curves between the two groups were significantly different, and patients with CV events had a significantly decreased probability of surviving (Fig 1, A). A median survival period for patients with CV events was 18 days, and a median survival period for patients without CV events was 100 days. For the entire cohort, the median LOS was significantly increased for patients who suffered CV events when compared with patients without CV events (nine days *v* five days). However, there was no difference for days to mortality for non-survivors between the two groups. The authors then performed disease severity comparisons between patients with and without CV events. The percentage for patients with CV events needing treatment in the ICU was significantly higher than that for patients without CV events (68.3% *v* 30%, $p < 0.001$), and the percentage for patients with CV events needing invasive mechanical ventilation was also significantly higher than that for patients without CV events (55.6% *v* 15.5%, $p < 0.001$). Forty-six (8.0%) non-CV-event patients experienced septic shock, and 40 (31.7%) CV patients experienced septic shock ($p < 0.001$). Fifty-eight (10.1%) non-CV-event patients experienced ARDS, and 41 (32.5%) CV-event patients experienced ARDS ($p < 0.001$). Three (0.5%) non-CV-event patients experienced DIC, and two (1.6%) CV- event patients experienced DIC ($p = 0.22$) (Table 3).

Clinical Outcomes Subgroup Analysis

Similarly to the entire cohort, the authors found that African American COVID-19 patients with CV events suffered significantly more death than those without CV events (43.9% *v* 7.8%). The Kaplan-Meier curves and log-rank test demonstrated that African American COVID-19 patients with CV events had a much lower chance of survival (Fig 1, B). White COVID-19 patients' mortality rates were 46.3% and 9.0% for those with and without CV events, respectively, and patients with CV events had only a 20% chance of survival beyond 24 days, while patients without CV events had an 80% chance of survival beyond 100 days (Fig 1, C). However, there was no significant mortality difference between African American and white COVID-19 patients with or without CV events, based on the log-rank test as well as the weighted Kaplan-Meier statistics. Median LOS was significantly longer in patients with CV events in both African American and white COVID-19 patients (11 *v* five days for African American patients and nine *v* five days for white patients) (Table 4). However, there was no difference between African American and white groups. Days to mortality were significantly shorter in African American COVID-19 patients with CV events when compared with white patients with CV events (six *v* 12 days) (Table 4); however, the difference (six *v* ten days) was not significant anymore after adjusting confounding variables using a propensity score-matching method (Table 5).

Risk Factors of Cardiovascular Events in COVID-19 for the Entire Cohort

The authors found the following factors were highly associated with the odds of new-onset CV events (patients with *v* without CV events) in the present sample population: advanced age, males, White patients, pulmonary comorbidities, CV comorbidities, renal disease, diabetes, neoplastic and/or immune-compromised diseases (Table 1). Multiple clinical and laboratory biomarkers also showed significant differences between COVID-19 patients with and without CV events (Table 2).

Multiple logistics regression analysis was used to examine the joint effect of these risk factors (Table 6), which suggested that sex (male), race (African American compared with Hispanic patients), lower $SaO2/F_IO2$, higher serum potassium, lower serum albumin, and number of CV comorbidities were highly associated with the occurrence of CV events in COVID-19 patients.

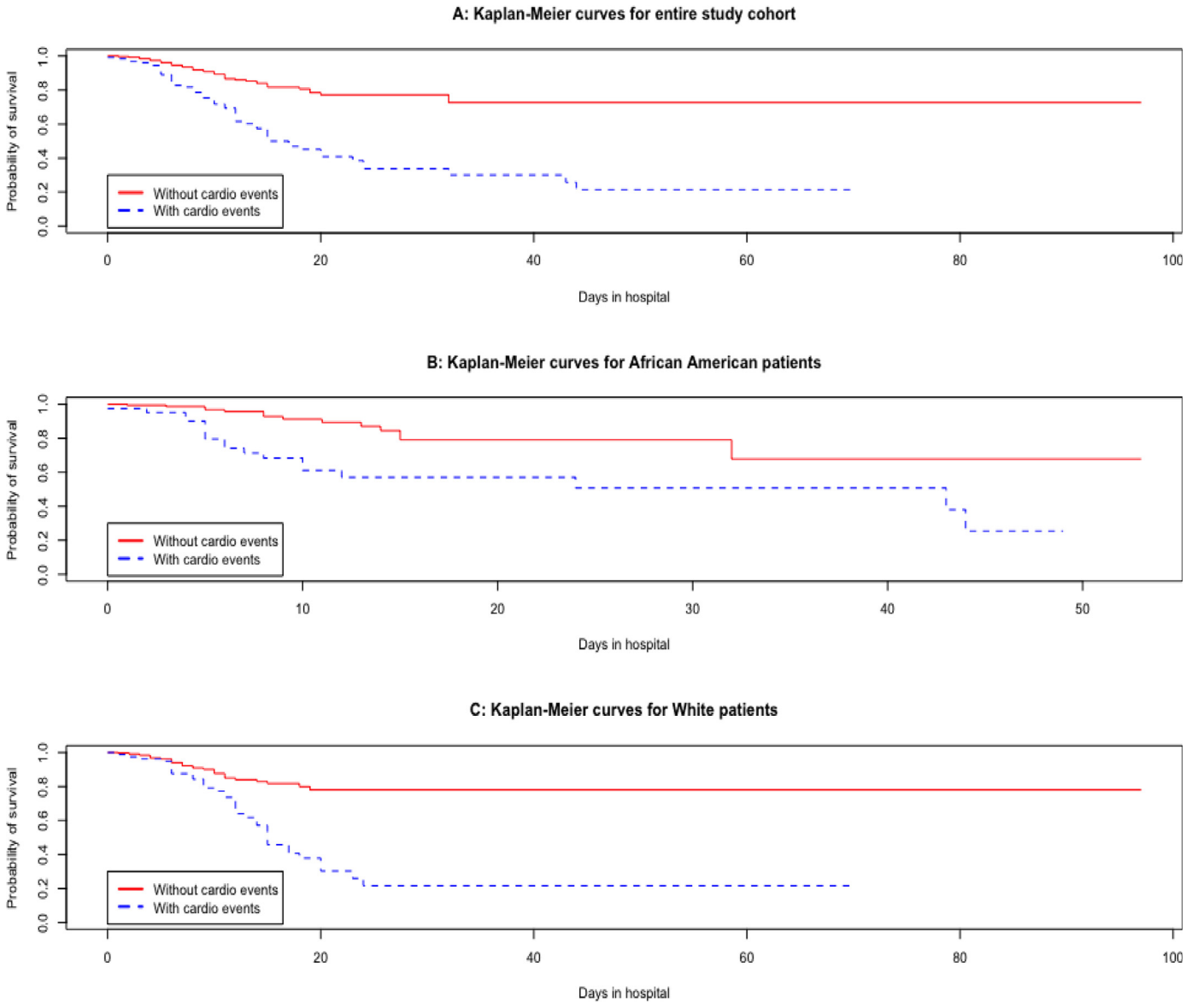

Fig 1. (A) Kaplan-Meier survival probability estimates for hospitalized COVID-19 patients stratified with or without cardiovascular events for entire cohort. (B) African Americans patients. (C) White patients.

Risk Factors of Cardiovascular Events in COVID-19 Subgroup Analysis

A subgroup analysis for African American patients with COVID-19 was performed that included 41 patients with CV events and 179 patients without CV events. Demographics, laboratory variables, and comorbidities were compared between African American patients with CV events and those without CV events. The following factors were highly associated with the odds of suffering CV events for African

Table 3
Disease Severity Comparisons Between COVID-19 Patients With and Without CV Events (N = 700)

Variables	Cases without CV Events (n = 574)	Cases with CV Events (n = 126)	p Value
ICU, n (%)	172 (30.0)	86 (68.3)	<0.001
Invasive mechanical ventilation, n (%)	89 (15.5)	70 (55.6)	<0.001
Septic shock, n (%)	46 (8.0)	40 (31.7)	<0.001
DIC, n (%)	3 (0.5)	2 (1.6)	0.222
ARDS, n (%)	58 (10.1)	41 (32.5)	<0.001

Abbreviations: CV, cardiovascular; ARDS, acute respiratory distress syndrome; DIC, disseminated intravascular coagulation; ICU, intensive care unit.

Table 4
Death, Length of Stay, and Days to Mortality Between African American and White COVID-19 Patients With and Without Cardiovascular Events (N = 644).

Variables	African American Patients (N = 220)			White Patients (N = 424) (Non-Hispanic White and Hispanic)			African American Versus White Patients	
	Without CV Events (n = 179)	With CV Events (n = 41)	p Value	Without CV Events (n = 344)	With CV Events (n = 80)	p Value	p Value Without CV Events	p Value With CV Events
Death, n (%)	14 (7.8)	18 (43.9)	<0.001	31 (9.0)	37 (46.3)	<0.001	0.767	0.958
	Median (IQR)	Median (IQR)		Median (IQR)	Median (IQR)			
LOS for survivors, d (IQR)	5 (2-11)	11 (7.5-23.5)	<0.001	5 (3-12)	9 (5.5-16)	<0.001	0.419	0.257
Days to mortality for non-survivors, d (IQR)	8.5 (5.25-13.75)	6 (5-10)	0.391	7 (410.5)	12 (8-5)	0.004	0.320	0.031*

NOTE. Especially in the last columns, the authors compared between African American COVID-19 patients without CV events and white COVID-19 patients without CV events and found no significant outcome difference. The authors then compared between African American COVID-19 patients with CV events and white COVID-19 patients with CV events and found no significant outcome difference except days to mortality for non-survivors.

* Indicates that the difference was not significant after using propensity score matching techniques. Abbreviations: CV, cardiovascular events; LOS, Length of Stay, IQR, interquartile range. Bold value indicate statistically significant.

American COVID-19 patients (described as patients with *v* without CV events): advanced age males, CV comorbidities (in particular with two or more CV comorbidity conditions), diabetes, neoplastic and/or immune-compromised diseases (Table 7). Multiple clinical and laboratory biomarkers also showed significant differences between African American COVID-19 patients with and without CV events (Table 8).

The authors carried out similar analyses for white COVID-19 patients, and compared African American to white patients with and without CV events (see the column "p values without CV events" and "p values with CV events"). There were several important differences between the white and African American races in terms of risk factors for CV events in COVID-19. Neoplastic and/or immune-compromised patients, higher WBC, higher glucose level, lower albumin, lower bilirubin, and higher AST were risk factors in African American COVID-19 patients, but not in white patients. Pulmonary comorbidity, renal disease, AST and/or ALT ratio and lower hemoglobin were risk factors for white COVID-19 patients, but not for African American patients (Table 7). Glucose and creatinine differed significantly between white and African American COVID-19 patients with CV events (Table 8). CV comorbidity, renal disease, neutrophil-lymphocyte ratio (NLR), AST and /or ALT ratio, SaO2/F_IO2 ratio, hemoglobin, and creatinine differed significantly between white and African American patients without CV events (Table 8). The similarities and differences in risks factors for African American and white COVID-19 patients are summarized in Figure 2.

A multiple logistics analysis was used to examine the joint effect of the risk factors (Table 6), which suggested that lower serum albumin (odds ratio [OR] 0.165, 95% confidence interval [CI] 0.06-0.454) and neoplastic and/or immune-compromised diseases count (OR 5.157, 95% CI 1.074-24.77) were highly associated with CV events for African American COVID-19 patients. SaO2/F_IO2 ratio (OR 0.994, 95% CI 0.991-0.997) and CV comorbidity count (OR 1.326, 95% CI 1.069-1.645) were significantly associated with CV events for white patients.

Discussion

This study was unique in several ways. First, this was a large database of 700 hospitalized COVID-19 patients from one metropolitan city in the United States. The geography, medical care, and socioeconomic status was relatively uniform and/or known so that the authors could focus on individual level risk factors for CV events in COVID-19. Second, more than 31% of the cohort patients were African Americans, allowing an adequate sample size to compare African American to white races in subgroup outcomes and risk factors analysis. Third, DVT was included, pulmonary embolism, and cerebrovascular events in the analysis because they shared similar pathogenic factors to cardiac injuries.

The median length of hospitalization among survivors was ten-to-13 days in the United States. (Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19)

Table 5
Outcome Comparisons Between African American and White COVID-19 Patients by Propensity-Score Matching (N = 121)

Outcomes	African American Patients With CV Events (n = 41)	White Patients With CV Events (n = 80)	p value
Matched sample size	41	41	
Death at discharge, n (%)	18 (43.9)	19 (46.3)	1
LOS for survivors in Days, median (IQR)	11.0 (7.5-23.5)	9.5 (6.0-14.5)	0.301
Days to mortality for non-survivors, median (IQR)	6 (5-10)	10 (6.0-14.5)	0.272

Abbreviations: CV, cardiovascular; IQR, interquartile range.

https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html Accessed Feb. 6 2021). The shorter LOS in the COVID-19 patients could have been due to the severity of illness or local practice patterns. The significantly lower LOS in COVID-19 patients with CV events might have been from that fact that 45% patients died during hospitalization and, therefore, reduced the overall LOS. In this cohort, the NLR was 6.4 ± 7.69 in COVID-19 patients without CV events and nine ± 10.74 patients with CV events. In severe or non-survival patients with COVID-19, the lymphocytes count decreases progressively, while the neutrophils count gradually increases. This may be due to excessive inflammation and immune suppression caused by SARS CoV-2 infection. Recent meta-analysis suggested that NLR can not only be a good biomarker predicting disease severity in patients with COVID-19, but also have value in predicting mortality. The NLR cutoff to predict disease severity was 4.5 and the cutoff to predict mortality was 6.5.[17]

An observational study by Guo et al showed a six-fold higher in-hospital mortality in patients with elevated cardiac troponin T (a marker of cardiac injury) in comparison to patients with normal cardiac troponin T level.[5] A study of 169 patients from Wuhan, China, found that acute myocardial injury significantly increased the death risk.[8] Another study from China showed cardiac injury was common (19.7%) in 416 hospitalized COVID-19 patients and was associated with a higher risk of in-hospital mortality.[9] Hypertension, diabetes, coronary disease, heart failure, and cerebrovascular disease were found to be more prevalent in patients with cardiac injury.[10] The same authors described that older age, comorbidities (eg, hypertension, coronary heart disease, chronic renal failure, and chronic obstructive pulmonary disease), and high levels of C-reactive protein were predictors of myocardial injury, using a multivariate logistic regression.[11] Salvatici et al. demonstrated that increased troponin levels were associated with elevated mortality in patients with COVID-19 and found it to be a useful biomarker of disease progression and worse prognosis in patients with COVID-19.[12] In a study of 113 patients, a logistic regression model identified pre-existing hypertension and a higher sequential organ failure assessment score as independent risk factors for patients with COVID-19 in developing cardiac injury.[18] In all cited studies, cardiac injury has been defined as serum levels of cardiac biomarkers above the 99th percentile reference limit, regardless of abnormalities on electrocardiography and/or echocardiography. However, critically ill patients could have elevated cardiac markers from mismatch between myocardial oxygen supply and demand without structural CV abnormalities. The prevalence of cardiac injury was reported to be 19% in total COVID-19 patients, 36% in severe COVID-19 patients, and 48% in non-survivors.[19] Furthermore, cardiac injury was found to be associated with a significant increase in the risk of poor outcomes, severe disease, admission to ICU, and mortality.[17] Another study reported 21.7% cardiac injury incidence and identified age, hypertension, chronic heart failure, diabetes, chronic obstructive pulmonary disease and/or asthma as risk factors for cardiac injury in COVID-19. Outcomes for patients with CV injuries were worse including increased incidence of mechanical ventilation, acute respiratory distress syndrome, acute kidney injury, anemia, and death.[20] An international, multicenter cohort study, including seven hospitals consisting of 305 hospitalized COVID-19 patients in New York City and Milan, found myocardial injury was observed in 62.3% of patients. Rates of in-hospital mortality were 31.7% in patients with myocardial injury and TTE abnormalities.[21] In a study of ICU-admitted COVID-19 patients, authors found that 49% of patients demonstrated a cardiac injury at baseline, and 70% of

Table 6
Multiple Logistic Regression Model of Factors Associated With Cardiovascular Events From the Entire Cohort, African American, and White COVID-19 Patients

	Entire Cohort (N = 700)		African American Patients (N = 220)		White Patients (N = 424) (Hispanic + Non-Hispanic)	
Variable	OR	95% CI	OR	95% CI	OR	95% CI
Race Non-Hispanic African American vs. Hispanic	4.888	(1.01-23.66)				
Male (vs Female)	1.737	(1.003-3.01)	1.417	(0.505-3.979)	1.318	(0.620-2.802)
SaO2/F_IO2 ratio	0.995	(0.993-0.997)	0.996	(0.991-1.001)	0.994	(0.991-0.997)
Serum potassium	1.557	(1.056-2.296)	2.156	(0.878-5.293)	1.463	(0.868-2.464)
Albumin	0.623	(0.411-0.945)	0.165	(0.06-0.454)	1.048	(0.564-1.946)
Cardiovascular comorbidity count	1.297	(1.106-1.521)	1.258	(0.897-1.763)	1.326	(1.069-1.645)
Neoplastic/immune compromised diseases count	1.622	(0.86-3.059)	5.157	(1.074-24.77)	1.967	(0.854-4.53)

Abbreviations: F_IO2, fraction of inspired oxygen; SaO2, saturation of oxygen in arterial blood.
Bold value indicate statistically significant.

Table 7
Demographic and Comorbidity Comparisons Between African American and White COVID-19 Patients With and Without Cardiovascular Events (N = 644)

Variables	African American Patients (N = 220)			White Patients (N = 424) (Non-Hispanic White and Hispanic)			African American Versus White Patients (N = 644)	
	Without CV Events	With CV Events	p value	Without CV Events	With CV Events	p Value	p Value Without CV Events	p Value With CV Events
Sample size, n (%)	179 (81.4%)	41 (18.6%)		344 (81.1%)	80 (18.9%)		1	
Age, mean ± SD	57.2 ± 17.67	68.5 ± 12.26	**<0.001**	59 ± 20.22	66 ± 15.58	**0.003**	0.318	0.667
Sex, n (%)								
Female	107 (59.8)	16 (39.0)	**0.025**	189 (54.9)	36 (45.0)	0.139	0.334	0.664
Male	72 (40.2)	25 (61.0)		155 (45.1)	44 (55.0)			
Body mass index, ± SD	33.5 ± 9.51	33.1 ± 8.62	0.855	30 ± 8.27	30.9 ± 7.42	0.177	<0.001	0.256
Comorbidities, n (%)								
Pulmonary	93 (52.0)	23 (56.1)	0.760	147 (42.7)	57 (71.3)	**<0.001**	0.055	0.143
Cardiovascular	120 (67.0)	36 (87.8)	**0.014**	194 (56.4)	64 (80.0)	**<0.001**	**0.024**	0.413
Renal disease	39 (21.8)	13 (31.7)	0.252	46 (13.4)	26 (32.5)	**<0.001**	**0.019**	1
Diabetes	62 (34.6)	24 (58.5)	**0.008**	90 (26.2)	36 (45.0)	**0.001**	0.054	0.223
Neoplastic/immune compromised diseases	14 (7.8)	8 (19.5)	**0.039**	31 (9.0)	11 (13.8)	0.214	0.767	0.575

NOTE. Within each race, the patients with CV events were compared with those without CV events. African American and white patients were also compared among those without events (see the column "p value without CV") and among those with CV events (see the column "p value with CV"), respectively.
Abbreviation: CV, cardiovascular.
Bold value indicate statistically significant.

patients experienced cardiac injury within the first 14 days of ICU stay, with a median time of occurrence of three days. The most frequent abnormalities were left ventricular (LV) abnormalities (87% of patients with cardiac injury), right ventricular systolic dysfunction (47%), pericardial effusion (43%), new-onset atrial arrhythmias (33%), LV relaxation impairment (33%), and LV systolic dysfunction (13%). Between baseline and day 14, the incidences of pericardial effusion and of new-onset atrial arrhythmias increased.[22] The international patient registry CAPACITY-COVID of 3,011 hospitalized patients with COVID-19 from 79 centers across 13 countries (Belgium, Egypt, France, Iran, Israel, Italy, Netherlands, Portugal, Russia, Saudi Arabia, Spain, Switzerland, and the United Kingdom) found that cardiac complications were diagnosed in 11.6% patients, with atrial fibrillation being the most common (4.7%). Interestingly, Linschoten et al. suggested that the high frequency of raised troponin levels in previous studies may predominantly reflect the occurrence of demand ischemia and non-cardiac causes rather than acute myocardial infarction and myocarditis.[23]

This study demonstrated an 18% incidence of CV events and carried a 45.2% mortality rate in this metropolitan sample population cohort. COVID-19 can cause CV complications or deterioration of coexisting CV diseases through direct or indirect mechanisms, including viral toxicity, dysregulation of the renin-angiotensin-aldosterone system, endothelial cell damage and thromboinflammation, cytokine storm, and oxygen supply and/or demand mismatch.[24,25] Published clinical studies suggested COVID-19 itself might induce myocardial injury, arrhythmia, acute coronary syndrome, and venous thromboembolism.[5,26,27] Additionally, medications that have been proposed as treatments for COVID-19, such as hydroxychloroquine and azithromycin, have pro-arrhythmic effects.[26] It is also suggested that a high level of systemic inflammation from COVID-19 can accelerate the development of subclinical disorders or cause new CV damage.[7,28] Cardiac cells have higher expression of ACE2 receptors and may, therefore, facilitate cellular entry of the virus, endothelial dysfunction, and myocardial damage.[29] Furthermore, pericytes were suspected to be target host cells of SARS-CoV-2 and could lead to coronary microvascular dysfunction and cardiac injury. Recent pathology reports found that endothelial inflammation could contribute to the destabilization of coronary plaques, atherothrombosis, and vascular disease.[30,31] Type II myocardial infarction due to the imbalance of myocardial oxygen supply and demand, as well as stress cardiomyopathy, also can occur in COVID-19 due to the hyperdynamic response to hypoxia and stress.[10]

The authors identified multiple risk factors for developing CV events in hospitalized COVID-19 patients including various demographic, comorbidities, and laboratory testing results. A multiple logistics analysis showed gender (male), race (African American compared with Hispanic patients), lower SaO2/F_IO2, higher serum potassium, lower serum albumin, number of CV comorbidities and neoplastic and/or immune-compromised diseases were highly associated with the occurrence of CV events in COVID-19 patients. Males and African

Table 8
Admission Clinical and Laboratory Biomarker Comparisons Between African American and White COVID-19 Patients With and Without Cardiovascular Events (N = 644)

Variables	African American Patients (N = 220)			White Patients (N = 424) (Non-Hispanic White and Hispanic)			African American Versus White Patients	
	Without CV Events (n = 179) Mean ± SD	With CV Events (n = 41) Mean ± SD	p Value	Without CV Events (n = 344) Mean ± SD	With CV Events (n = 80) Mean ± SD	p value	p Value Without CV Events	p Value With CV Events
AST/ALT ratio	1.7 ± 1	1.6 ± 0.63	0.507	1.4 ± 0.63	1.8 ± 0.92	<**0.001**	**0.011**	0.733
Neutrophil-lymphocyte ratio	6.3 ± 10.49	8.5 ± 6.79	**0.002**	6.5 ± 6.06	9.6 ± 12.44	**0.006**	**0.025**	0.974
SaO2/F_IO2 ratio	396.6 ± 91.08	294.6 ± 142.5	<**0.001**	377.5 ± 108.0	268.1 ± 132.9	<**0.001**	0.056	0.254
WBC, $10^3/mm^3$	7.5 ± 5.5	8.9 ± 6.11	**0.017**	7.4 ± 3.85	8.6 ± 5.61	0.164	0.599	0.492
Hemoglobin, g/dL	12.4 ± 2.02	12.3 ± 2.41	0.952	13 ± 2.01	12.4 ± 2.38	**0.026**	<**0.001**	0.795
Neutrophil, %	70.3 ± 13.07	75.3 ± 13.36	**0.017**	72 ± 13.78	76.4 ± 14.08	**0.009**	0.135	0.566
Lymphocyte, %	19.3 ± 10.99	13.7 ± 7.4	**0.004**	18.1 ± 10.73	15.1 ± 11	**0.015**	0.223	0.958
Neutrophil, $10^3/mm^3$	7.8 ± 14.07	7.4 ± 6.89	**0.013**	7.8 ± 12.47	8.5 ± 10.96	**0.097**	0.08	0.975
Lymphocyte, $10^3/mm^3$	1.7 ± 2.86	1.1 ± 0.65	**0.079**	1.7 ± 3.5	1.6 ± 3.6	**0.006**	0.23	0.547
Serum potassium, mmol/L	3.8 ± 0.63	4.3 ± 0.74	**0.001**	3.9 ± 0.63	4.1 ± 0.73	**0.04**	0.865	0.091
Glucose[@], mg/dL	142.5 ± 76.29	193 ± 113	<**0.001**	147.1 ± 84.0	153.3 ± 78.0	0.255	0.601	**0.004**
BUN, mg/dL	22.5 ± 17.9	37.6 ± 32.8	<**0.001**	21.3 ± 19.17	29.9 ± 18.6	<**0.001**	0.509	0.393
Creatinine, mg/dL	1.9 ± 2.48	2.1 ± 1.53	**0.001**	1.2 ± 1.32	1.6 ± 1.09	<**0.001**	<**0.001**	**0.005**
Albumin, g/dL	3.6 ± 0.6	3.2 ± 0.73	**0.001**	3.6 ± 0.65	3.4 ± 0.65	0.068	0.926	0.093
Bilirubin, mg/dL	1.5 ± 7.12	0.9 ± 0.57	**0.019**	0.7 ± 0.64	1.2 ± 3.91	0.069	0.285	0.119
AST, units/L	58.4 ± 81.0	89.8 ± 158.4	**0.029**	55.5 ± 58.5	81.9 ± 177.6	0.325	0.093	0.517
Procalcitonin, ng/m	4.1 ± 34.14	1.2 ± 2.58	<**0.001**	1.6 ± 15.15	2.7 ± 7.4	<**0.001**	0.214	0.445
D-dimer, μg/mL fibrinogen equivalent units	2216 ± 5512	6945 ± 18717	**0.024**	1482 ± 4462	3575 ± 8726	<**0.001**	0.292	0.641
Interleukin-6, pg/mL	82.2 ± 115.9	158.1 ± 178.4	**0.012**	97.9 ± 116.1	205.5 ± 299.0	**0.039**	0.306	0.913
CRP, mg/L	37.2 ± 59.51	65 ± 69.47	**0.008**	43 ± 114.11	47.4 ± 73.95	**0.025**	0.717	0.248
BNP, pg/mL	2749 ± 17225	926.8 ± 1396	**0.002**	439.3 ± 1013	798.6 ± 873.0	**0.002**	0.220	0.952
NT-proBNP, pg/mL	4097 ± 21360	2632 ± 3772	**0.008**	3099 ± 16290	7750 ± 17860	<**0.001**	0.351	0.806

Abbreviations: ABG, arterial blood gas; ALT, alanine transaminase; AST, aspartate transaminase; BNP, Brain-type natriuretic peptide; BUN, blood urea nitrogen; CRP, C-reactive protein; CV, cardiovascular; D-dimer, domain-dimer; F_IO2, fraction of inspired oxygen; INR, international normalized ratio; NT-proBNP, N-terminal pro hormone brain-type natriuretic peptide; SaO2, saturation of oxygen in arterial blood; WBC, white blood cell count.
Bold value indicate statistically significant.

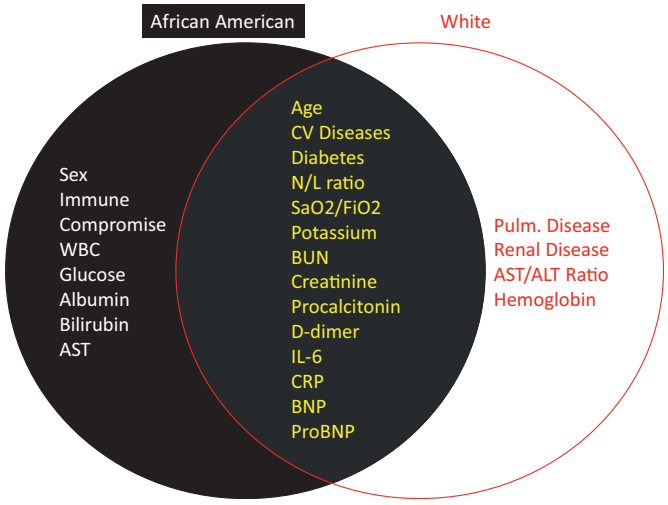

Fig 2. Summary of similar and different risk factors in African American and white COVID-19 patients. WBC, White Blood Cell count; AST, aspartate aminotransferase; CV, cardiovascular; N/L ratio, Neutrophil-Lymphocyte ratio; D-Dimer, D-domain-dimer (D-dimer); BNP, B-type natriuretic peptide; ProBNP, N-terminal pro b-type natriuretic peptide; IL-6, interleukin-6; CRP, C-reactive protein; ALT, alanine aminotransferase.

Americans may have higher levels of undiagnosed baseline CV disease, and the hyperdynamic stress and/or immunothrombosis from COVID-19 pneumonia may worsen their already marginal CV functions. Higher potassium could be due to worsening kidney dysfunction from dehydration, gastrointestinal symptoms, and poor perfusion from CV dysfunction. Lower SaO2/F_IO2 ratios are indicators of the severity of COVID-19 pneumonia at the time of presentation and could cause hypoxia-induced myocardial ischemia, septic cardiomyopathy, and stress cardiomyopathy.[32] Lower albumin could be indicative of pre-existing poor nutritional status prior to COVID-19 infection, as well as a weaker immune system to combat SARS-CoV-2 infections. Pre-existing CV comorbidities are expected to get worse from the stress, hypoxia, and immune dysregulation. Recent clinical studies have shown that pre-existing CV disease was associated with worse outcomes and increased risk of death in patients with COVID-19.[33-35] Those with neoplastic disease and who are immunocompromised represent a patient subgroup that is likely susceptible to viral infections secondary to an altered immune response.

Multiple studies have suggested disparities between African Americans and other populations in relation to COIVD-19 outcomes. African Americans are overrepresented among reported COVID-19 deaths in the United States.[36] In addition, African Americans have a disproportionately higher incidence of underlying health conditions like diabetes mellitus, hypertension, obesity, asthma, and CV disease.[37] Given the known risk factors for COVID-19 complications, the confluence of hypertension, diabetes, obesity, and the higher prevalence of CV disease among African Americans may help explain their worsened COVID-19 outcomes. African American residents were at the highest risk of death from COVID-19, and Hispanic and/or Latino residents died from COVID-19 at an appreciably younger age than all other ethnic groups. Higher COVID-19 mortality was seen in neighborhoods with heightened barriers to social distancing and low health insurance coverage.[38] A study from New York City characterized neighborhood traits associated with COVID-19 infection and found that housing value, housing density, and income were protective against infection, while crowded households were associated with increased risks.[39]

The authors found several important similarities and differences between the white and African American races in terms of outcomes and risk factors of CV events in COVID-19. For clinical outcomes, there was no difference in mortality, LOS for survivors, and days to mortality for non-survivors between African American and white COVID-19 patients after propensity score matching. This was different from several previous studies and could be from the relative standard of care once patients are hospitalized regardless of race. Genetic and social economic differences between races might be masked by the serious damages from the CV events.

In terms of risk factors, glucose and creatinine differed significantly between African American and white COVID-19 patients with CV events. Neoplastic and/or immune-compromised patients, higher WBC, higher glucose level, lower albumin, lower bilirubin, and higher AST were CV event risk factors for African American COVID-19 patients, but not in white patients. Pulmonary comorbidities, renal disease, AST/ALT ratio, and hemoglobin were risk factors for white COVID-19 patients, but not in African American patients. CV comorbidity, renal disease, NLR, AST/ALT ratio, SaO2/F_IO2 ratio, hemoglobin, and creatinine differed significantly between white and African American patients without CV events. A multiple logistics analysis suggested that lower serum albumin and neoplastic and/or immune-compromised diseases count were highly associated with CV events in African American COVID-19 patients. SaO2/F_IO2 ratio and CV comorbidity were significantly associated with CV events for white patients. These similar and differential risk factors between African American and white COVID-19 patients might reflect common pathophysiology of COVID-19 and potentially unique disease states or management strategy differences between races. In particular, glucose and creatinine were significantly higher in African American patients with CV events, which could reflect underlying or poorly controlled diabetes or renal diseases, delayed medical care due to socioeconomic factors, and/or different medication regimens. Particularly, the increased creatinine in African American COVID-19 patients could be due to poor control of hypertension, differences in anti-hypertension treatment algorithms (ACE inhibitors, angiotensin-receptor blockers, calcium-channel blockers, diuretics) and the combination of ACE inhibitors and/or angiotensin-receptor blockers, diuretic(s) + non-steroidal anti-inflammatory drugs, which could severely impair renal functions and be linked to acute renal failure episodes in older COVID-19 adults.

A recent study using CV magnetic resonance imaging revealed cardiac involvement in 78% patients and ongoing myocardial inflammation in 60% patients independent of pre-

existing conditions, severity and overall course of the acute illness, and time from the original diagnosis.[4] Another study of 26 recovered patients who had all been hospitalized for COVID-19 showed myocardial edema on magnetic resonance imaging in 57% of patients.[40] Due to the high mortality with CV events in COVID-19, patients with pre-existing CV comorbidities should be monitored closely with a low threshold for performing diagnostic studies. Patients recovering from COVID-19 need to be followed for long-term CV complications. This study revealed common and unique risk factors for African American COVID-19 patients, which could be used to guide prediction and management of individual patients. However, whether modifying and treating these risks factors could reduce CV events or mortality is unknown and should be studied further.

Limitations

This study had several limitations. First, due to the retrospective study design nature, there were missing laboratory values in some patients, which could not be obtained for analysis. Second, reports of comorbidities were obtained from the EMRs and relied on accurate medical record documentation. Third, treatment details, which may have contributed to the outcomes reported, were not analyzed in this manuscript. However, local COVID-19 management patterns were relatively consistent in Louisville, KY. Fourth, the authors did not have the long-term follow-up data on these events and the long-term sequela of COVID-19 on cardiac health; thus, long-term mortality could not be assessed. Fifth, only hospitalized COVID-19 patients were studied, and non-hospitalized patients were not included.

Strength

One of the strengths of the present study was that it was a population-based large COVID-19 cohort study with 700 patients. Another strength was a large African American population within the study cohort that allowed for further subgroup analysis.

Conclusion

CV events were prevalent and associated with worse outcomes in hospitalized patients with COVID-19. Outcomes of CV events in African American and white COVID-19 patients were similar. There were common and unique risk factors for CV events in African American COVID-19 patients when compared with white patients.

Acknowledgments

The authors acknowledge the excellent efforts of University of Louisville CERID group and Kornhauser Health Sciences Library to assist with this project.

Conflict of Interest

None.

References

1 Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Biomed 2020;91:157–60.
2 Johns Hopkins Coronavirus Resource Center. COVID-19 map. Available at: https://coronavirus.jhu.edu/map.html. Accessed December 14, 2020.
3 Cao W, Li T. COVID-19: Towards understanding of pathogenesis. Cell Res 2020;30:367–9.
4 Puntmann VO, Carerj ML, Wieters I, et al. Outcomes of Cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5:1265–73.
5 Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5:811–8.
6 Lippi G, Lavie CJ. Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis. Progress in cardiovascular diseases 2020;63:390–1.
7 Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential effects of coronaviruses on the cardiovascular system: A review. JAMA Cardiol 2020;5:831–40.
8 Ni W, Yang X, Liu J, et al. Acute myocardial injury at hospital admission is associated with all-cause mortality in COVID-19. J Am Coll Cardiol 2020;76:124–5.
9 Shi S, Qin M, Yang B. Coronavirus disease 2019 (COVID-19) and cardiac injury—Reply. JAMA Cardiol 2020;5:1199–200.
10 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.
11 Shi S, Qin M, Cai Y, et al. Characteristics and clinical significance of myocardial injury in patients with severe coronavirus disease 2019. Eur Heart J 2020;41:2070–9.
12 Salvatici M, Barbieri B, Cioffi SMG, et al. Association between cardiac troponin I and mortality in patients with COVID-19. Biomarkers 2020;25:634–40.
13 Heffernan KS, Michos ED, Gump BB. Coronavirus disease 2019 (COVID-19) and Cardiac injury. JAMA Cardiol 2020;5:1198.
14 Zakeri R, Bendayan R, Ashworth M, et al. A case-control and cohort study to determine the relationship between ethnic background and severe COVID-19. EClinicalMedicine 2020;28:100574.
15 Carrico R. Implementation of the Louisville COVID-19 surveillance protocol: Experiences from the University of Louisville Center of Excellence for Research in Infectious Diseases [CERID]. J Resp Infect 2020;4.
16 Ramirez J. Defining the burden of COVID-19 in the Kentuckiana area: Incidence, epidemiology & clinical outcomes of patients with COVID-19. J Resp Infect 2020;4.
17 Li X, Liu C, Mao Z, et al. Predictive values of neutrophil-to-lymphocyte ratio on disease severity and mortality in COVID-19 patients: A systematic review and meta-analysis. Crit Care 2020;24:647.
18 Mu S, Wei W, Jin C, et al. Risk factors for COVID-19 patients with cardiac injury: Pulmonary ventilation dysfunction and oxygen inhalation insufficiency are not the direct causes. Aging (Albany NY) 2020;12:23464–77.
19 Huang Z, Huang P, Du B, et al. Prevalence and clinical outcomes of cardiac injury in patients with COVID-19: A systematic review and meta-analysis. Nutr Metab Cardiovasc Dis 2021;31:2–13.
20 Al-Wahaibi K, Al-Wahshi Y, Mohamed Elfadil O. Myocardial injury is associated with higher morbidity and mortality in patients with 2019 novel coronavirus disease (COVID-19). SN Compr Clin Med 2020:1–7.
21 Giustino G, Croft LB, Stefanini GG, et al. Characterization of myocardial injury in patients with COVID-19. J Am Coll Cardiol 2020;76:2043–55.
22 Doyen D, Dupland P, Morand L, et al. Characteristics of cardiac injury in critically ill patients with coronavirus disease 2019. Chest 2020. https://doi.org/10.1016/j.chest.2020.10.056. Accessed on April 11, 2021. [e-pub ahead of print].

23 Linschoten M, Peters S, van Smeden M, et al. Cardiac complications in patients hospitalised with COVID-19. Eur Heart J Acute Cardiovasc Care 2020;9:817–23.
24 Dou Q, Wei X, Zhou K, et al. Cardiovascular manifestations and mechanisms in patients with COVID-19. Trends Endocrinol Metab 2020;31:893–904.
25 Unudurthi SD, Luthra P, Bose RJC, et al. Cardiac inflammation in COVID-19: Lessons from heart failure. Life Sci 2020;260:118482.
26 Nishiga M, Wang DW, Han Y, et al. COVID-19 and cardiovascular disease: From basic mechanisms to clinical perspectives. Nat Rev Cardiol 2020;17:543–58.
27 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.
28 Tay MZ, Poh CM, Rénia L, et al. The trinity of COVID-19: Immunity, inflammation and intervention. Nat Rev Immunol 2020;20:363–74.
29 Chen L, Li X, Chen M, et al. The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2. Cardiovasc Res 2020;116:1097–100.
30 Lazaridis C, Vlachogiannis NI, Bakogiannis C, et al. Involvement of cardiovascular system as the critical point in coronavirus disease 2019 (COVID-19) prognosis and recovery. Hellenic J Cardiol 2020;61:381–95.
31 Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet 2020;395:1417–8.
32 Xie J, Covassin N, Fan Z, et al. Association Between hypoxemia and mortality in patients with COVID-19. Mayo Clin Proc 2020;95:1138–47.
33 Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506.
34 Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA 2020;323:1061–9.
35 Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. Lancet 2020;395:1054–62.
36 Yancy CW. COVID-19 and African Americans. JAMA 2020;323:1891–2.
37 National Academies of Sciences Engineering, and Medicine; Health and Medicine Division. In: Baciu A, Negussie Y, Geller A, Weinstein JN, editors. Communities in Action: Pathways to Health Equity, Washington (DC): National Academies Press; 2017.
38 Bryan MS, Sun J, Jagai J, et al. COVID-19 mortality and neighborhood characteristics in Chicago. Ann Epidemiol 2021;56;47-54.e5.
39 Emeruwa UN, Ona S, Shaman JL, et al. Associations between built environment, neighborhood socioeconomic status, and SARS-CoV-2 infection among pregnant women in New York City. JAMA 2020;324:390–2.
40 Huang L, Zhao P, Tang D, et al. Cardiac involvement in patients recovered from COVID-2019 identified using magnetic resonance imaging. JACC Cardiovasc Imaging 2020;13:2330–9.