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Original Article

Pre-existing cardiovascular disease, acute kidney injury, and cardiovascular outcomes in hospitalized blacks with COVID-19 infection

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Abstract: Background: The Corona Virus 19 (COVID-19) infection is associated with worse outcomes in blacks, although the mechanisms are unclear. We sought to determine the significance of black race, pre-existing cardiovascular disease (pCVD), and acute kidney injury (AKI) on cardiopulmonary outcomes and in-hospital mortality of COVID-19 patients. Methods: We conducted a retrospective cohort study of blacks with/without pCVD and with/without in-hospital AKI, hospitalized within Grady Memorial Hospital in Georgia between February and July 2020, who tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on qualitative polymerase-chain-reaction assay. The primary outcome was a composite of in-hospital cardiac events. Results: Of the 293 patients hospitalized with COVID-19 in this study, 71 were excluded from the primary analysis (for race/ethnicity other than black non-Hispanic). Of the 222 hospitalized COVID-19 patients included in our analyses, 41.4% were female, 78.8% had pCVD, and 30.6% developed AKI during the admission. In multivariable analyses, pCVD (OR 4.7, 95% CI 1.5-14.8, P=0.008) and AKI (OR 2.7, 95% CI 1.3-5.5, P=0.006) were associated with increased odds of in-hospital cardiac events. AKI was associated with increased odds of in-hospital mortality (OR 8.9, 95% CI 3.3-23.9, P<0.0001). The presence of AKI was associated with increased odds of ICU stay, mechanical ventilation, and acute respiratory distress syndrome (ARDS). Conclusion: pCVD and AKI were associated with higher risk of in-hospital cardiac events, and AKI was associated with a higher risk of in-hospital mortality in blacks.

Keywords: Pre-existing CVD, acute kidney injury, mortality, COVID-19, blacks

Introduction

The SARS-CoV-2, responsible for COVID-19 infection, is an ongoing cause of global morbidity and mortality [1]. SARS-CoV-2 is an enveloped single-stranded RNA virus which can cause mild or no symptoms at all, respiratory illness such as severe acute respiratory distress syndrome (ARDS), and in the most complex cases, fatal multi-organ failure and death [2]. As of January 24, 2021, there were 97,264,519 confirmed cases and 2,107,554 reported deaths worldwide [3]. Several studies suggest the presence of cardiovascular comorbidities can increase the susceptibility to contracting COVID-19 [4, 5]. Cardiometabolic comorbidities such as obesity, hypertension (HTN), and Type 2 diabetes (T2D) have also been associated with greater disease severity and higher fatality rates in patients infected with the virus [6]. Other hematologic findings related to cytokine storm, inflammatory states, hypercoagulable conditions, and lymphopenia are also associated with significant mortality of

infected patients [7]. In general, hospitalized patients with COVID-19 are found to have higher associations of diabetes, hypertension and cardiovascular disease (CVD) [6, 7]. Several observational studies in predominantly white and Asian populations have demonstrated a nearly five-fold increase in mortality for patients with pre-existing CVD (pCVD) when compared with patients without CVD [8-12]. According to the "Diagnosis and Treatment of Novel Coronavirus Pneumonia (Trial Version 4)", elderly patients with HTN, coronary artery disease (CAD), and T2D are also more likely to be infected with SARS-CoV-2 and suffer a worse prognosis [13, 14].

As of January 24, 2021, according to the World Health Organization, there have been a total of 24,604,325 confirmed cases and 410,667 reported deaths in the United States [3]. Several studies suggest significantly higher transmission and hospitalizations rates in blacks when compared with other populations [4, 15, 16]. In Atlanta, GA, a recent study suggests black race was associated with a significantly higher odds of hospitalization (aOR 3.2 95% CI 1.5-5.8) [15]. In patients hospitalized with COVID-19, CVD is the most common comorbidity associated with cardiac complications, worsening hospital course, and death [13, 17]. Other studies suggest higher in-hospital mortality in patients with pCVD and acute myocardial injury [6, 18]. This observation suggests that while both pCVD and cardiac injury independently portend worse outcomes, the occurrence of both conditions simultaneously may convey a synergistic interaction in predicting these adverse outcomes. The exact mechanism of the worsening prognosis associated with pCVD and COVID-19 remain unclear.

In addition, the data are limited on the effects of other acute organ injury, such as the renal system, in patients hospitalized for COVID-19 infection. Although several studies have associated black race with worse outcomes in COVID-19 affected patients, these data are also limited as to why this association is seen. To date, the available literature on the effects of COVID-19 on black race and the effects of CVD and acute kidney injury (AKI) are not robust. Thus, the objective in this study is to evaluate the impact of pCVD and AKI on cardiopulmonary outcomes among a black patient cohort hospitalized with COVID-19 infection.

Methods

This retrospective cohort study included patients seen at Grady Health System between February 1 and July 31, 2020, who tested positive for SARs-CoV-2 on qualitative polymerase chain-reaction assay and were hospitalized for symptomatic COVID-19 infection. This cohort study includes patients of black non-Hispanic race, admitted to the hospital for acute COVID-19 infection. All non-black or Hispanic patients were excluded from the final analysis. The race/ethnicity of the patients was self-identified previously within the hospital records. This study was approved by the Grady Health System ethical committee and Morehouse School of Medicine institutional review board (IRB).

Data collection

Clinical data were extracted from the health system's electronic medical record system, Epic, with the use of trained graduate and undergraduate medical education physicians. The data extracted included the following: demographic characteristics (patient-reported race, age, sex, ethnic group, insurance status); chronic conditions documented in the most current problem list diagnoses and from the last encounter prior to admission, body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) recorded at the time of index admission, selected outpatient medications (aspirin, beta-blockers, angiotensin-converting enzyme [ACE] inhibitors, angiotensin receptor blockers [ARBs], statin use, calcium channel blockers, P2Y12 platelet inhibitors), COVID-19 testing and other laboratory data (serum sodium, potassium, blood urea nitrogen, creatinine, complete blood count, liver function tests, erythrocyte sedimentation rate, c-reactive protein, total serum protein and albumin), in-hospital medication treatment (oxygen support, use of corticosteroids, hydroxychloroquine, azithromycin, remdesivir, and heparin anticoagulation use), use of non-invasive and mechanical ventilation, and clinical symptoms during admission. Quality control of the extracted data was ensured by 3 independent physician investigators who were blinded to the originally extracted datapoints by counterchecking the datapoints of randomly selected participants. COVID-19 was confirmed with a viral nucleic acid [reverse-transcriptase-polymerase-chain-

reaction (RT-PCR)] assay of samples obtained from nasopharyngeal swab. Patients were included in the analysis if they tested positive for the COVID-19 virus and were admitted for symptom management. Pre-existing cardiovascular disease was defined as presence of at least one of cardiac diagnoses within the medical record which included coronary artery disease, heart failure or evidence of left ventricular dysfunction on previous echocardiography within the past 12 months, valvular heart disease with at least moderate severity, cardiomyopathy, atrial fibrillation, and hypertension prior to being diagnosed with COVID-19. The outcome of myocardial injury was defined as blood levels of cardiac biomarker (troponin) above the 99th-percentile upper reference limit. Myocardial infarction was defined as myocardial injury in the presence of either typical angina, new ischemic ST-T wave changes on electrocardiography, new regional wall motion abnormality on echocardiography, or angiographic evidence of an acute coronary event. Acute myocarditis was clinically defined as myocardial injury in the presence of either one of acute heart failure (AHF), new onset fatal and non-fatal arrhythmias including atrial fibrillation and high degree conduction system disease, cardiogenic shock, or unexplained cardiac arrest. AKI was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) guideline as increase in serum creatinine by 0.3 mg/dl or more within 48 hours; or increase in serum creatinine up to or more than 1.5 times baseline which is known or presumed to have occurred within the prior 7 days [19]. Acute respiratory distress syndrome (ARDS) was defined according to the 2013 Berlin definition [20]. In-hospital mortality data and time in days to occurrence of specific outcome measures were monitored up to August 25, 2020 or the last day of follow-up.

Outcome measures and covariates

The primary outcome measure was a composite of acute cardiovascular diagnoses during the hospitalization which included the diagnoses of acute heart failure, myocardial injury, acute myocardial infarction, cardiogenic shock, fatal and non-fatal arrhythmias, or death from any cause. The secondary outcomes measures included in-hospital mortality, myocardial injury, acute myocarditis, ARDS, and ICU stay. In a subgroup analysis of only individuals with pCVD, we evaluated the impact of myocardial injury and, separately, the presence of AKI on in-hospital all-cause mortality.

Statistical analysis

We compared characteristics of the patients with pCVD and the patients who developed AKI during the hospital admission. Measures of location, dispersion, and proportion were used to describe all study variables. COVID-19 positive patients who were not hospitalized, or identified themselves as white, Asian, Hispanic, or did not have a recorded race or ethnic group were excluded from the analyses. Independent sample T-test (or Wilcoxon Rank Sum test where appropriate) and Chi-square (or Fisher's exact where appropriate) tests were used to compare continuous and binary variables respectively by the levels of the primary and secondary outcome variables. All outcome variables were defined on a binary scale. Multivariable binary logistic regression was used to assess the association between pCVD and outcome measures adjusting for covariates using backwards selection with 5% stay criteria. Similarly, a logistic regression model was fitted with in-hospital AKI as the main predictor. No multiple imputation was made for missing data. Fisher's exact test was used to assess the association between AKI, as well as myocardial injury, and all-cause mortality among the subset of patients with pCVD. SAS 9.4 software was used for all data analyses. For all the statistical analyses, 2-sided *P*-value ≤0.05 was considered significant.

Results

Demographics

Data was collected on 293 hospitalized patients admitted from February 2020 through July 2020. Of the 293 patients, 71 were excluded due to non-black race. Of the remaining 222 patients, 189 patients were successfully treated and discharged, and 33 (14.9%) patients died. This cohort included 130 (58.6%) men and 92 (41.4%) women, with a mean ± SD age of all included patients 63.1±16.4. Of the 222 patients, 175 (78.8%) had pCVD and 68 (30.6%) had AKI while hospitalized. Baseline characteristics with descriptive analyses are summarized in **Table 1**. Patients with pCVD were more

Table 1. Baseline characteristics of black patients hospitalized with COVID-19 (n=222)

Variable	All Patients (n=222)	pCVD (n=175)	In-hospital AKI (n=68)
Gender, male	130 (59%)	102 (58%)	42 (62%)
Age, mean (SD)	63.1 (16.4)	65.7 (14.5)	66.5 (15.0)
Admission Vital Signs, mean (SD)			
Systolic Blood Pressure	134.0 (23.8)	136.6 (24.7)	129.2 (20.9)
Diastolic Blood Pressure	80.0 (16.4)	80.9 (16.9)	80.3 (18.2)
Heart Rate	90.2 (17.9)	90.1 (17.4)	91.0 (16.6)
Respiratory Rate	21.6 (7.4)	21.7 (7.8)	22.0 (5.5)
Pulse Oximetry	95.9 (5.1)	95.6 (5.5)	94.4 (7.8)
Medical/Social History			
Hypertension	172 (77%)	172 (98%)	59 (87%)
Type 2 Diabetes	92 (41%)	89 (51%)	34 (50%)
Dyslipidemia	81 (36%)	75 (43%)	31 (46%)
CAD	27 (12%)	27 (15%)	13 (19%)
Atrial Fibrillation	23 (10%)	23 (13%)	13 (19%)
CHF	39 (18%)	39 (22%)	21 (31%)
VHD	12 (5%)	12 (7%)	7 (10%)
Prior CVA	45 (20%	38 (22%)	17 (25%)
COPD	26 (12%)	24 (14%)	8 (12%)
Asthma	16 (7%)	11 (6%)	4 (6%)
Obesity	91 (41%)	76 (43%)	34 (50%)
HIV	12 (5%)	8 (5%)	3 (4%)
Chronic Liver Disease	10 (5%)	9 (5%)	6 (9%)
Chronic Kidney Disease	44 (20%)	44 (25%)	18 (26%)
History of DVT/PE	31 (14%)	25 (14%)	9 (13%)
Alcohol Use	49 (22%)	40 (23%)	10 (15%)
Tobacco Use	67 (30%)	59 (34%)	22 (32%)
Medications			
Aspirin	76 (34%)	72 (41%)	26 (38%)
Statin	102 (46%)	92 (53%)	37 (54%)
Beta-Blocker	79 (36%)	77 (44%)	34 (50%)
ACE-Inhibitor	37 (17%)	36 (21%)	13 (19%)
Angiotensin Receptor Blocker	25 (11%)	24 (14%)	11 (16%)
Calcium Channel Blocker	79 (36%)	76 (43%)	27 (40%)
P2Y12 Platelet Inhibitor	16 (7%)	15 (9%)	4 (6%)

likely to have a history of HTN, Aspirin, and ACE-Inhibitor use. However, the patients with AKI were slightly older with a higher proportion of obesity and beta-blocker use (**Table 1**).

Treatment variables

In-hospital treatment variables are listed in **Table 2**. Of the 222 patients, 129 (58%) required oxygen support, and 42 (19%) of the cohort required mechanical ventilation during the hospitalization. In terms of medical treatment, 37 (17%) patients received Hydroxychloroquine, while 40 (18%) patients received Remdesivir. Corticosteroids were administered to 37 (17%) of all patients. There were a higher proportion of patients in the AKI group who required mechanical ventilation, when compared to the patients with pCVD (41% vs. 21%, respectively).

In-hospital cardiopulmonary endpoints

The proportions of in-hospital outcomes are listed in **Table 3**. Overall, the AKI group had higher proportions of ARDS, myocardial injury,

Table 2. In-hospital treatment

Therapy	All (n=222)	pCVD (n=175)	In-hospital AKI (n=68)
Oxygen, NC	129 (58%)	113 (65%)	48 (71%)
Non-Invasive Ventilation	77 (35%)	65 (37%)	28 (41%)
Mechanical Ventilation	42 (19%)	37 (21%)	28 (41%)
Corticosteroid	37 (17%)	25 (14%)	9 (13%)
Hydroxychloroquine	37 (17%)	31 (18%)	17 (25%)
Azithromycin	65 (29%)	56 (32%)	28 (41%)
Remdesivir	40 (18%)	28 (16%)	14 (21%)
Anticoagulation (heparin)	165 (74%)	130 (74%)	52 (76%)

Table 3. In-hospital outcomes

Outcome	All (n=222)	pCVD (n=175)	In-hospital AKI (n=68)
ARDS	84 (38%)	72 (41%)	43 (63%)
Myocardial Injury	86 (39%)	76 (43%)	37 (54%)
Myocardial Infarction	11 (5%)	11 (6%)	4 (6%)
Heart Failure	16 (7%)	16 (9%)	9 (13%)
Length of Stay (median ± SD)	12.1 (12.2)	12.9 (13.0)	14.4 (11.7)
In-hospital Death	33 (15%)	30 (17%)	21 (31%)

and in-hospital death when compared with the pCVD group. The primary outcome of composite in-hospital cardiovascular events were significant in both the pCVD and AKI groups (see **Table 4**). In adjusted analysis, the patients with pCVD were much more likely to have a cardiac event during hospitalization compared with patients without pCVD (aOR 4.7, 95% CI 1.5-14.8, P=0.008). Patients who developed AKI during the admission were also more likely to experience a cardiac event compared to patients with stable renal function (aOR 2.7, 95% CI 1.3-5.5, P=0.006). Patients who developed AKI also had higher odds of requiring an ICU stay (OR 6.9, 95% CI 3.3-14.5, P<0.0001), mechanical ventilation (aOR 11.3, 95% CI 4.5-28.3, P<0.0001), and developing ARDS (aOR 6.4, 95% CI 3.1-13.1, P<0.0001) compared to patients with stable renal function (see **Table 4**). The case fatality rate (CFR) in our overall black cohort was 14.9%. In a multivariable analysis, AKI patients had a significantly higher odds of in-hospital death when compared with patients without AKI (aOR 8.9, 95% CI 3.3-23.9, P<0.0001). The patients with pCVD were not more likely to require ICU stay, mechanical ventilation, develop ARDS, or die in-hospital when compared with patients without pCVD.

The additional mortality impact of AKI and myocardial injury in patients with pCVD

A subset of analysis of the deaths in the pCVD cohort is seen in **Table 5**. AKI (aOR, 3.8, 95% 1.5-9.8, P=0.006) and myocardial injury (aOR 7.1, 95% CI 2.6-19.5, P<0.001) in patients with pCVD were associated with higher odds of death when compared with patients having pCVD without these predictor variables (See **Table 5**). Overall, cardiorenal disease portends worse cardiovascular hard outcomes in COVID-19 infection.

Discussion

This analysis suggests significantly higher odds of cardiac events for black patients with pCVD or in-hospital AKI during hospitalization for COVID-19 infection. The presence of AKI in black patients hospitalized for COVID-19 was also significantly associated with increased odds of requiring an ICU stay, mechanical ventilation, and developing ARDS. Although ARDS and respiratory failure were considered the main cause of admission to an intensive care unit in patients with COVID-19, cardiovascular complications appear to contribute significantly to the disease morbidity and mortality. Reports have demonstrated an independent association between acute cardiac injury and increased risk of mortality in patients with COVID-19 [6, 14, 18, 21]. In these studies, investigators suggest patients with pCVD were more likely to have cardiac injury, evidenced by elevation of troponin-T levels, compared to patients without pCVD [14, 18]. However, these observations were seen in a primarily Asian population. Until now, the data of worsened hospital course in black patients with pCVD were limited. Although there were no differences of in-hospital mortality for black patients with pCVD compared to those without, our study suggests significant higher odds of black patients with pCVD experiencing a cardiac event during hospitalization for COVID-19 infection. These findings suggest it may be reasonable to consider interventions such as

Table 4. Adjusted odds ratio for outcomes by pCVD and in-hospital AKI

Outcome	pCVD OR (95% CI), *p*-value	In-Hospital AKI OR (95% CI), *p*-value
Primary Outcome	4.7 (1.5, 14.8), 0.008	2.7 (1.3, 5.5), 0.006
ARDS	1.2 (0.5, 3.1), 0.685	6.4 (3.1, 13.1), <0.0001
ICU Stay	3.0 (0.8, 11.1), 0.092	6.9 (3.3, 14.5), <0.0001
Mechanical Ventilation	1.6 (0.4, 6.3), 0.490	11.3 (4.5, 28.3), <0.0001
Myocardial Injury	3.3 (1.1, 10.4), 0.04	2.2 (1.1, 4.3), 0.025
In-hospital Death	4.5 (0.6, 35.8), 0.159	8.9 (3.3, 23.9), <0.0001

Table 5. Adjusted Odd Ratio for In-hospital all-cause mortality for Patients with pCVD and Myocardial Injury, or AKI

Predictor Variables and In-hospital Death	Odd Ratio (95% CI), *p*-value
pCVD with Acute Myocardial Injury (21/175)	3.8 (1.5, 9.8), 0.006
pCVD with AKI (20/175)	7.1 (2.6, 19.5), <0.001

telemetry for hospitalized black patients at higher risk for cardiac events. Our study also suggests that a heightened susceptibility to the viropathic effects of SARS-CoV-2, in this cohort known to have high CVD burden, may account for the higher incidence of cardiac injury in black populations as well.

The patients in this study with in-hospital AKI seemed to experience a much higher hospital morbidity during COVID-19 infection. The findings with in-hospital AKI were significant for a higher in-hospital death, and also higher odds of requiring escalations of care. Although the association of in-hospital AKI with increased morbidity and mortality require further investigation, these findings may present a plausible hypothesis for the worsened prognosis of black patients compared to some other racial groups.

Similarly, other inpatient studies of cardiovascular outcomes in patients infected with other coronaviruses like SARS-CoV and MERS-CoV, have shown higher incidence of cardiac events among patients with pCVD and/or cardiac injury. However, these observed event rates appear to be lower when compared to SARS-COV-2 infection [22-29].

The mechanisms of cardiac injury among patients with COVID-19 are not completely understood, however several pathogenic mechanisms including direct damage by the virus, systemic inflammatory response [30], destabilization of coronary plaque, and aggravated hypoxia [18] have been proposed. Elevated inflammatory markers like C-reactive protein in patients with COVID-19 have been positively correlated with troponin-T levels in a linear fashion [18], indicating that cardiac injury may be related to the heightened inflammatory processes and cytokine storm during COVID-19 infection. In addition, studies have reported a hypercoagulable milieu associated with COVID-19 infection [2, 6, 23, 31, 32]. It remains unclear if this results as a sequela of the inflammatory process or as part of the multiple organ dysfunction syndrome (MODS) seen with COVID-19. The heightened inflammatory and hypercoagulable states induced by COVID-19 infection may promote micro-thrombogenesis, resulting in decreased blood flow and ischemia in the distal coronary bed. Also, patients with pre-existing coronary heart disease (CHD) are more likely to have a significant amount of stable plaque burden compared to patients without pre-existing CHD. Other studies have suggested that procoagulant effects of systemic inflammation may increase the likelihood of stent thrombosis in those with a history of previous percutaneous coronary intervention [2, 33].

Similar to SARS-CoV and MERS-CoV, direct cytokine-mediated myocyte damage has been implicated as an important non-ischemic pathogenic mechanism of cardiac injury in patients with SARS-CoV-2 infection [6, 14]. Myocardial oxygen demand supply mismatch [34], hypoxia-induced myocyte apoptosis [35], and stress-induced cardiomyopathy in the phase of severe inflammatory response with cytokine storm have been reported as potential alternative mechanisms that contribute either to myocardial injury or directly to the cardiac dysfunction seen in COVID-19 [14]. Our study demonstrated that both pCVD and AKI are independently associated with composite cardiovascular endpoint that includes cardiac dysfunction in blacks with COVID-19. In patients with pCVD, the higher risk of myocardial injury compared to blacks without pCVD as shown in

our study may explain, in part, the observed elevated risk of clinical cardiac dysfunction. We speculate that similar pathogenic mechanisms of cardiac dysfunction occurring in other end organs may contribute to the MODS commonly seen in hospitalized patients with COVID-19.

Several studies report a high CVD burden in blacks [36-38]. As demonstrated in our study, pCVD increases the risk of myocardial injury in blacks. In our study, myocardial injury by itself is a strong predictor of all-cause mortality in black cohort with pCVD. These reports suggest that blacks with pCVD may be more likely to have myocardial injury when they develop COVID-19 and therefore more likely to die from any cause. This may partly explain why the CFR of COVID-19 is several folds higher in blacks when compared to the general population [39]. Higher prevalence of CVD in blacks or worse CVD outcomes, psychosocial factors including poor self-care, stress, inaccessibility to healthcare, health inequality, poor socioeconomic status, educational level, and lack of health insurance may contribute to the observed difference in CFR. Blacks have also been cited as being more likely to have higher social vulnerabilities including overcrowded housing and living in densely populated areas where optimal social-distancing practices may be at best difficult to attain [40]. This may increase the virus transmission rate and disease burden in this population where adverse cardiopulmonary outcomes after infection with SARS-CoV-2 have been demonstrated.

Although we demonstrate a higher risk of adverse outcomes in blacks with pCVD who develop COVID-19, whether this elevated risk of in-hospital cardiac events or other metabolic derangements persists long after resolution of the acute COVID-19 infection remains unknown. When likened to prior corona viruses, a cardiometabolic study amongst 25 SARS-CoV survivors revealed that lipid metabolism remained disrupted up till 12 years after clinical recovery from viral infection [33]. Since CVD is highly prevalent and one of the leading causes of death in blacks [41], SARS-CoV-2 infection may have longer-term implications for overall cardiovascular health in black populations.

Our study also evaluated the association of AKI with cardiopulmonary endpoints. In a subgroup analysis, black patients with pCVD who have COVID-19 have a much higher odds of death if their disease is complicated by AKI when compared to those without AKI. Unlike myocardial injury, similar mortality trend was not observed in the subset of patients without pre-existing CVD. The explanation for this finding is uncertain. However, it is plausible that AKI causing fluid retention, depending on the severity, can worsen clinical cardiac dysfunction and ARDS. Similar pathophysiologic mechanisms as described for cardiac dysfunction may also apply to kidney dysfunction, and multiple organ dysfunction occurring simultaneously may have an additive or synergistic interaction that portend more adverse clinical outcomes. It is also possible that in-hospital AKI is simply a marker of disease severity in patients who develop multiple organ dysfunction. In addition to other risk factors, black race has been reported as an independent risk factor of COVID-19 associated AKI [42]. In their systematic review, Fabrizi et al noted that the frequency of AKI is much greater with severe disease and is directly related to death rate in hospitalized patients with COVID-19 [43]. Substantial geographic variation in rates and severity of AKI have been reported, and nearly half of the patients with AKI did not recover to baseline at the time of discharge [44].

In our study, it appears that AKI is a stronger predictor of mortality than myocardial injury in black patients with pCVD who develop COVID-19. To our knowledge, no previous study has evaluated the individual association of pre-existing CVD and AKI with specific cardiopulmonary endpoints solely in black population.

Limitations

Our study had a sample size of 222 patients. A more robust study with a larger sample size is needed to support our findings. We included only a black population from a single medical center, so our findings may not be generalized to the entire black race. Our study was retrospective in nature, with inherent limitations that accompany such analyses. Although attempts were made to capture data on consecutive patients, there were likely patients that were missed for analysis in this cohort due to short hospital or observation stays. We did not include information from other serological datapoints or variables due to heavy missing values. This limits determination of potential

pathogenic mechanisms of the observed associations. Our study evaluates the association of pCVD and AKI with clinical outcomes including in-hospital mortality. We cannot exclude the possibility of unmeasured confounding in the analysis involving a novel viral infection. Although inferred, we did not evaluate cause-specific mortality. The causes of death may include ARDS, acute kidney failure, thromboembolic events from hypercoagulable milieu, or MODS, and not necessarily due to cardiac injury and dysfunction. Finally, we did not include patients who were asymptomatic or had only mild disease and were treated at home or in the emergency department alone. Therefore, our study findings may be more reflective of those who had a more severe form of COVID-19. Albeit these limitations, our study is the first of its kind linking possible etiologies to the outcomes seen in blacks.

Conclusion

In blacks with COVID-19, pCVD is associated with myocardial injury and composite cardiopulmonary endpoint but not with all-cause mortality or ARDS. In-hospital AKI is a strong predictor of ARDS, ICU stay, in-hospital cardiac events, and all-cause mortality in blacks hospitalized with COVID-19. Compared to the general population, black patients with pCVD or in-hospital AKI are more likely to suffer acute cardiovascular complications, and in some instances, in-hospital death. When compared to myocardial injury, in-hospital AKI is a stronger predictor of mortality in black patients with pCVD. Aggressive treatment and preemptive care should be strongly considered in black patients who have pCVD or in-hospital AKI during hospitalization for COVID-19 treatment. As the long-term course for these patients is still unknown, prolonged clinical follow-up amongst survivors of COVID-19 is therefore essential.

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This study was approved by the Grady Health System research ethical committee (ROC) and Morehouse School of Medicine institutional review board (IRB). Waiver of consent was also approved by the research oversight committee of the hospital system. Please refer to the following approval numbers FWA # 4535. IRB ID # 674.

Disclosure of conflict of interest

None.

Abbreviations

COVID-19, Corona Virus Disease-2019; pCVD, Pre-existing cardiovascular disease; AKI, Acute kidney injury; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; ARDS, Acute respiratory distress syndrome; IRB, Institutional review board; BMI, Body-mass index; RT-PCR, Reverse-transcriptase-polymerase-chain-reaction; AHF, Acute heart failure; KDIGO, Kidney Disease Improving Global Outcomes; CFR, Case fatality rate; MODS, Multiple organ dysfunction syndrome; CHD, Coronary heart disease; MERS-CoV, Middle east respiratory syndrome-corona virus; ICU, Intensive care unit.

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