Keywords
Acute kidney injury · Acute respiratory distress syndrome · Coronavirus disease 19 · In-hospital mortality

Abstract
Background: Although diffuse alveolar damage and respiratory failure are the key features of coronavirus disease 2019 (COVID-19), the involvement of other organs such as the kidney has also been reported. The reports of the incidence of acute kidney injury (AKI) in COVID-19 patients vary widely. In this study, we report our unique experience with AKI in COVID-19 patients in a low socioeconomic and predominantly ethnic minority group and provide its incidence, risk factors, and prognosis to expand the current understanding of this complication. Methods: In this single-center, retrospective cohort study, we analyzed the data of 469 COVID-19 patients admitted to the Brookdale University Hospital in Brooklyn, NY, from March 18 through April 23, 2020. Information regarding demographics, comorbidities, medications, clinical and laboratory data, and outcomes was collected from the electronic medical records. Both univariate and multivariate analyses were performed to determine the association of AKI with in-hospital mortality. Results: The median age was 66 years (interquartile range [IQR] 25–75; range 19–101 years), and 268 (57.14%) patients were male. Estimated glomerular filtration rate (eGFR) as determined by the Modification of Diet in Renal Disease Study Equation was low (<60 mL/min/1.73 m²) in 207 (44.1%) patients. During hospitalization, 128 (27.3%) patients developed AKI, and the incidence was significantly higher in those patients presenting with a low eGFR (N = 81, 39.1%; p < 0.001). Male sex, hypertension, the use of angiotensin-converting enzyme inhibitors and non-steroidal anti-inflammatory drugs, hemodynamic instability, mechanical ventilation, acute respiratory distress syndrome, and admission elevated ferritin, creatinine kinase, brain natriuretic peptide, and troponin 1 were identified as the risk factors for in-hospital AKI. Ninety-seven (28.45%) patients died in the non-AKI group versus 91 (71.1%) in the AKI group (p < 0.001). The Cox proportional hazard model after adjusting for age, gender, comorbidities, hemodynamic status, and PF ratio (arterial oxygen partial pressure [PaO₂]/fractional inspired oxygen [FiO₂]) determined that on admission, an elevated blood urea nitrogen (hazard ratio [HR]: 1.75; 95% confidence interval [CI] 1.23–2.48), a low eGFR (HR 1.43; CI 1.1–2.03), AKI stage 1 (HR 1.14; CI 0.64–2.03), AKI stage 2 (HR 1.86; CI 1.03–3.56), and AKI stage 3 (HR 2.1; CI 1.3–2.81) were independent risk factors for in-hospital mortality. Renal re-
placement therapy (RRT) did not improve survival in stage III AKI. **Conclusion:** AKI in our hospitalized COVID-19 patients was common and carried a high mortality, especially in patients with AKI stage 3. RRT did not improve survival. Policy changes and planning for this high incidence of AKI in COVID-19 patients and its associated high mortality are necessary at the local and national levels. © 2020 S. Karger AG, Basel

**Introduction**

Coronavirus disease 2019 (COVID-19) is associated with a high morbidity and mortality with a disproportionately poor outcome in the minority and low socioeconomic groups [1–3]. As reported by some, the association of acute kidney injury (AKI) and COVID-19 has a high mortality [4]. However, the incidence of reported AKI associated with COVID-19 varies widely [4–9]. It would be expected that kidney involvement is frequent since the virus enters the cell through the angiotensin-converting enzyme 2 (ACE2), which is expressed, in addition to pulmonary type 2 alveolar cells, on renal proximal tubular epithelial cells, glomerular visceral and parietal epithelium, and the cytoplasm of the distal tubules and collecting ducts [10–13]. In addition, COVID-19 induces hemodynamic instability and severe inflammation, which, in addition to direct renal infection, can induce acute tubular necrosis (ATN). We report our experience with AKI in COVID-19 patients in an inner city, predominantly minority, and a low socioeconomic group and compare our experience with other studies in significantly different cohorts of patients. We identify the incidence, risk factors, and prognosis of AKI and thus provide a broader understanding of this complication in a group of patients not specifically reported upon to date.

**Methods**

**Study Design and Participants**

All adult patients >18 years of age admitted to the Brookdale University Hospital and Medical Center with COVID-19 infection from March 18 through April 23, 2020, were studied in this retrospective analysis done in a single medical center serving a low-income minority population in Brooklyn, NY. It was one of the single centers with the most admissions of COVID-19 patients. COVID-19 infection was diagnosed based on clinical presentation, radiographic lung abnormalities, and a positive result of real time PCR. We excluded COVID-19 patients from our study if they were on maintenance hemodialysis or were renal transplant recipients. This study was approved by the Institutional Review Board of Brookdale Hospital and did not require patient consent because of its retrospective design.

**Data Source**

We collected the demographics, the presenting clinical symptoms when available, prior medical history including outpatient medications and prior level of renal function, comorbidities, and in-hospital laboratory data from the electronic medical record (Epic Hyperspace, 2015). Laboratory data consisted of complete blood count, hemostasis parameters, renal and liver function, PF ratio (arterial oxygen partial pressure [PaO₂]/fractional inspired oxygen [FiO₂]), creatinine kinase, lactate dehydrogenase, and inflammatory markers including high-sensitivity C-reactive protein (hs-CRP), ferritin, and D-dimer. Normal range of these measures was provided by our laboratory.

The Kidney Disease: Improving Global Outcome (KDIGO) [14] definition was used to identify AKI. Estimated glomerular filtration rate (eGFR) on admission was taken as baseline eGFR and was divided into <60 and ≥60 mL/min/1.73 m². eGFR was estimated using the Modification of Diet in Renal Disease Study (MDRD) equation. The earliest day of the serum creatinine change that met the KDIGO criteria for AKI was selected as day 1 of AKI. The peak serum creatinine value was used to determine the stage of AKI, with an increase in the serum creatinine of 1.5–1.9, 2.0–2.9, and ≥3 times the baseline serum creatinine defined as AKI stages 1, 2, and 3 respectively.

**Objective**

The primary objective of the study was to determine the incidence of in-hospital AKI in COVID-19 patients and to study baseline characteristics and laboratory data associated with its development. The secondary objective of the study was in-hospital mortality associated with AKI in COVID-19 patients determined by both a univariate and an adjusted regression model.

**Statistical Analysis**

Continuous variables were described as mean ± standard deviation for normally distributed data, or median and interquartile range (IQR) values for non-normal distribution. Categorical variables were presented as frequency and percentage. The mean of continuous variables was compared by using independent t tests, the Wilcoxon rank sum test, and the Kruskal-Wallis test (across the stages of AKI). The proportion of categorical variables was compared by using χ² test. Fischer’s exact test was used when there were only limited data available. The Kaplan-Meier method (log-rank test) was used to determine the cumulative incidence of in-hospital mortality. We used the Cox proportional hazard (PH) regression to determine the association of kidney disease indicators and in-hospital mortality. The assumptions of the Cox PH
Table 1. Baseline characteristics of COVID-19 patients admitted in the hospital stratified by baseline eGFR

| Characteristic                              | All patients | eGFR ≥60 mL/min/1.73 m² | eGFR <60 mL/min/1.73 m² | p value |
|---------------------------------------------|--------------|-------------------------|-------------------------|---------|
| Age, mean (SD)                              | 64.2 (15.55) | 61.22 (16.63)           | 68.03 (13.15)           | <0.0001 |
| Age, median (IQR)                           | 66 (55–75)   | 62 (51–73)              | 69 (60–77)              | <0.0001 |
| Gender, n (%)                               |              |                         |                         |         |
| Male                                        | 268 (57.14)  | 130 (49.62)             | 138 (66.67)             | <0.001  |
| Female                                      | 201 (42.86)  | 132 (50.38)             | 69 (33.33)              |         |
| Race, n (%)                                 |              |                         |                         |         |
| African American                            | 341 (72.71)  | 179 (68.32)             | 162 (78.26)             | 0.034   |
| Hispanic                                    | 67 (14.29)   | 39 (14.89)              | 28 (13.53)              |         |
| Asian                                       | 17 (3.62)    | 14 (5.34)               | 3 (1.45)                |         |
| Caucasian                                   | 7 (1.49)     | 6 (2.29)                | 1 (0.48)                |         |
| Other                                       | 37 (7.89)    | 24 (9.16)               | 13 (6.28)               |         |
| BMI, mean (SD)                              | 30.63 (7.73) | 30.67 (7.07)            | 30.58 (8.49)            | 0.81    |
| BMI, median (IQR)                           | 29 (25.6–34.2)| 29.2 (25.7–34.3)       | 28.2 (25.6–33.8)        | 0.25    |
| Preexisting comorbidities, n (%)            |              |                         |                         |         |
| Smoker                                      | 38 (8.10)    | 20 (7.63)               | 18 (8.70)               | 0.67    |
| Hypertension                                | 323 (68.87)  | 158 (60.31)             | 165 (79.71)             | <0.001  |
| Diabetes                                    | 219 (46.70)  | 105 (40.08)             | 114 (55.07)             | 0.002   |
| Hyperlipidemia                              | 147 (31.41)  | 70 (26.72)              | 77 (37.38)              | 0.014   |
| Coronary artery disease                     | 74 (15.81)   | 28 (10.69)              | 46 (22.33)              | 0.001   |
| Stroke                                      | 37 (7.91)    | 18 (6.87)               | 19 (9.22)               | 0.35    |
| COPD                                        | 34 (7.26)    | 21 (8.02)               | 13 (6.31)               | 0.48    |
| Asthma                                      | 63 (13.49)   | 43 (16.48)              | 20 (9.71)               | 0.03    |
| HIV                                         | 8 (1.85)     | 4 (1.65)                | 4 (2.11)                | 0.73    |
| Cancer                                      | 31 (6.62)    | 18 (6.87)               | 13 (6.31)               | 0.81    |
| Signs and symptoms, n (%)                   |              |                         |                         |         |
| Nausea/vomiting                             | 45 (9.59)    | 25 (9.54)               | 20 (9.66)               | 0.96    |
| Diarrhea                                    | 52 (11.09)   | 29 (11.07)              | 23 (11.11)              | 0.98    |
| Cough                                       | 248 (52.88)  | 156 (59.44)             | 92 (44.44)              | 0.001   |
| Dyspnea                                     | 312 (66.52)  | 183 (69.85)             | 129 (62.32)             | 0.09    |
| Fever                                       | 236 (50.32)  | 143 (54.58)             | 93 (44.93)              | 0.04    |
| Sore throat                                 | 18 (3.84)    | 12 (4.58)               | 6 (2.90)                | 0.35    |
| Fatigue                                     | 176 (37.53)  | 89 (33.97)              | 87 (42.03)              | 0.07    |
| Myalgia                                     | 118 (25.16)  | 66 (25.19)              | 52 (25.12)              | 0.96    |
| Altered mental status                       | 91 (19.40)   | 35 (13.36)              | 56 (27.05)              | <0.001  |
| Syncope                                     | 11 (2.35)    | 4 (1.53)                | 7 (3.38)                | 0.18    |
| Chest pain                                  | 25 (5.33)    | 19 (7.25)               | 6 (2.90)                | 0.04    |
| Drugs, n (%)                                |              |                         |                         |         |
| Statin                                      | 171 (36.46)  | 79 (30.15)              | 92 (44.44)              | 0.001   |
| ACEi                                        | 98 (20.98)   | 43 (16.41)              | 55 (26.57)              | 0.007   |
| ARB                                         | 50 (10.66)   | 24 (9.16)               | 26 (12.56)              | 0.24    |
| NSAID                                       | 48 (10.23)   | 26 (9.92)               | 22 (10.63)              | 0.80    |
| Aspirin                                     | 128 (27.29)  | 56 (21.37)              | 72 (34.78)              | 0.001   |
| Hemodynamic instability at presentation, n (%)| 70 (14.93)  | 31 (11.89)              | 39 (18.84)              | 0.03    |
| PF ratio                                    |              |                         |                         |         |
| >300 mm Hg                                  | 70 (25.36)   | 40 (27.59)              | 30 (22.90)              | 0.034   |
| 200–300 mm Hg                               | 45 (16.30)   | 31 (21.38)              | 14 (10.69)              |         |
| 100–200 mm Hg                               | 74 (26.81)   | 32 (22.07)              | 42 (32.06)              |         |
| <100 mm Hg                                  | 87 (31.52)   | 42 (28.97)              | 45 (34.35)              |         |
| AKI during hospitalization                  | 128 (27.29)  | 47 (17.94)              | 81 (39.13)              | <0.001  |
| Stage 1                                     | 43 (9.17)    | 16 (6.11)               | 27 (13.04)              | <0.001  |
| Stage 2                                     | 20 (4.26)    | 10 (3.82)               | 10 (4.83)               |         |
| Stage 3                                     | 65 (13.86)   | 21 (8.02)               | 44 (21.26)              |         |
| Day of AKI, median (IQR)                    | 3 (2–5)      | 4 (3–7)                 | 2 (1–4)                 | 0.04    |
| Administration of mechanical ventilation     | 100 (21.32)  | 47 (17.94)              | 53 (25.60)              | 0.044   |
model were checked using the Schoenfeld residuals, and no violations of the assumptions were present. In the multivariable analysis, separate Cox PH models were used to determine the association of baseline eGFR and blood urea nitrogen (BUN) on admission, proteinuria, hematuria, and stages of AKI with in-hospital mortality since these variables showed a highly significant correlation. Variables for Cox PH regression were selected using stepwise regression. Variables with a level of risk factor <0.10 were entered into the model. While evaluating the association of hematuria and proteinuria with in-hospital mortality by the Cox PH model, patients with missing values (n = 256) were excluded from the analysis. All statistical analyses were performed using the STATA version 14.2 software and a p value of <0.05 was used to determine statistical significance.

### Results

#### Sample Size and Baseline Characteristics

In this study, 500 adult confirmed cases of COVID-19 were initially reviewed. Patients on maintenance hemodialysis (n = 31) were excluded from the study and 469 patients were used for the analysis. Baseline characteristics of these patients are shown in Table 1. 72.7% of our cohort were African Americans and 14.3% were Hispanics. The median age of the patients was 66 years (IQR 55–75), and 57.1% of them were male. Most of these patients presented with dyspnea (66.5%), cough (52.9%), and fever (50.3%). 14.9% of the patients had a systolic blood pressure below 100 mm Hg at presentation. 21.3% (n = 100) of all patients were mechanically ventilated during the hospitalization. The median values of ferritin, D-dimer, hs-CRP, creatinine kinase and lactate dehydrogenase were elevated above their reference ranges (see online suppl. Table 1; for all online suppl. material, see www.karger.com/doi/10.1115/000511160). 54.3% (n = 255) of all the patients studied were discharged, 5.6% (n = 26) were transferred to the other institution, and 40.1% (n = 188) died during hospitalization.

#### Renal Dysfunction

On admission, eGFR was <60 mL/min/1.73 m² in 44.1% (n = 207) of the patients. 70.4 and 52.5% of the patients, in which these data were available (45.4% of the

Table 1 (continued)

| Characteristic                        | All patients N = 469 (100%) | eGFR ≥60 mL/min/1.73 m² N = 262 (55.9%) | eGFR <60 mL/min/1.73 m² N = 207 (44.1%) | p value |
|--------------------------------------|-----------------------------|----------------------------------------|----------------------------------------|---------|
| Disposition on discharge, n (%)      |                             |                                        |                                        |         |
| Home                                 | 228 (48.61)                 | 154 (58.78)                            | 74 (35.75)                             | <0.001  |
| NH                                   | 27 (5.76)                   | 16 (6.11)                              | 11 (5.31)                              |         |
| Transferred to other hospitals       | 26 (5.54)                   | 13 (4.96)                              | 13 (6.28)                              |         |
| In hospital death                    | 188 (40.09)                 | 79 (30.15)                             | 109 (52.66)                            |         |
| Length of stay in days, median (IQR)| 6.5 (3–10)                  | 6 (3–10)                               | 7 (4–10)                               | 0.64    |

PF ratio, arterial oxygen partial pressure (PaO₂)/fractional inspired oxygen (FiO₂). eGFR, estimated glomerular filtration rate; AKI, acute kidney injury; SD, standard deviation; IQR, interquartile range; BMI, basal metabolic index; COPD, chronic obstructive pulmonary disease; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blockers; NSAID, non-steroidal anti-inflammatory drug; NH, nursing home.

Fig. 1. Cumulative incidence of acute kidney injury in COVID-19 patients admitted in the hospital stratified by baseline admission estimated glomerular filtration rate (eGFR) in mL/min/1.73 m².
Table 2. Baseline characteristics of COVID-19 patients stratified by in-hospital AKI status

| Characteristics                                      | All patients | No-AKI \((N = 341)\) | AKI \((N = 128)\) | \(p\) value |
|------------------------------------------------------|--------------|------------------------|-------------------|-------------|
| Age, median (IQR)                                    | 66 (55–75)   | 65 (55–74)             | 67 (55–76)        | 0.26        |
| Gender, \(n\) (%)                                    |              |                        |                   |             |
| Male                                                 | 268 (57.14)  | 179 (52.49)            | 89 (69.53)        | 0.001       |
| Female                                               | 201 (42.86)  | 162 (47.51)            | 39 (30.47)        |             |
| Race, \(n\) (%)                                      |              |                        |                   |             |
| African American                                     | 341 (72.71)  | 242 (70.97)            | 99 (77.34)        | 0.15        |
| Hispanic                                             | 67 (14.29)   | 50 (14.66)             | 17 (13.28)        |             |
| Asian                                                | 17 (3.62)    | 16 (4.69)              | 1 (0.78)          |             |
| Caucasian                                            | 7 (1.49)     | 4 (1.17)               | 3 (2.34)          |             |
| Other                                                | 37 (7.89)    | 29 (8.50)              | 8 (6.25)          |             |
| BMI, median (IQR)                                    | 29 (25.6–34.2) | 28.9 (25.2–34.3) | 29.2 (27.1–34.1) | 0.14        |
| Preexisting comorbidities, \(n\) (%)                 |              |                        |                   |             |
| Smoker                                               | 38 (8.10)    | 30 (8.80)              | 8 (6.25)          | 0.36        |
| Hypertension                                         | 323 (68.87)  | 226 (66.28)            | 97 (75.78)        | 0.048       |
| Diabetes                                             | 219 (46.70)  | 152 (44.57)            | 67 (52.34)        | 0.14        |
| Hyperlipidemia                                       | 147 (31.41)  | 106 (31.09)            | 41 (32.28)        | 0.82        |
| Coronary artery disease                              | 74 (15.81)   | 48 (14.08)             | 26 (20.47)        | 0.09        |
| Stroke                                               | 37 (7.91)    | 25 (7.33)              | 12 (9.45)         | 0.45        |
| COPD                                                 | 34 (7.26)    | 24 (7.04)              | 10 (7.87)         | 0.84        |
| Asthma                                               | 63 (13.49)   | 51 (14.96)             | 12 (9.52)         | 0.13        |
| HIV                                                  | 8 (1.85)     | 6 (1.94)               | 2 (1.63)          | 0.98        |
| Cancer                                               | 31 (6.62)    | 23 (6.74)              | 8 (6.30)          | 0.98        |
| CKD                                                  | 50 (10.66)   | 32 (9.38)              | 18 (14.06)        | 0.14        |
| Home medications, \(n\) (%)                          |              |                        |                   |             |
| Statin                                               | 171 (36.46)  | 123 (36.07)            | 48 (37.50)        | 0.74        |
| ACEi                                                 | 98 (20.98)   | 63 (18.48)             | 35 (27.34)        | 0.035       |
| ARB                                                  | 50 (10.66)   | 33 (9.68)              | 17 (13.28)        | 0.26        |
| NSAID                                                | 48 (10.23)   | 28 (8.21)              | 20 (15.63)        | 0.02        |
| Aspirin                                              | 128 (27.29)  | 87 (25.51)             | 41 (32.03)        | 0.16        |
| Hemodynamic instability at presentation, \(n\) (%)   | 70 (14.93)   | 37 (10.85)             | 33 (25.78)        | <0.001      |
| PF ratio, \(n\) (%)                                  |              |                        |                   |             |
| >300 mm Hg                                           | 70 (25.36)   | 55 (31.61)             | 15 (14.71)        | 0.001       |
| 200–300 mm Hg                                        | 45 (16.30)   | 34 (19.54)             | 11 (10.78)        |             |
| 100–200 mm Hg                                        | 74 (26.81)   | 39 (22.41)             | 35 (34.31)        |             |
| <100 mm Hg                                           | 87 (31.52)   | 46 (26.44)             | 41 (40.20)        |             |
| Administration of mechanical ventilation, \(n\) (%)  | 100 (21.32)  | 32 (9.38)              | 68 (53.13)        | <0.001      |
| Disposition on discharge, \(n\) (%)                  |              |                        |                   |             |
| Discharged                                           | 228 (48.61)  | 203 (59.53)            | 25 (19.53)        | <0.001      |
| Transferred to other hospital                        | 26 (5.54)    | 20 (5.87)              | 6 (4.69)          |             |
| NH/shelter                                           | 27 (5.76)    | 21 (6.16)              | 6 (4.69)          |             |
| In-hospital death                                    | 188 (40.09)  | 97 (28.450)            | 91 (71.09)        |             |
| Length of stay, median (IQR)                         | 6.5 (3–10)   | 6 (3–9)                | 8 (5–12)          | <0.001      |
| Recovery of renal functions during hospitalization   |              |                        |                   |             |
| Full recovery                                        | –            | –                      | 20 (15.6)         | –           |
| Partial recovery                                     | –            | –                      | 15 (11.7)         | –           |

PF ratio, arterial oxygen partial pressure (\(\text{PaO}_2\))/fractional inspired oxygen (\(\text{FiO}_2\)). BMI, basal metabolic index; COPD, chronic obstructive pulmonary disease; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blockers; NSAID, non-steroidal anti-inflammatory drug; NH, nursing home.
cohort), had proteinuria and hematuria, respectively. Patients with an eGFR <60 mL/min/1.73 m² at presentation were significantly older (median age 69 vs. 62 years; \( p < 0.0001 \)), more likely to be males (66.7 vs. 33.3%), and have hypertension (HTN), diabetes, hyperlipidemia, and coronary artery disease among other preexisting comorbidities (Table 1). Patients with a presenting eGFR <60 mL/min/1.73 m² had associated elevated ferritin, D-dimer, hs-CRP, creatinine kinase, lactate, lactate dehydrogenase, and troponin on admission (\( p < 0.05 \)) (online suppl. Table 1).

The incidence of AKI during hospitalization was 27.3% (\( n = 128 \)) and was significantly higher in patients who presented with eGFR <60 mL/min/1.73 m² (39.1 vs. 17.9%) (Table 1; Fig. 1). 33.6, 15.6, and 50.8% of these patients had AKI stages 1, 2 and 3, respectively. The development of AKI was seen earlier in the course in patients with an eGFR <60 mL/min/1.73 m² at presentation (53.1 vs. 23.4%) and occurred within 48 h of admission. Patients who developed AKI during the hospitalization were more likely to have a systolic blood pressure of <100 mm Hg at presentation and a lesser PF ratio and were more likely to be intubated during the course of hospitalization (Table 2). Eighteen out of 50 patients with documented chronic kidney disease (CKD) prior to admission developed AKI during the hospitalization. Baseline laboratory values of these patients who developed AKI during hospitalization and those who did not are presented in online suppl. Table 2.

The number of patients requiring renal replacement therapy (RRT) during the hospitalization was 22. This represented 4.7% of all patients and 17.2% of those with AKI. All the patients who required RRT by definition had stage 3 AKI. The modalities of RRT were continuous RRT in 12 patients (54.5% of all those who required RRT) and intermittent hemodialysis in 8 patients (36.4%). Two patients (9.1%) required both modalities of RRT. 68% (68 out of 100) of those patients who required mechanical ventilation developed AKI compared with 16.3% (60 out of 369) of nonventilated patients. Of these 68 patients, 19 (27.9%) required RRT. The majority of AKI stage 3 pa-

**Fig. 2.** Cumulative incidence of in-hospital mortality in COVID-19 patient by acute kidney injury (a) and admitting estimated glomerular filtration rate (eGFR) (b). Shadows show the 95% confidence interval.
tients requiring RRT were on mechanical ventilation (19 out of 22 requiring RRT). 81.8% of the patients who were treated with RRT (18 out of 22 patients) died during the hospitalization. Of those with stage 3 AKI who were not dialyzed, 90% died. Renal function recovered sufficiently in 2 patients treated with RRT and both no longer required dialysis upon discharge.

Urine studies were available for 45.5% of all patients (n = 213), and in 60.1% (77 out of 128) of those patients who developed AKI. Hematuria of 2+ to 3+ was found by urine dipstick in 46.8% of AKI patients, while proteinuria of 2+ to 3+ was detected in 53.2% of the patients with AKI.

**AKI and In-Hospital Mortality**

Overall, the in-hospital mortality was 40.1% in COVID-19 patients. The in-hospital mortality was significantly higher in patients with an eGFR <60 mL/min/1.73 m<sup>2</sup> (52.6%) than in patients with an eGFR ≥60 mL/min/1.73 m<sup>2</sup> (30.2%) at presentation. The in-hospital mortality of AKI patients was 71.1% (91 out of 128 who developed AKI died) (Table 2).

A significantly higher in-hospital mortality was observed in patients with an eGFR <60 mL/min/1.73 m<sup>2</sup> at presentation, elevated BUN at presentation, and in-hospital AKI using the Kaplan-Meier analysis (Fig. 2). Age ≥75 years (hazard ratio [HR] 2.2; p < 0.001), preexisting comorbidities (diabetes mellitus [DM], HR 1.44; stroke, HR 1.97; and malignancy, HR 1.72; p < 0.05), PF ratio <200 (HR 1.73; p < 0.001), initial systolic blood pressure of <100 mm Hg (HR 2.3; p < 0.001), elevated presenting BUN (HR 1.73; p < 0.001), eGFR <60 mL/min/1.73 m<sup>2</sup> at presentation (HR 1.73; p < 0.001), and in-hospital AKI stage 2 (HR 1.96; p = 0.02) and stage 3 (HR 2.3; p < 0.001) were all associated with a higher in-hospital mortality by univariate Cox regression analysis (online suppl. Table 3). In a multivariable Cox PH model, adjusted for age, gender, PF ratio, hemodynamic status, and comorbidities (diabetes, HTN, hyperlipidemia, cancer, and stroke), eGFR <60 mL/min/1.73 m<sup>2</sup> at presentation, BUN on admission, and AKI greater than or equal to stage 2 was associated with a higher risk of in-hospital mortality. There was no significant association between in-hospital mortality and proteinuria and/or hematuria (Table 4).

**Discussion**

AKI is common among hospitalized patients (incidence 8–22%) and is associated with increased morbidity and mortality [15–17]. In our cohort of 469 COV-19 patients, a relatively higher percentage of patients (27.3%, 128 of 469) developed in-hospital AKI. Current evidence suggests that AKI in COVID-19 patients is a result of an interplay of virus-mediated injury, a dysregulated inflammatory response, angiotensin II pathway activation, hypercoagulation, and microangiopathy [18]. These COVID-19-specific factors likely interact with the other known risk factors for AKI, such as hemodynamic instability, hypoxia, and sepsis, which increased over time. The increase in the cumulative incidence of AKI over time in our cohort is likely associated with concomitant clinical deterioration and less likely represent a unique renal effect of COVID-19. Compared to studies of AKI in COVID-19 patients from other countries, we found our incidence to be higher than that reported from 2 Asian countries (0–9.2%), and is similar to that in an Italian study (27.8%) [5–9]. However, it is lower than that in the more recent report by Hirsch et al. [4] who detailed their experience in 13 academic and community hospitals in metropolitan New York (36.6%), none of which are located in the inner city, lower socioeconomic neighborhoods with a predominant minority population. As compared with the above-cited studies, the incidence of stage 3 AKI (13.9%) was highest in our cohort. It is not possible to determine with certainty the cause(s) of this wide variation. However, we did note a higher prevalence of comorbid conditions in our group. For example, Cheng et al. [5] reported a 5.1% incidence of AKI, with a 33.4% prevalence of HTN and a 14.3% prevalence of DM in their study population. In our cohort, roughly twice as many (68.9%) had HTN, and more than 3 times as many (46.7%) were diabetic (Table 1). Also, the incidence of severe lung involvement that required mechanical ventilation was lower (13.4%) than ours (21.3%) (Table 1). Mechanical ventilation per se has been reported to be strongly associated with AKI [4]. In our cohort, the incidence of AKI was also higher among those requiring mechanical ventilation (68%).

We identified various risk factors for AKI in our study (Tables 2, 3). Similar to previous reports, our patients with AKI were more likely to be male, have a history of HTN, and have severe respiratory failure requiring mechanical ventilation [4, 5]. In our study, higher BMI increased the likelihood of developing severe AKI. A low eGFR at presentation more than doubled the risk of developing AKI (p < 0.001) (Table 1). Patients with lower eGFR had a significantly higher cumulative incidence of AKI than those with eGFR >60 mL/min/1.73 m<sup>2</sup> (p < 0.001; Fig. 1). Thus, there was a synergistic effect of reduced baseline kidney function and subsequent AKI. We
| Characteristics                     | All AKI \((N = 128)\) | stage 1 \((N = 43)\) | stage 2 \((N = 20)\) | stage 3 \((N = 65)\) | p value (stages of AKI) | p value (no-RRT vs. RRT) |
|-------------------------------------|------------------------|----------------------|----------------------|----------------------|------------------------|------------------------|
| Age, median (IQR)                  | 67 (55–76)             | 7 (58–80)            | 65.5 (54–74)         | 67 (54–74)           | 0.19                   | 0.005                  |
| Gender, n (%)                      | Male 89 (69.53)        | 29 (67.44)           | 14 (32.6)            | 46 (70.77)           | 0.011                  | 0.98                   |
|                                     | Female 39 (30.47)      | 14 (32.56)           | 6 (30.0)             | 13 (30.23)           |                        |                        |
| Race, n (%)                        | African American 59 (46.03) | 17 (39.53)          | 6 (30.0)             | 8 (12.31)            | 0.19                   | 0.78                   |
|                                     | Hispanic 17 (13.28)    | 3 (6.99)             | 0 (0.00)             | 0 (0.00)             |                        |                        |
|                                     | Asian 1 (0.78)         | 1 (2.33)             | 0 (0.00)             | 0 (0.00)             |                        |                        |
|                                     | Caucasian 8 (6.30)     | 3 (6.99)             | 2 (10.00)            | 3 (4.61)             |                        |                        |
|                                     | Other 2 (1.63)         | 1 (2.33)             | 1 (5.00)             | 0 (0.00)             |                        |                        |
| BMI, median (IQR)                  | 29.2 (27.2–34.1)       | 27.9 (25.5–34.5)     | 29.2 (27.4–32.6)     | 31.5 (27.6–35.5)     | 0.041                  | 0.11                   |
| Preexisting comorbidities, n (%)   | Smoker 8 (6.30)        | 2 (4.65)             | 1 (5.00)             | 5 (7.69)             | 0.04                   | 0.035                  |
|                                     | Hypertension 97 (75.78) | 36 (83.72)           | 12 (60.0)            | 55 (85.38)           | 0.052                  | 0.017                  |
|                                     | Diabetes 67 (52.34)    | 21 (68.48)           | 10 (50.0)            | 35 (55.38)           | 0.32                   | 0.04                   |
|                                     | Hyperlipidemia 41 (32.28) | 10 (23.26)          | 6 (30.0)             | 24 (37.50)           | 0.46                   | 0.04                   |
|                                     | Coronary artery disease 5 (3.92) | 1 (2.33)          | 0 (0.00)             | 4 (6.25)             | 0.38                   | 0.08                   |
|                                     | Stroke 12 (9.45)       | 4 (9.30)             | 2 (10.00)            | 10 (15.38)           | 0.56                   | 0.65                   |
|                                     | COPD 10 (7.87)         | 4 (9.30)             | 0 (0.00)             | 6 (9.38)             | 0.35                   | 0.41                   |
|                                     | Asthma 12 (9.45)       | 1 (2.33)             | 3 (15.00)            | 7 (11.23)            | 0.78                   | 0.53                   |
|                                     | HIV 10 (7.87)          | 4 (9.30)             | 0 (0.00)             | 6 (9.38)             | 0.82                   | 0.29                   |
|                                     | Cancer 8 (6.30)        | 2 (4.65)             | 0 (0.00)             | 6 (9.38)             | 0.82                   | 0.29                   |
|                                     | CKD 18 (14.06)         | 7 (16.28)            | 0 (0.00)             | 11 (16.92)           | 0.06                   | 0.11                   |
| Hemodynamic instability at presentation, n (%) | Statin 48 (37.50) | 14 (32.6)            | 7 (35.0)             | 27 (41.53)           | 0.029                  | 0.055                  |
|                                     | ACEI 35 (27.34)        | 13 (30.23)           | 6 (30.00)            | 16 (24.62)           | 0.17                   | 0.37                   |
|                                     | ARB 17 (13.28)         | 5 (11.63)            | 2 (10.00)            | 10 (15.38)           | 0.41                   | 0.71                   |
|                                     | NSAID 30 (23.03)       | 10 (23.26)           | 9 (45.00)            | 11 (16.92)           | 0.04                   | 0.71                   |
|                                     | Aspirin 41 (32.28)     | 13 (30.23)           | 6 (30.00)            | 16 (24.62)           | 0.54                   | 0.58                   |
|                                     | Hemodynamic instability at presentation, n (%) | Statin 48 (37.50) | 14 (32.6)            | 7 (35.0)             | 27 (41.53)           | 0.029                  | 0.055                  |
|                                     | ACEI 35 (27.34)        | 13 (30.23)           | 6 (30.00)            | 16 (24.62)           | 0.17                   | 0.37                   |
|                                     | ARB 17 (13.28)         | 5 (11.63)            | 2 (10.00)            | 10 (15.38)           | 0.41                   | 0.71                   |
|                                     | NSAID 30 (23.03)       | 10 (23.26)           | 9 (45.00)            | 11 (16.92)           | 0.04                   | 0.71                   |
|                                     | Aspirin 41 (32.28)     | 13 (30.23)           | 6 (30.00)            | 16 (24.62)           | 0.54                   | 0.58                   |
did not find an association between diabetes and in-hospital AKI.

The role of angiotensin-converting enzyme inhibitors (ACEi) in COVID-19 is a subject of ongoing debate. ACEi can increase the expression of ACE2, the receptor used by SARS-CoV-2 to enter target cells [19, 20]. However, ACE2 has been shown to be beneficial in acute respiratory distress syndrome when replaced [21, 22]. This possible protective effect is attributed to the degradation of proinflammatory angiotensin II to angiotensin by ACE2. At present, it remains unclear if ACEi facilitate severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cellular entry and intracellular virus replication and whether ACEi improve acute respiratory distress syndrome outcomes. In our cohort, the use of ACEi was significantly higher in patients with a lower admitting eGFR (Table 1) and in those who experienced AKI (Table 2). We found a similar association between AKI and non-steroidal anti-inflammatory drugs, but not with angiotensin II receptor blockers (ARBs) in our cohort (Table 2). Further studies are necessary to delineate the relationship between ACEi, angiotensin II receptor blockers, and COVID-19 outcomes.

Markers of acute inflammation (ferritin and CRP), muscle injury (creatinine kinase), myocardial injury, and D-dimer levels were significantly higher in patients with a low eGFR at presentation (online suppl. Table 1) and in those with AKI (online suppl. Table 2), suggesting causality by a dysregulated immune/inflammatory response, the so-called “cytokine storm.”

We found an extremely high incidence of mortality in our study cohort. High presenting BUN and low eGFR (<60 mL/min/1.73 m²) were significantly associated with
increased mortality (Table 1). AKI was significantly associated with increased mortality. The mortality risk was highest in stage 3 AKI (HR 2.1; CI 1.3–2.81) (Table 4). Mortality was 71.1% in the AKI group and 28.5% in the non-AKI group (p < 0.001). Mortality rose concurrently with the AKI stages, 44.2, 75, and 87.7% for stages 1, 2, and 3, respectively (Table 3). These rates were over 2- and 5-fold higher than those reported by Hirsch et al. [4] (34.8% AKI, 5.6% in non-AKI). However, our cohort’s high mortality is similar to the findings of Johns Hopkins University and the American Community Survey. They reported a 3- and 6-fold higher COVID-19 infection and mortality rate in predominantly African American counties than in predominantly white counties [2]. Wadhera et al. [23] also reported a death rate of 181 per 100,000 in Brooklyn, about 50% higher than that of Manhattan. Moreover, in New York City, current age-adjusted mortality is highest among African Americans and about 1.5 times that of whites [24].

Our hospital provides medical services for an ethnic minority and a low-income population in the most impoverished neighborhood in Brooklyn, where 37% of the residents live below the Federal Poverty Level as per a 2015 report [25]. 72.7% of our patients identified themselves as African Americans. In comparison, in the study by Hirsch et al. [4], 38.8% identified themselves as whites, and only 20.6% identified themselves as African Americans. The high representation of ethnic minorities in our study population may have contributed to the increased mortality. This association has been widely publicized and is likely the result of a complex interplay of multiple factors. These include, but are not limited to, a high burden of comorbidities, genetics, the pernicious influence of adverse socioeconomic determinants of health, the absence of the privilege to work from home, and the ability to follow the recommended social distancing [3].

In our cohort, 22 (17.2%) of the 128 patients with AKI required RRT. Nineteen out of these 22 patients (86.4%) were mechanically ventilated. Thus, almost all of the additional requirements for acute dialysis during the COVID-19 pandemic at our institution were in intensive care units. Overall, 27.9% (19 out of 68) of mechanically ventilated patients required RRT. Elevated ferritin was associated with an increased risk of all stages of AKI and an extremely high mortality, especially in AKI stage 3. Unfortunately, RRT provided little survival benefit. Policy changes and planning in preparation for this high incidence of AKI in COVID-19 patients are necessary at the local and national levels.
Statement of Ethics
Study was approved by Institutional Review Board (IRB), Brookdale Hospital.

Conflict of Interest Statement
The authors have no conflicts of interests to declare.

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Author Contributions
U.Z. – wrote manuscript and literature review; P.R. – IRB approval and data and manuscript review; S.S., L.A., P.K. – manuscript review; A.C., M.A., G.M., A.S., and J.T.N. – data collection; and P.B. – supervisor.