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# Outcomes Among Patients Hospitalized With COVID-19 and Acute Kidney Injury

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**Rationale & Objective:** Outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19) and acute kidney injury (AKI) are not well understood. The goal of this study was to investigate the survival and kidney outcomes of these patients.

**Study Design:** Retrospective cohort study.

**Setting & Participants:** Patients (aged ≥18 years) hospitalized with COVID-19 at 13 hospitals in metropolitan New York between March 1, 2020, and April 27, 2020, followed up until hospital discharge.

**Exposure:** AKI.

**Outcomes:** Primary outcome: in-hospital death. Secondary outcomes: requiring dialysis at discharge, recovery of kidney function.

**Analytical Approach:** Univariable and multivariable time-to-event analysis and logistic regression.

**Results:** Among 9,657 patients admitted with COVID-19, the AKI incidence rate was 38.4/1,000 patient-days. Incidence rates of in-hospital death among patients without AKI, with AKI not requiring dialysis (AKI stages 1-3), and with AKI receiving dialysis (AKI 3D) were 10.8, 31.1, and 37.5/1,000 patient-days, respectively. Taking those without AKI as the reference group, we observed greater risks for in-hospital death for patients with AKI 1-3 and AKI 3D (HRs of 5.6 [95% CI, 5.0-6.3] and 11.3 [95% CI, 9.6-13.1], respectively). After adjusting for demographics, comorbid conditions, and illness severity, the risk for death remained higher among those with AKI 1-3 (adjusted HR, 3.4 [95% CI, 3.0-3.9]) and AKI 3D (adjusted HR, 6.4 [95% CI, 5.5-7.6]) compared with those without AKI. Among patients with AKI 1-3 who survived, 74.1% achieved kidney recovery by the time of discharge. Among those with AKI 3D who survived, 30.6% remained on dialysis at discharge, and prehospitalization chronic kidney disease was the only independent risk factor associated with needing dialysis at discharge (adjusted OR, 9.3 [95% CI, 2.3-37.8]).

**Limitations:** Observational retrospective study, limited to the NY metropolitan area during the peak of the COVID-19 pandemic.

**Conclusions:** AKI in hospitalized patients with COVID-19 was associated with significant risk for death.

Visual Abstract online

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Acute kidney injury (AKI) is a common complication among hospitalized patients with severe coronavirus disease 2019 (COVID-19) infection. Although the reported incidence of AKI among hospitalized patients with COVID-19 varies widely, recent studies from the United States have suggested an incidence as high as 37% to 40%.[1-3] AKI among hospitalized patients is associated with poor prognosis,[4] increased length of stay, and increased health care costs.[5] Patients who survive AKI appear to be at increased risk for death and incident chronic kidney disease (CKD).[6]

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Outcomes among hospitalized patients with COVID-19 and AKI are incompletely understood. Published studies on AKI in COVID-19 to date have been hindered by relatively small sample sizes or incomplete clinical courses with patients still receiving treatment in the hospital.[7-10] Because recovery from severe COVID-19 often takes weeks in the hospital, previously published studies may result in a skewed view of end points, potentially biasing toward adverse outcomes.[11-13] Additionally, prior publications have not addressed varied timelines of AKI development during hospitalization or the varied duration of follow-up.

In our previously reported study on AKI in COVID-19 among 5,449 patients, 39% of patients remained hospitalized and thus outcomes were not determined.[1] Accordingly, we provided only limited results and discussion pertaining to outcomes. In this current study, we include 9,657 patients with COVID-19, in which >99% have completed outcomes. The purpose of the current study therefore was to rigorously analyze in-hospital mortality and kidney outcomes among patients with COVID-19 and AKI.

## Methods

### Study Design and Cohort

This was a retrospective observational cohort study of a large New York health system. Data for this study were obtained from 13 hospitals using the enterprise inpatient electronic health record Sunrise Clinical Manager (Allscripts). All adult (aged ≥ 18 years) patients with positive

**PLAIN-LANGUAGE SUMMARY**

In a large New York health system, a significant proportion of patients hospitalized for coronavirus disease 2019 (COVID-19) infection experienced acute kidney injury (AKI), but their overall and kidney-related outcomes were unknown. Given the prolonged hospitalizations for these critically ill patients, studies to date have been hampered by a lack of complete follow-up and outcome ascertainment. We found that the risk for dying in the hospital was significantly higher if one developed AKI and particularly so for those who needed dialytic support. Most patients with AKI who survived to hospital discharge had kidney recovery, although among patients with AKI requiring dialysis, ~31% still needed outpatient dialysis at the time of discharge. Chronic kidney disease was the only independent risk factor associated with requiring dialysis at discharge.

results by polymerase chain reaction testing of a nasopharyngeal sample for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) who were hospitalized from March 1, 2020, to April 27, 2020, were eligible. Patients who were transferred between hospitals within the health system were treated as 1 hospital encounter. For patients who had multiple qualifying hospital admissions, we included only the first hospitalization. Patients were excluded if they were transferred to hospitals out of the health system, admitted to inpatient obstetric services, had kidney failure, had a prior kidney transplant, or had fewer than 2 serum creatinine (Scr) measurements during the admission. The identification and exclusion of patients with kidney failure and kidney transplant recipients are described fully in Item S1. The latest date of discharge for patients enrolled in the study was June 4, 2020. The Institutional Review Board of Northwell Health approved the study protocol before the commencement of the study. Individual-level informed consent was not obtained given the retrospective nature of the analysis of a large electronic medical record.

## Outcomes

The primary outcome was in-hospital death. Secondary outcomes comprised the following kidney outcomes: (1) the need for dialysis at discharge among patients who had developed AKI 3D (stage 3, receiving dialysis) and survived and (2) recovery of kidney function at discharge among patients who had developed AKI (both AKI 1-3 [stages 1 -3 not receiving dialysis] and AKI 3D) and survived.

## Definitions and Measurements

AKI was defined according to KDIGO (Kidney Disease: Improving Global Outcomes) criteria as follows: stage 1, as an increase in Scr level by 0.3 mg/dL within 48 hours or 1.5 to 1.9 times increase in Scr level from baseline within 7 days; stage 2, as 2 to 2.9 times increase in Scr level within 7 days; and stage 3, as 3 or more times increase in Scr level within 7 days or initiation of dialysis.[14] Patients were stratified according to the most severe AKI stage attained during their hospital stay. Baseline Scr level and adjudication of AKI were automatically calculated from a prebuilt operational algorithm, available internally since June 2019 (Item S1; Fig S1), which is based on KDIGO AKI criteria and the United Kingdom National Health Service AKI algorithm.[15] Any patient receiving dialysis, regardless of automated AKI stage reporting, was defined as AKI stage 3 (specifically AKI 3D), as per KDIGO criteria. We did not use the urine output criteria to define AKI because documentation of urine output in the electronic health record was unreliable. Estimated glomerular filtration rate was calculated using the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation.[16]

For the AKI 1-3 group, recovery of kidney function at discharge was defined as a decline of 33% in discharge Scr level from the peak Scr level. Given that patients with AKI stage 1 may recover kidney function without meeting the 33% decline in Scr level, those with AKI stage 1 also met the definition of recovery of kidney function with a decline in Scr level ≥ 0.3 mg/dL (ie, reversal of AKI stage 1).[17] For the AKI 3D group, kidney recovery was defined as no longer needing dialysis at discharge, as well as a decline of at least 33% in discharge Scr level from peak Scr level. The peak Scr level was based on the highest Scr value before initiating dialysis.

The definition of CKD was based on provider-entered medical history documentation and included *International Classification of Diseases, Tenth Revision* (ICD-10) codes N18.3, N18.4, and N18.5. Because prehospitalization baseline Scr level was available for only 18.6% of the cohort, we were unable to determine CKD diagnosis based on KDIGO criteria.[18] For patients with AKI 3D who survived, the study investigators performed manual chart review to determine the presence and stage of CKD (Item S1). Because the adjudication process was labor intensive, manual verification was limited to this subset of patients.

## Measurement of Incidence

We measured incidence rates of AKI and in-hospital death using patient-days as the denominator.

## Covariates

We collected data for patient demographics, baseline history of comorbid conditions, home medications, and details on hospital admissions. Comorbid conditions and home medications were determined from provider-entered medical history and admission medication reconciliation. We collected details of hospital admission such as intensive care unit (ICU) stay, mechanical ventilation,

vasopressor support, and baseline laboratory test results within 48 hours of hospital admission. The duration of time off dialysis and need for dialysis on hospital discharge were determined through manual chart reviews of hospital progress notes, discharge notes, and social worker notes.

### Statistical Analysis

We report descriptive statistics including median and interquartile range (IQR) for skewed continuous measures and proportions for categorical measures. We compared baseline patient characteristics between patients with or without AKI using Fisher exact tests for categorical variables and nonparametric Kruskal-Wallis tests for continuous variables.

To evaluate the relationship between AKI and in-hospital death, we performed univariable and multivariable Cox regression models by treating AKI status as a time-varying exposure and in-hospital death as the outcome.[19] The exposure of interest for in-hospital death was a 3-level AKI status: no AKI, AKI stages 1-3 but not receiving dialysis (AKI 1-3), and AKI receiving dialysis (AKI 3D). Patients were censored on the day of discharge or June 4, 2020, whichever came first. We chose the models a priori based on known risk factors for AKI-associated mortality in hospitalized patients.[6,20,21] In model 1, we adjusted for demographics, including age, sex, and race/ethnicity. In model 2, we adjusted for demographics and comorbid conditions, including body mass index, diabetes mellitus, hypertension, cardiovascular diseases (coronary artery disease, heart failure, and peripheral vascular disease), respiratory disease (asthma and chronic obstructive pulmonary disease), CKD, chronic liver disease, and cancer. In model 3, we added variables pertaining to illness severity, including values for admission oxygen saturation, hemoglobin, lymphocyte count, platelet count, serum urea nitrogen, serum bilirubin, serum albumin, C-reactive protein, and serum ferritin and the need for mechanical ventilation and vasoactive medication. Because D-dimer had a substantial degree of missingness (no AKI group [38.5%], AKI 1-3 [33%], and AKI 3D [27.4%]), we did not include it into our models. Mechanical ventilation and vasoactive medication use were treated as time-varying covariates.

To determine kidney outcomes of patients who developed AKI (both AKI 1-3 and AKI 3D) and survived, we evaluated the proportion of patients who had recovery of kidney function. Among patients who developed AKI 3D and survived, we performed univariable and multivariable logistic regression to identify risk factors for needing dialysis on discharge. The variables selected into the multivariable regression analysis were decided a priori and chosen based on known factors for nonrecovery of kidney function, including age, cardiovascular disease, known kidney disease, and need for vasopressor and mechanical ventilation.[22,23]

Missing data in regression models were handled using multiple imputation (Item S1). All statistical tests were 2 sided, and $P < 0.05$ was considered statistically significant. All analyses were performed using R, version 3.6.3 (R Foundation for Statistical Computing).

## Results

### Study Participants and Characteristics

From March 1, 2020, to April 27, 2020, a total of 11,635 patients were admitted to 13 health system hospitals with a diagnosis of COVID-19. Of these, 9,657 were included in the final cohort (Fig 1) and were followed up to June 4, 2020, day of death, or the day of discharge, whichever came earlier. A total of 2,409 (24.9%) patients were admitted to an ICU, 2,033 (21.1%) were treated with mechanical ventilation, and 2,075 (21.5%) required vasopressor support during the hospital stay. Within the cohort, 2,418 (25.0%) died, 7,149 (74.0%) were discharged home, and 90 (0.9%) were still admitted. Complete hospital disposition data were available for 99.6% of patients without AKI, 98.1% of patients with AKI 1-3, and 96.2% of patients with AKI 3D (Fig 2).

A total of 3,854/9,657 (39.9%) patients developed AKI, of whom 3,216/9,657 (33.3%) had AKI 1-3 (1,644 with stage 1 [17%], 840 with stage 2 [8.7%], and 732 with stage 3 [7.6%]) and 638 (6.6%) had AKI 3D. After accounting for follow-up time, the incidence rate of AKI was 38.3/1,000 patient-days, with an incidence rate of AKI 1-3 and AKI 3D of 32.0 and 6.3/1,000 patient-days, respectively. Table 1 shows clinical characteristics of patients by AKI status. Patients who developed AKI had a higher proportion with comorbid conditions including diabetes mellitus, coronary artery disease, heart failure, and CKD. Additionally, the AKI 3D group had the highest levels of inflammatory markers (D-dimer, C-reactive protein, and serum ferritin) followed by the AKI 1-3 group and the non-AKI group.

We found that in the AKI 1-3 group, 1,313/3,216 (40.8%) patients required mechanical ventilation and 1,354/3,216 (42.1%) required vasopressors, whereas in the AKI 3D group, these proportions were 581/638 (91.0%) and 584/638 (91.5%), respectively. Median time to diagnosis of AKI was 10.3 hours after initiation of mechanical ventilation (IQR, −0.1 to 30.4) and 7.3 (IQR, −2.5 to 29.4) hours after initiation of vasopressor therapy. Among patients who required mechanical ventilation and had AKI, most (1,415/1,894; 74.7%) developed AKI after initiation of mechanical ventilation. Similarly, among those with AKI and who required vasopressors, 1,357/1,938 (70%) developed AKI after vasopressor therapy initiation.

### In-Hospital Death and Length of Stay

Among the 5,801 without AKI, 421 (7.3%) experienced in-hospital death, a rate of 10.8 deaths/1,000 patient-days. For the 3,216 patients with AKI 1-3, a total of 1,491 (46.4%) died (31.1 deaths/1,000 patient-days). Taking

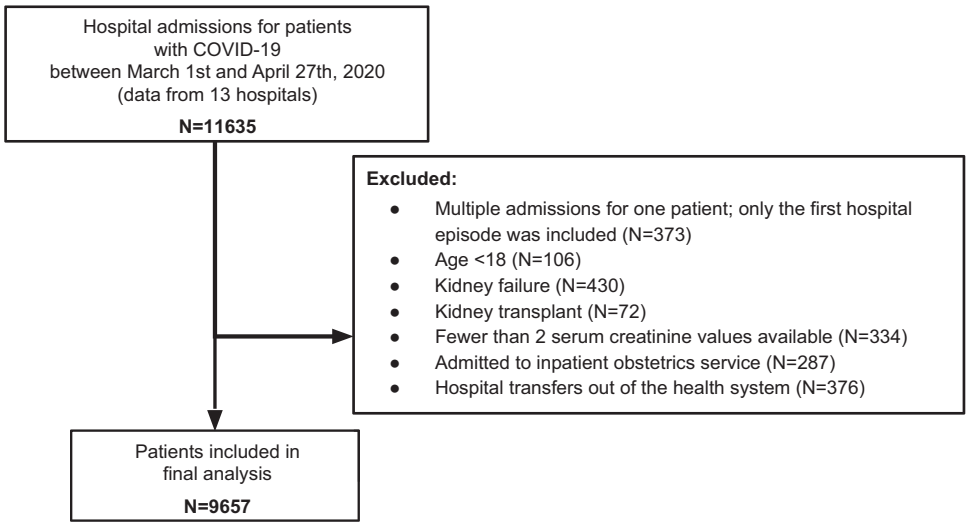


**Figure 1.** Flow chart of study cohort. Abbreviation: COVID-19, coronavirus disease 2019.

the group without AKI as the reference group, the unadjusted hazard ratio (HR) for in-hospital death was 5.6 (95% CI, 5.0-6.3) in the AKI 1-3 group. The risk for in-hospital death remained significant following adjustments for baseline demographics (model 1: adjusted HR, 4.9 [95% CI, 4.3-5.5]), demographics and comorbid conditions (model 2: adjusted HR, 4.9 [95% CI, 4.4-5.5]), and demographics, comorbid conditions, and illness severity (model 3: adjusted HR, 3.4 [95% CI, 3.0-3.9]). Among the 638 patients with AKI 3D, 506 (79.3%) died (37.5 deaths/1,000 patient-days). Using the group without AKI as the reference group, the unadjusted HR for in-hospital death was 11.3 (95% CI, 9.6-13.1) for those with AKI 3D. The risk for in-hospital death remained significant in all 3 adjusted models (model 1: adjusted HR, 11.7 [95% CI, 9.9-13.7]; model 2: adjusted HR, 11.7 [95% CI, 10.1-13.6]; and model 3: adjusted HR, 6.5 [95% CI, 5.5-7.6]; Table 2).

Median length of stay of patients who were discharged alive differed significantly based on AKI status. Patients with AKI 3D had the longest median length of stay (29.2 [IQR, 19.0-46.1] days), followed by patients with AKI 1-3 (11.6 [IQR, 6.9-20.9] days) and patients without AKI (5.2 [IQR, 3.0-8.6] days).

## Kidney Outcomes

Of 3,854 adults meeting our eligibility criteria for AKI, 3,216 (83.4%) developed AKI 1-3 during their

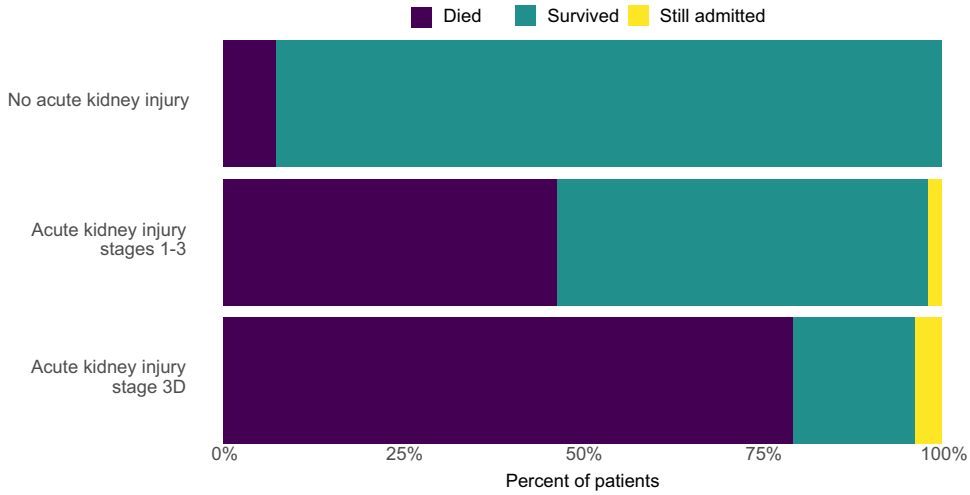


**Figure 2.** Hospital disposition by status of acute kidney injury (AKI). Of the 9,657 patients in the study cohort, 7.3% of those without AKI died, whereas the proportion of patients who died was higher among those with AKI stages 1 - 3 not receiving dialysis (AKI 1-3) (46.4%) and AKI receiving dialysis (AKI 3D) (79.3%). Among the entire cohort, only 0.9% of patients remained hospitalized.

**Table 1.** Clinical Characteristics by Worst AKI Status During Hospitalization

| Variables[a] | No AKI (n = 5,803) | AKI 1-3 (n = 3,216) | AKI 3D (n = 638) | *P*[b] |
|---|---|---|---|---|
| Age, y[c] | 62.0 [51.0-75.0] | 71.0 [61.0-81.0] | 64.0 [57.0-72.0] | <0.001 |
| Age category | | | | <0.001 |
| <40 y | 548 (9.4%) | 125 (3.9%) | 18 (2.8%) | |
| 40-49 y | 745 (12.8%) | 186 (5.8%) | 51 (8.0%) | |
| 50-59 y | 1,226 (21.1%) | 434 (13.5%) | 146 (22.9%) | |
| 60-69 y | 1,269 (21.9%) | 715 (22.2%) | 215 (33.7%) | |
| 70-79 y | 1,024 (17.6%) | 841 (26.2%) | 159 (24.9%) | |
| ≥80 y | 991 (17.1%) | 915 (28.5%) | 49 (7.7%) | |
| Male sex | 3,366 (58.0%) | 1,879 (58.4%) | 502 (78.7%) | <0.001 |
| Race/ethnicity | | | | <0.001 |
| Non-Hispanic White | 1,946 (33.5%) | 1,226 (37.9%) | 156 (25.3%) | |
| Non-Hispanic Black | 1,103 (19.0%) | 669 (20.7%) | 138 (22.4%) | |
| Hispanic | 1,282 (22.1%) | 599 (18.5%) | 138 (22.4%) | |
| Other | 1,060 (18.3%) | 531 (16.4%) | 124 (20.1%) | |
| Unknown | 412 (7.1%) | 213 (6.6%) | 60 (9.7%) | |
| Insurance | | | | <0.001 |
| Commercial | 2,062 (35.5%) | 724 (22.5%) | 225 (35.3%) | |
| Medicaid | 1,288 (22.2%) | 537 (16.7%) | 138 (21.6%) | |
| Medicare | 2,300 (39.6%) | 1,894 (58.9%) | 261 (40.9%) | |
| Self-pay | 74 (1.3%) | 30 (0.9%) | 7 (1.1%) | |
| Other | 79 (1.4%) | 31 (1.0%) | 7 (1.1%) | |
| Tertiary care center | 3,984 (68.7%) | 2,133 (66.3%) | 451 (70.7%) | 0.03 |
| BMI, kg/m$^2$[c] | 28.3 [25.1-32.5] | 27.6 [24.2-32.3] | 30.1 [26.6-35.4] | <0.001 |
| BMI category | | | | <0.001 |
| <18.5 kg/m$^2$ | 83 (1.4%) | 91 (2.8%) | 5 (0.8%) | |
| 18.5-9.9 kg/m$^2$ | 3,085 (53.2%) | 1,781 (55.4%) | 263 (41.2%) | |
| ≥30.0 kg/m$^2$ | 1,994 (34.4%) | 1,043 (32.4%) | 286 (44.8%) | |
| Unknown | 641 (11.0%) | 301 (9.4%) | 84 (13.2%) | |
| Tobacco status | | | | <0.001 |
| Never | 4,605 (79.4%) | 2,154 (67.0%) | 411 (64.4%) | |
| Smoker | 1,091 (18.8%) | 733 (22.8%) | 138 (21.6%) | |
| Unknown | 107 (1.8%) | 329 (10.2%) | 89 (13.9%) | |
| CCI[c] | 3.0 [2.0-6.0] | 6.0 [3.0-8.0] | 4.0 [3.0-6.0] | <0.001 |
| Comorbid conditions | | | | |
| Diabetes | 1,770 (30.5%) | 1,401 (43.3%) | 298 (48.4%) | <0.001 |
| Hypertension | 3,117 (53.7%) | 2,218 (68.5%) | 395 (64.1%) | <0.001 |
| CAD | 599 (10.3%) | 570 (17.6%) | 80 (13.0%) | <0.001 |
| Heart failure | 290 (5.0%) | 435 (13.4%) | 66 (10.7%) | <0.001 |
| PVD | 91 (1.6%) | 118 (3.6%) | 15 (2.4%) | <0.001 |
| Asthma | 537 (9.3%) | 216 (6.7%) | 44 (7.1%) | <0.001 |
| COPD | 300 (5.2%) | 273 (8.4%) | 37 (6.0%) | <0.001 |
| Chronic liver disease | 157 (2.7%) | 93 (2.9%) | 14 (2.3%) | 0.7 |
| Cancer | 413 (7.1%) | 295 (9.1%) | 46 (7.5%) | 0.003 |
| CKD[d] | 169 (2.9%) | 279 (8.6%) | 44 (7.1%) | <0.001 |
| Home medications | | | | |
| No. of medications[c] | 4.0 [1.0-8.0] | 7.0 [3.0, -10.0] | 4.0 [1.0-8.0] | <0.001 |
| ACEi | 717 (13.0%) | 435 (15.3%) | 89 (17.7%) | 0.001 |
| ARB | 884 (16.0%) | 603 (21.2%) | 102 (21.5%) | <0.001 |
| β-Blocker | 1,305 (23.7%) | 1,085 (38.1%) | 138 (27.4%) | <0.001 |
| CCB | 1,107 (20.1%) | 777 (27.3%) | 153 (31.4%) | <0.001 |
| Thiazide | 520 (9.4%) | 329 (11.6%) | 48 (9.5%) | 0.005 |
| MRA | 66 (1.2%) | 77 (2.7%) | 12 (2.6%) | <0.001 |
| Loop diuretics | 381 (6.9%) | 453 (15.9%) | 69 (13.7%) | <0.001 |
| Anticoagulation | 453 (8.2%) | 377 (13.2%) | 40 (8.0%) | <0.001 |
| Antiplatelet | 1,242 (22.5%) | 956 (33.6%) | 145 (28.8%) | <0.001 |

*(Continued)*

**Table 1 (Cont'd).** Clinical Characteristics by Worst AKI Status During Hospitalization

| Variables[a] | No AKI (n = 5,803) | AKI 1-3 (n = 3,216) | AKI 3D (n = 638) | P[b] |
|---|---|---|---|---|
| Statin | 1,904 (34.5%) | 1,320 (46.4%) | 209 (42.5%) | <0.001 |
| Admission vital signs[c] | | | | |
| Systolic BP, mm Hg | 129.0 [116.0-145.0] | 126.0 [111.0-144.0] | 134.0 [120.0-152.0] | <0.001 |
| Diastolic BP, mm Hg | 76.0 [68.0-84.0] | 73.0 [64.0-82.0] | 76.0 [68.0-84.8] | <0.001 |
| Heart rate, bpm | 98.0 [85.0-110.0] | 98.0 [84.0-111.0] | 102.0 [88.0-115.0] | <0.001 |
| Respiratory rate, breaths/min | 20.0 [18.0-22.0] | 20.0 [18.0-24.0] | 22.0 [19.0-28.0] | <0.001 |
| $S_{PO_2}$, % | 95.0 [91.0-97.0] | 94.0 [88.8-97.0] | 92.0 [85.0-95.0] | <0.001 |
| Temperature, ° C | 37.4 [36.9-38.1] | 37.3 [36.8-38.1] | 37.4 [36.9-38.3] | <0.001 |
| Severity of illness | | | | |
| ICU | 367 (6.3%) | 1453 (45.2%) | 589 (92.3%) | <0.001 |
| Mechanical ventilation | 139 (2.4%) | 1313 (40.8%) | 584 (91.5%) | <0.001 |
| Use of vasopressors | 151 (2.6%) | 1354 (42.1%) | 584 (91.5%) | <0.001 |
| eGFR from nadir Scr | | | | <0.001 |
| ≥60 mL/min/1.73 $m^2$ | 5,136 (88.5%) | 2,237 (69.6%) | 404 (63.3%) | |
| 45-59 mL/min/1.73 $m^2$ | 354 (6.1%) | 305 (9.5%) | 69 (10.8%) | |
| 30-45 mL/min/1.73 $m^2$ | 192 (3.3%) | 312 (9.7%) | 54 (8.5%) | |
| 15-29 mL/min/1.73 $m^2$ | 91 (1.6%) | 249 (7.7%) | 63 (9.9%) | |
| <15 mL/min/1.73 $m^2$ | 30 (0.5%) | 113 (3.5%) | 48 (7.5%) | |
| Laboratory test results within 48 h of hospital admission[c] | | | | |
| Complete blood cell count | | | | |
| WBC count, $\times 10^3/\mu L$ | 7.1 [5.4-9.5] | 8.1 [5.9-11.3] | 8.2 [6.1-11.4] | <0.001 |
| Lymphocyte count, $\times 10^3/\mu L$ | 0.9 [0.7-1.3] | 0.8 [0.6-1.2] | 0.8 [0.6-1.1] | <0.001 |
| Hemoglobin, g/L | 13.3 [12.1-14.4] | 13.1 [11.6-14.4] | 13.6 [12.0-14.8] | <0.001 |
| Platelet count, $\times 10^3/\mu L$ | 213.0 [165.0-278.0] | 207.0 [156.0-272.0] | 210.0 [153.3-262.0] | <0.001 |
| Metabolic panel | | | | |
| Sodium, mmol/L | 136.0 [133.0-139.0] | 136.0 [133.0-140.0] | 135.0 [132.0-138.0] | <0.001 |
| Potassium, mmol/L | 4.0 [3.7-4.4] | 4.2 [3.8-4.7] | 4.2 [3.8-4.7] | <0.001 |
| Carbon dioxide, mmol/L | 24.0 [22.0-26.0] | 23.0 [20.0-25.0] | 21.0 [19.0-24.0] | <0.001 |
| SUN, mg/dL | 15.0 [11.0-21.0] | 25.0 [16.0-44.0] | 24.0 [15.0-43.0] | <0.001 |
| Scr, mg/dL | 1.0 [0.8-1.2] | 1.3 [0.9-2.0] | 1.3 [1.0-2.4] | <0.001 |
| Albumin, g/L | 3.5 [3.1-3.8] | 3.3 [2.8-3.7] | 3.3 [2.8-3.7] | <0.001 |
| Total bilirubin, mg/dL | 0.5 [0.4-0.7] | 0.5 [0.4-0.7] | 0.6 [0.4-0.8] | <0.001 |
| D-Dimer assay, ng/mL | 386.0 [243.0-732.5] | 582.5 [344.5-1,275.0] | 622.0 [355.0-1,866.0] | <0.001 |
| Missing | 2,232 (38.5%) | 1,085 (33.7%) | 175 (27.4%) | |
| C-Reactive protein, mg/dL | 9.5 [5.0-16.2] | 12.7 [7.0-21.0] | 15.9 [9.4-24.0] | <0.001 |
| Missing | 1281 (22.1%) | 629 (19.6%) | 91 (14.3%) | |
| Ferritin, ng/mL | 698.9 [356.0-1,282.0] | 854.3 [459.0-1,459.0] | 1,024.5 [632.5-1,892.3] | <0.001 |
| Missing | 1,340 (23.1%) | 718 (22.3%) | 1,036 (16.6%) | |

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; AKI 1-3, AKI stages 1-3 but not receiving dialysis; AKI 3D, AKI stage 3 receiving dialysis; ARB, angiotensin II receptor blocker; BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; CCB, calcium channel blocker; CCI, Charlson Comorbidity Index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; MRA, mineralocorticoid receptor antagonist; PVD, peripheral vascular disease; Scr, serum creatinine; $S_{PO_2}$, oxygen saturation as measured by pulse oximetry; SUN, serum urea nitrogen; WBC, white blood cell.
[a]The proportion of missing data is shown if missingness is >1%.
[b]We compared the different groups using Kruskal-Wallis rank sum test.
[c]Data expressed as median [interquartile range].
[d]CKD is defined here as per *International Classification of Diseases, Tenth Revision* code.

admission, and of these, 1,663/3,216 (51.7%) survived and 1,233/1,663 (74.1%) recovered kidney function (Fig 3). Across all stages of AKI, median Scr level on discharge was lower than median admission and peak Scr levels (Fig 4).

For patients with AKI 3D, 108/638 (16.9%) patients survived and 24 (3.7%) remained hospitalized (Figs 2 and 3). Among those who survived, 72/108 (66.7%) had recovery of kidney function, that is, not needing dialysis at discharge and a minimum of 33% decline in discharge Scr level from peak Scr level (Fig 3). Among the 72 patients with recovery of kidney function, 54 (75%) had a discharge Scr level lower than the admission and peak levels (Fig 4). In the AKI 3D group who survived, the remaining 36/108 (33.3%) did not achieve recovery of kidney function; of these, 33/36 still needed dialysis at discharge and 3/36 were discharged off dialysis but did not have at least 33% decline in discharge Scr level from

**Table 2.** HRs for In-Hospital Death Among Patients With AKI

| | AKI 1-3 | | AKI 3D | |
|---|---|---|---|---|
| | HR (95% CI) | *P* | HR (95% CI) | *P* |
| Unadjusted | 5.6 (5.0-6.3) | <0.001 | 11.3 (9.6-13.1) | <0.001 |
| Adjusted with model 1 | 4.9 (4.3-5.5) | <0.001 | 11.7 (9.9-13.7) | <0.001 |
| Adjusted with model 2 | 4.9 (4.4-5.5) | <0.001 | 11.7 (10.1-13.6) | <0.001 |
| Adjusted with model 3 | 3.4 (3.0-3.9) | <0.001 | 6.5 (5.5-7.7) | <0.001 |

*Note:* The exposure of interest was a 3-level AKI status: no AKI, AKI 1-3, and AKI 3D, all of which were treated as time-varying exposure. The reference used was no AKI status. Model 1 variables include age, sex, and race/ethnicity. Model 2 variables include those in model 1 and the following: body mass index, diabetes mellitus, hypertension, cardiovascular diseases (coronary artery disease, heart failure, and peripheral vascular disease), respiratory diseases (asthma and chronic obstructive pulmonary disease), chronic kidney disease (defined here as per *International Classification of Diseases, Tenth Revision* code), chronic liver disease, and cancer. Model 3 variables include those in model 2 and the following: values for oxygen saturation, hemoglobin, lymphocyte, platelet, serum urea nitrogen, bilirubin, albumin, C-reactive protein, and ferritin and need for mechanical ventilator and vasoactive medications.
Abbreviations: AKI, acute kidney injury; AKI 1-3, AKI stages 1-3 but not receiving dialysis; AKI 3D, AKI stage 3 receiving dialysis; HR, hazard ratio.

peak Scr level (Fig 3). Median time off dialysis before hospital discharge was 17.0 (IQR, 7.3-25) days.

Among the 108 patients with AKI 3D who survived, we studied potential risk factors for the need for dialysis on discharge. Nephrologist-adjudicated CKD status and stage were feasible for 101/108 (93.5%) patients. In the remaining 7 patients, we were unable to determine CKD status due to the lack of estimated glomerular filtration rate values outside the hospital admission.

Among patients who still needed dialysis at discharge, most (19/33 [58%]) had underlying CKD on admission (10, 7, and 2 with CKD stages 5, 4, and 3, respectively). Another 10/33 (30%) did not have CKD on admission, and 4/33 (12%) had indeterminate status (Table 3). Notably, 17/19 (90%) patients with underlying CKD stages 4 and 5 who had AKI 3D needed dialysis on discharge.

By univariable analysis, increased age, cardiovascular disease, and CKD were risk factors associated with the need for dialysis at discharge, whereas need for mechanical ventilation and vasoactive medications were associated with lower risk (Table 4). In multivariable analysis, the only independent risk factor for needing dialysis at discharge was the presence of CKD at hospital admission (adjusted odds ratio, 9.3 [95% CI, 2.3-37.8]). Mechanical ventilation and vasoactive medication use were no longer significant predictors.

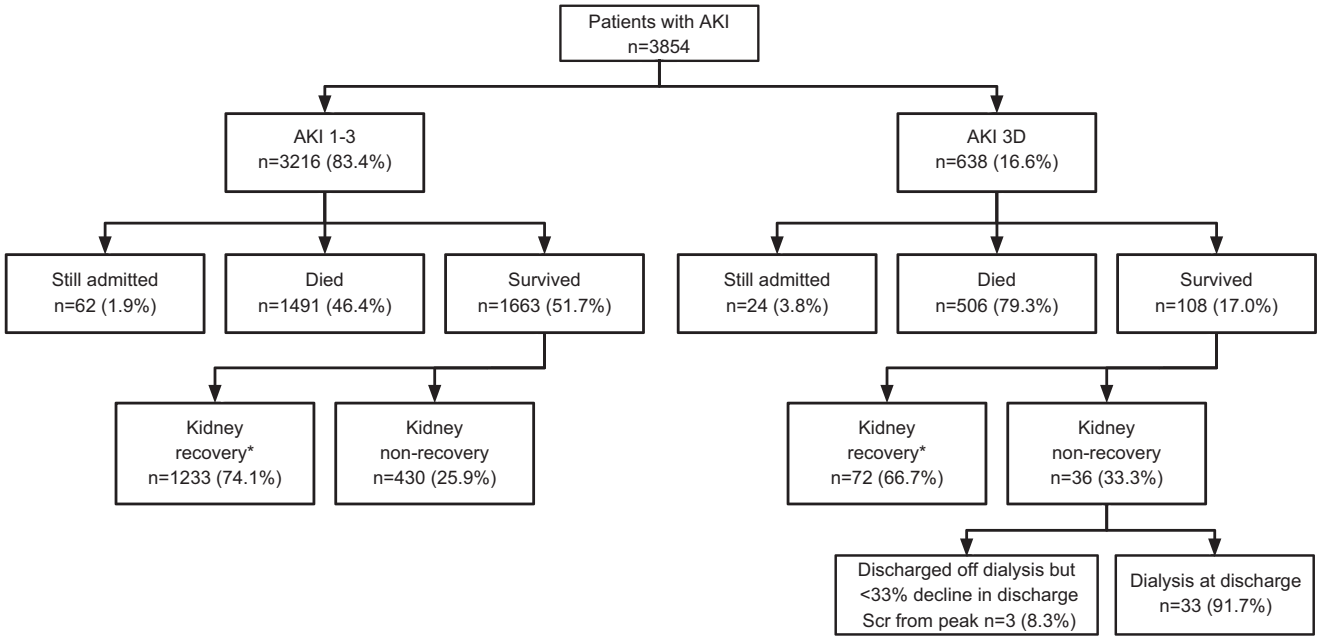


**Figure 3.** Flow chart of survival and kidney outcomes for patients with acute kidney injury (AKI) stages 1 to 3 but not receiving dialysis (AKI 1-3) and AKI stage 3 receiving dialysis (AKI 3D). Of 3,854 patients with AKI (39.9% of initial cohort [n = 9,657]), most (83.4%) had AKI 1-3, while 16.6% had AKI 3D. In the AKI 1-3 group, 46.4% died and 51.7% survived, of whom 74.1% had kidney recovery. Among AKI 3D, 79.3% died and 17% survived. Of the survivors, 66.7% had kidney recovery and 33.3% did not. Most (92%) of those without kidney recovery continued to require dialysis at discharge. *Kidney recovery defined as decline of at least 33% from peak serum creatinine level and not receiving dialysis at the time of discharge.

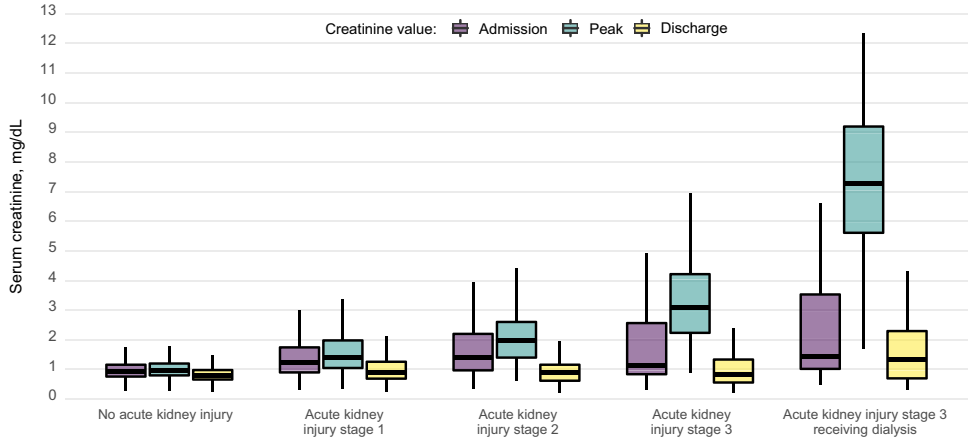


**Figure 4.** Admission, peak, and discharge serum creatinine levels among patients discharged alive, by stages of acute kidney injury (AKI). Across all stages of AKI, median serum creatinine level on discharge was lower than the median serum creatinine level at hospital admission or the median peak serum creatinine level. AKI stage 3 denotes only those who did not receive dialysis.

## Discussion

Due to the high rate of AKI among patients with COVID-19, it is important to understand how AKI affects survival and kidney outcomes.[1,7] Previous studies have been limited by small sample size or incomplete follow-up or have not focused primarily on survival or kidney outcomes.[24-26] Our current study of almost 10,000 hospitalized patients with COVID-19 with 99% completed end points and a survival analysis that incorporated the time-varying component of AKI allows for a clear assessment of survival and kidney outcomes in this patient population.

We found that the incidence rate of in-hospital death was highest among patients with AKI 3D, followed by AKI 1-3 and those without AKI (37.5 vs 31.1 vs 10.8 deaths/1,000 patient-days, respectively). It is clear that in-hospital death among patients with COVID-19 who develop AKI, and in particular those who received dialysis, is substantial, underscoring the need for shared decision making in these critically ill patients.

We used 3 survival models to adjust for confounding variables related to the association between AKI and increased mortality risk in COVID-19. The first 2 models focused on demographics and comorbid conditions and did little to change the observed risk relationships. The third model included markers of illness severity, including baseline laboratory test results, inflammatory marker levels, and the need for mechanical ventilation and vasopressor medications. Although this latter model greatly reduced the HRs for in-hospital death, both AKI 1-3 and AKI 3D remained significant risk factors for in-hospital death (HRs of 3.4 [95% CI, 3.0-3.9] and 6.4 [95% CI, 5.5-7.6], respectively, compared with those without AKI). This suggests that in addition to its independent association with risk for death, AKI may be an indicator of greater COVID-19–related disease severity. Although causality

**Table 3.** Characteristics of Patients Who Developed AKI 3D and Survived, Stratified by CKD Status

| | CKD | | | | |
|---|---|---|---|---|---|
| Variable | Stage 3 (n = 6) | Stage 4 (n = 9) | Stage 5 (n = 10) | No CKD (n = 76) | Indeterminate (n = 7) |
| Age, y[a] | 68.5 [59.0-83.3] | 68.0 [64.0-71.5] | 62.0 [54.0-68.5] | 62.0 [54.0-68.5] | 68.0 [64.0-71.5] |
| Male sex | 2 (33%) | 7 (100%) | 62 (82%) | 62 (82%) | 7 (100%) |
| Mechanical ventilation | 3 (50%) | 2 (29%) | 65 (86%) | 65 (86%) | 2 (29%) |
| Vasopressor | 2 (33%) | 2 (29%) | 64 (84%) | 64 (84%) | 2 (29%) |
| Serum creatinine, mg/dL[a] | | | | | |
| Admission | 3.5 [2.3-5.6] | 4.5 [3.7-9.0] | 1.3 [1.0-2.9] | 1.3 [1.0-2.9] | 4.5 [3.7-9.0] |
| Peak | 5.9 [4.3-7.0] | 9.0 [6.5-9.8] | 7.7 [6.0-9.7] | 7.7 [6.0-9.7] | 9.0 [6.5-9.8] |
| Discharge | 1.7 [1.6-4.0] | 3.4 [3.0-5.8] | 1.4 [0.7-2.5] | 1.4 [0.7-2.5] | 3.4 [3.0-5.8] |
| Dialysis on discharge | 2 (33%) | 4 (57%) | 10 (13%) | 10 (13%) | 4 (57%) |

*Note:* CKD status was defined here based on adjudicated review of the chart.
Abbreviations: AKI 3D, acute kidney injury stage 3 receiving dialysis; CKD, chronic kidney disease.
[a]Data are expressed as median [interquartile range].

**Table 4.** Univariable and Multivariable Logistic Regression Analyses of Risk Factors Associated With Need for Dialysis at Discharge Among Patients Who Had Developed AKI 3D and Survived

| | Unadjusted | | Adjusted | |
|---|---|---|---|---|
| **Variable** | **OR (95% CI)** | ***P*** | **OR (95% CI)** | ***P*** |
| Age, per 1 y older | 1.0 (1.0-1.1) | 0.02 | 1.0 (1.0-1.1) | 0.7 |
| Male sex | 0.8 (0.3-2.0) | 0.6 | — | — |
| Race/ethnicity | | | | |
| Non-Hispanic White | 1.0 (reference) | — | — | — |
| Non-Hispanic Black | 1.6 (0.5-4.8) | 0.4 | — | — |
| Hispanic | 0.9 (0.3-3.1) | 0.9 | — | — |
| Other | 1.7 (0.1-1.7) | 0.2 | — | — |
| Unknown | 1.7 (0.4-7.0) | 0.5 | — | — |
| Diabetes | 1.7 (0.7-4.0) | 0.2 | — | — |
| Hypertension | 2.6 (0.9-7.7) | 0.08 | — | — |
| Cardiovascular disease[a] | 4.9 (2.0-12.4) | <0.001 | 2.0 (0.6-7.3) | 0.3 |
| Respiratory disease[b] | 2.5 (0.7-9.3) | 0.2 | — | — |
| Chronic liver disease | 2.4 (0.3-17.5) | 0.4 | — | — |
| Cancer | 2.1 (0.6-7.3) | 0.3 | — | — |
| Kidney disease | | | | |
| Chronic kidney disease[c] | 20.9 (6.7-64.9) | <0.001 | 9.3 (2.3-37.8) | 0.002 |
| Indeterminate | 8.8 (1.7-45.3) | 0.009 | 4.5 (0.7-27.7) | 0.1 |
| Mechanical ventilation | 0.1 (0.0-0.3) | <0.001 | 1.6 (0.2-13.1) | 0.6 |
| Vasoactive medication[d] | 0.1 (0.0-0.3) | <0.001 | 0.2 (0.0-1.7) | 0.2 |

Abbreviations: AKI 3D, acute kidney injury stage 3 receiving dialysis; OR, odds ratio.
[a]Includes coronary artery disease, heart failure, and peripheral vascular disease.
[b]Includes asthma and chronic obstructive pulmonary disease.
[c]Defined here based on adjudicated review of the chart.
[d]Includes inotropes and vasopressors.

cannot be inferred from an observational study, the uremic milieu caused by AKI can affect immune function,[27] inflammation,[28] and coagulation.[29]

Consistent with our findings, recent publications have reported on the association of AKI with in-hospital death among those hospitalized with COVID-19.[11] Early reports from Wuhan, China, found that even after adjusting for age, sex, disease severity, and comorbid conditions, risk for death was increased with AKI (HRs ranging from 1.9 to 4.7 for increasing stages of AKI).[24] A recent publication from New York comparing COVID-19 admissions with a historical cohort found that patients with AKI had significantly higher risk for death compared with those without AKI.[25] A multicenter study of ICU patients across 64 centers in the United States found that decreased kidney function (renal Sequential Organ Failure Assessment [SOFA] score of 4) at ICU admission was associated with higher odds of 28-day mortality (odds ratio, 2.4 [95% CI, 1.46-4.05]),[26] although true comparison with our findings is limited because this study focused on an ICU population and did not use KDIGO criteria for AKI. Despite the heterogeneity of published studies in terms of geographical location, patient population, and severity of illness, it is clear that AKI is associated with increased risk for death among patients with COVID-19.

Kidney outcomes of patients with COVID-19 who develop AKI are important for several reasons. First, the degree of recovery provides some insight into pathobiology and AKI cause. Although in some cases the injury was mild, in many cases patients developed acute tubular injury with or without concomitant pathology, including collapsing glomerulopathy or rarely, thrombotic microangiopathy.[30-33] Second, it is important to understand the degree to which posthospital nephrology follow-up care may be required and accordingly the potential burden that COVID-19 conveys on the nephrology community. Third, for patients with AKI 3D, knowledge of recovery and the ability to be discharged off dialysis can influence in-hospital decision making.

Kidney outcomes of patients with AKI varied and to a great extent depended on whether the patient received dialysis. Of 3,854 adults with AKI, 3,216 (83.4%) developed AKI 1-3 during their admission, and of these, 1,663/3,216 (51.7%) survived and 1,233/1,663 (74.1%) recovered kidney function. Additionally, median Scr level on discharge was lower than the median Scr level during admission, suggesting 1 of 2 possibilities: some patients had AKI on admission or there was protein malnutrition and loss of muscle mass during the prolonged hospitalization.[34,35]

Patients with AKI 3D had a notably difficult course. Of 3,854 with AKI, 638 (16.6%) received dialysis during admission, of whom 108/638 (17.0%) survived and 72/108 (66.7%) recovered kidney function. In the remaining 36/108 (33.3%) who did not recover kidney function, 33 (92%) required dialysis at discharge and 3 (8%) did not require dialysis at discharge but did not have a decline of at

least 33% in discharge Scr level from peak Scr level. For patients who need dialysis at discharge, placement in a dialysis center with an ability to manage patients with recent severe illness is essential. It is unclear how many of these patients may subsequently experience recovery of kidney function, although it should be noted that more than half of them had pre-existing advanced CKD.

Decision making regarding initiation of dialysis in COVID-19 can be difficult. The likelihood of death, as well as subsequent kidney disease outcomes, are important aspects of the discussion. Among the group with AKI 3D who survived, only a history of CKD was independently associated with needing dialysis at discharge by multivariable analysis. Consistent with what would be intuitively expected, persistent need for dialysis was particularly true among patients with CKD stage 4 or 5 at hospital admission. Accordingly, among patients without a history of severe CKD, decisions as to initiating dialysis in COVID-19 can focus mainly on mortality risk.

Regardless of the need for dialysis or recovery of kidney function at discharge, hospitalized patients with COVID-19 who experience any form of AKI should probably be followed up closely after discharge to assess ongoing kidney function. At present, we do not have sufficient outpatient follow-up data to inform an understanding of the impact of AKI in COVID-19 on the subsequent development of CKD. Long-term follow-up of such patients is crucial because prior AKI literature has demonstrated increased kidney injury progression persisting for up to 10 years following hospital admission with AKI despite an apparent normalization of kidney function postdischarge.[36]

Strengths of this study include a large racially and ethnically diverse sample size, with a mix of patients from community and tertiary hospitals. In contrast to several other recent publications, in which large numbers of patients did not have completed outcomes,[7,11,37] >99% of our patients had completed outcomes, with <1% still hospitalized. We used time-to-event analyses using AKI exposure as a time-varying covariate and thus avoiding immortal time bias.

Limitations of our study include the observational and retrospective study design. In addition, our 13 hospital sites were all in metropolitan New York during the early part of the pandemic and may not be representative of later outcomes due to changes in resource capacity, patient characteristics, treatment protocols, and therapeutic refinements. Because our study relied on automated electronic health record data extraction, information for goals of care discussions was not obtainable and we were unable to determine circumstances around withholding of dialysis. At the same time, our health system had adequate dialysis and continuous kidney replacement therapy supplies and did not specifically ration these procedures.[38] Finally, nephrologist adjudication of CKD diagnosis and stage was limited to patients with AKI 3D who survived, with the rest of the population relying on *ICD-10* coding.

In conclusion, we found that the development of AKI during hospitalization for COVID-19 was associated with a substantial increase in risk for death. This risk was amplified when AKI resulted in dialysis. Most surviving patients with COVID-19 and AKI experienced substantial kidney recovery before discharge. In contrast, among those who have AKI 3D and survived, 30.6% still needed dialysis at discharge, a group of patients whose subsequent outcomes will require further study.

## Supplementary Material

### Supplementary File (PDF)

**Figure S1:** Algorithm for detecting AKI using electronic health records.

**Item S1:** Supplementary methods.

## Article Information

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# Outcomes Among Hospitalized Patients With COVID-19 and AKI