Outcomes among Hospitalized Chronic Kidney Disease Patients with COVID-19

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Abstract

Background Patients with CKD have impaired immunity, increased risk of infection-related mortality, and worsened COVID-19 outcomes. However, data comparing nondialysis CKD and ESKD are sparse.

Methods Patients with COVID-19 admitted to three hospitals in the New York area, between March 2 and August 27, 2020, were retrospectively studied using electronic health records. Patients were classified as those without CKD, those with nondialysis CKD, and those with ESKD, with outcomes including hospital mortality, ICU admission, and mortality rates.

Results Of 3905 patients, 588 (15%) had nondialysis CKD and 128 (3%) had ESKD. The nondialysis CKD and ESKD groups had a greater prevalence of comorbidities and higher admission D-dimer levels, whereas patients with ESKD had lower C-reactive protein levels at admission. ICU admission rates were similar across all three groups (23%–25%). The overall, unadjusted hospital mortality was 25%, and the mortality was 24% for those without CKD, 34% for those with nondialysis CKD, and 27% for those with ESKD. Among patients in the ICU, mortality was 56%, 64%, and 56%, respectively. Although patients with nondialysis CKD had higher odds of overall mortality versus those without CKD in univariate analysis (OR, 1.58; 95% CI, 1.31 to 1.91), this was no longer significant in fully adjusted models (OR, 1.11; 95% CI, 0.88 to 1.40). Also, ESKD status did not associate with a higher risk of mortality compared with non-CKD in adjusted analyses, but did have reduced mortality when compared with nondialysis CKD (OR, 0.57; 95% CI, 0.33 to 0.95). Mortality rates declined precipitously after the first 2 months of the pandemic, from 26% to 14%, which was reflected in all three subgroups.

Conclusions In a diverse cohort of patients with COVID-19, we observed higher crude mortality rates for patients with nondialysis CKD and, to a lesser extent, ESKD, which were not significant after risk adjustment. Moreover, patients with ESKD appear to have better outcomes than those with nondialysis CKD.

Key Points
• Patients with ESKD had higher crude mortality rates than those without CKD, but this was no longer significant after multivariate adjustment.
• Patients with ESKD, when directly compared with those with nondialysis CKD, appeared to have reduced risk of mortality, despite adjusting for confounders.
• Mortality associated with coronavirus disease 2019 declined significantly during the pandemic, and initial reports likely overestimate mortality rates among patients with CKD.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has been accompanied by high rates of mortality and morbidity, with wide-ranging clinical manifestations (1–3). Those at highest risk for adverse outcomes include the elderly and those with preexisting health conditions (4,5), such as CKD, which is also a well-established risk factor for mortality and morbidity in the general population (6). This is especially true for patients with ESKD, who are more susceptible to sepsis (7), and are presumably at increased risk of contracting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) due to more frequent encounters with the healthcare system (8).
Several studies have shown a significant association between adverse COVID-19 outcomes and both acute kidney disease and CKD. AKI is commonly seen in patients hospitalized with COVID-19, and a meta-analysis demonstrated an overall prevalence of 17%, with significant variation among studies (9). Although AKI portends unfavorable outcomes (1,10,11), data concerning preexisting CKD in relationship to COVID-19 are more limited and discordant. An abbreviated meta-analysis of four studies from China suggested a three-fold greater association between AKI and severe COVID-19 disease (12), and several cohorts from the United States also showed increased odds of mortality and adverse outcomes with preexisting CKD (13–19). Conversely, a different study from New York did not show a significant association between CKD and mortality in patients who were critically ill (20). It is also uncertain whether there is a difference in outcomes between those with nondialysis CKD and ESKD, because many studies had inconsistent separation of nondialysis CKD from ESKD, or they were plagued by small sample sizes or lack of complete follow-up. Reports specifically from the ESKD community in Europe, the United States, and China have generally demonstrated a high mortality rate (nearly 30%) (21–25); however, one analysis from England showed a mortality rate of only 9%, albeit with a relatively high number of patients still being hospitalized (26).

Clinical characteristics specifically focused on nondialysis CKD and ESKD status have not been explicitly studied and compared in a large population, particularly in a cohort with complete follow-up to discharge or death. Moreover, previous studies in CKD were based on data from earlier in the pandemic, and there is a need to re-examine CKD outcomes in later months because there may be improvements in mortality over time (27). In this study, we examined presentations and outcomes among patients hospitalized with COVID-19 from March to August 2020.

Methods

Study Population

We conducted a retrospective analysis of patients admitted to three hospitals in the New York University (NYU) Langone healthcare system: Tisch Hospital in Manhattan, NYU Langone Hospital–Brooklyn in Brooklyn, and NYU Winthrop Hospital in Mineola, New York (located just outside of New York City). These institutions include an urban quaternary care facility, a suburban referral center, and an urban safety net hospital. The cohort included all patients, over the age of 18, admitted with positive testing for SARS-CoV-2 by real-time RT-PCR assay of nasopharyngeal or oropharyngeal swab specimens between March 1 and August 27, 2020. Exclusion criteria included patients who did not have a creatinine measurement or who were not admitted specifically for COVID-19 (Figure 1). To focus on the most relevant population and outcomes, we used admission diagnosis codes to help filter out patients who were only incidentally found to be PCR positive and were admitted for reasons other than COVID-19 (Supplemental Table 1). For patients admitted more than once with an associated positive SARS-CoV-2 PCR test, we used the hospitalization that involved the highest level of care or the worst outcome. Follow-up was available through January 15, 2021, and there were no patients still admitted at the end of this period. This study was approved with a waiver of informed consent and a Health Insurance Portability and Accountability Act waiver by the NYU Grossman School of Medicine Institutional Review Board.

Covariates

All data were extracted from the electronic health record (Epic Systems, Verona, WI). Diagnosis codes for stage 3–5 CKD and ESKD from the problem list and past medical history, and a Chronic Kidney Disease Epidemiology Collaboration (28) eGFR of ≤60 ml/min per 1.73 m², using the most recent outpatient creatinine within 6 months before hospitalization (if available), were used to classify CKD and ESKD. Selective manual chart review was used to verify that those with severe AKI requiring RRT were not misclassified as ESKD. In addition, we manually reviewed the charts of all patients who underwent RRT, or who died within the first 72 hours of admission, to further ensure there was no misclassification of patients with ESKD. Baseline outpatient creatinine was available on 820 (21%) patients. Data also included demographics (age, self-reported race/ethnicity, sex), body mass index, medical comorbidities (hypertension, hyperlipidemia, coronary artery disease, congestive heart failure, chronic obstructive pulmonary disease, asthma, malignancy [excluding non-metastatic, nonmelanoma skin cancer], type 1 and type 2 diabetes), laboratory results, admission vital signs, smoking status (never smoked, current smoker, former smoker), and significant hospitalization events (intensive care unit [ICU] admission, intubation, RRT, extracorporeal membrane oxygenation therapy, mortality). AKI was defined according to the creatinine criteria, as outlined by the Acute Kidney Injury Network (29), using the admission creatinine as the baseline creatinine. Medical comorbidities were identified using codes from the International Classification of Diseases, Tenth Revision (ICD-10).

Statistical Analyses

The distribution of baseline characteristics was summarized according to CKD status using medians with interquartile ranges for continuous variables, and frequencies for categoric variables. For laboratory variables, not all patients had data, and the varied sample size is listed first within each cell of the table. Patients with nondialysis CKD and those with ESKD were compared with patients without CKD using logistic regression models for overall hospital mortality and ICU admission. We also constructed logistic regression models excluding patients without CKD and directly compared those with ESKD with those with nondialysis CKD for the outcomes of overall mortality, ICU mortality, and ICU admission. Covariates for these models were selected a priori on the basis of established and plausible clinical relevance. We created three models for each outcome: (1) a univariate model; (2) a demographic and comorbidity-adjusted model; and (3) a fully adjusted model, including markers of disease severity on admission and week of admission. All statistical analyses were conducted using R version 4.0.3. Two-sided P values <0.05 were considered statistically significant. No adjustments were made for multiple comparisons.
**Results**

**Baseline Characteristics of Inpatients with COVID-19**

The final cohort included 3905 patients, and was stratified by non-CKD, nondialysis CKD, and ESKD status (Table 1). The median age for the cohort was 66 years; 60% were men, 37% were diabetic, 61% were hypertensive, and 84% had a major chronic condition. There were 588 (15%) patients with nondialysis CKD, and 128 (3%) patients with ESKD. Those with nondialysis CKD had a higher median age (74 years) than those with either ESKD (65.5 years) or those without CKD (64 years). The nondialysis CKD and ESKD groups were more likely to be Black; have higher rates of former or current smoking; have higher admission D-dimer and IL-6 levels; and have any chronic medical condition, particularly diabetes, hypertension, hyperlipidemia, and heart disease.

On the other hand, the ESKD subgroup tended to have lower admission C-reactive protein levels, less obesity, and more hypotension compared with those without CKD.

**Outcomes**

The overall, unadjusted hospital mortality (including discharge to hospice) was 25%, and mortality was 24% for patients without CKD, 34% for those with nondialysis CKD, and 27% for those with ESKD. However, there was a clear trend in all three subgroups for reduced mortality as the pandemic wore on. During the first 2 months, mortality was 25% for those without CKD, 35% for those with nondialysis CKD, and 29% for those with ESKD; compared with 14%, 15%, and 13%, respectively, over the last 4 months. ICU admission was similar among all three groups (23%–25%). Furthermore, there were no significant differences in length of stay or use of high-flow oxygen. A greater proportion of patients with ESKD did require mechanical ventilation (Table 1). AKI occurred more often for patients with nondialysis CKD than for those without CKD at baseline (57% versus 28%).

Outcomes for patients stratified by ICU admission are illustrated in Table 2. In both ICU and non-ICU settings,
| Characteristic | Total (N=3905) | No CKD (N=3189) | Nondialysis CKD (N=588) | ESKD (N=128) |
|---------------|----------------|-----------------|-------------------------|-------------|
| Age (yr), median (IQR) | 66 (54–77) | 64 (52–75) | 74 (66–83.5) | 65.5 (56–75) |
| Age (yr), n (%) | | | | |
| 19–44 | 466 (12) | 445 (14) | 13 (2) | 8 (6) |
| 45–54 | 546 (14) | 486 (15) | 39 (7) | 21 (16) |
| 55–64 | 805 (21) | 699 (22) | 80 (14) | 26 (20) |
| 65–74 | 926 (24) | 722 (23) | 168 (29) | 36 (28) |
| ≥75 | 1162 (30) | 837 (26) | 288 (49) | 37 (29) |
| Male, n (%) | 2352 (60) | 1930 (61) | 338 (57) | 84 (66) |
| Race/ethnicity, n (%) | | | | |
| Asian | 301 (8) | 255 (8) | 33 (6) | 13 (10) |
| Black | 597 (15) | 438 (14) | 118 (20) | 41 (32) |
| Hispanic | 1014 (26) | 861 (27) | 112 (19) | 41 (32) |
| Other/multiracial | 286 (7) | 256 (8) | 22 (4) | 8 (6) |
| Unknown | 132 (3) | 120 (4) | 9 (2) | 3 (2) |
| White | 1575 (40) | 1259 (39) | 294 (50) | 22 (17) |
| Tobacco use, n (%) | | | | |
| Current | 212 (5) | 159 (5) | 41 (7) | 12 (9) |
| Former | 873 (22) | 627 (20) | 209 (36) | 37 (29) |
| Never, including passive exposure | 2194 (56) | 1841 (58) | 290 (49) | 63 (49) |
| Unknown | 626 (16) | 562 (18) | 48 (8) | 16 (13) |
| Obesity, n (%) | | | | |
| BMI of 40 kg/m² | 322 (8) | 255 (8) | 58 (10) | 9 (7) |
| BMI of 30 to <40 kg/m² | 1279 (33) | 1052 (33) | 195 (33) | 32 (25) |
| BMI of 25 to <30 kg/m² | 1277 (33) | 1032 (32) | 204 (35) | 41 (32) |
| BMI of <25 kg/m² | 896 (23) | 727 (23) | 124 (21) | 45 (35) |
| Unknown | 131 (3) | 123 (4) | 7 (1) | 1 (0.78) |
| Any chronic condition, n (%) | 3287 (84) | 2572 (81) | 588 (100) | 127 (99) |
| Chronic obstructive pulmonary disorder | | | | |
| Cancer | 462 (12) | 332 (10) | 115 (20) | 15 (12) |
| Oxygen saturation <88% at presentation | 608 (16) | 512 (16) | 78 (13) | 18 (14) |
| Systolic BP <100 mm Hg at presentation | 247 (10) | 186 (6) | 46 (8) | 15 (12) |
| Laboratory data, N patients with available data; median value (IQR) | | | | |
| AKI, n (%) | 1222 (31) | 885 (28) | 337 (57) | N/A |
| Use of high-flow oxygen, n (%) | 307 (8) | 252 (8) | 46 (8) | 9 (7) |
| Mechanical ventilation, n (%) | 848 (22) | 685 (21) | 129 (22) | 34 (27) |
### Table 1. (Continued)

| Characteristic                           | Total (N=3905) | No CKD (N=3189) | Nondialysis CKD (N=588) | ESKD (N=128) |
|-----------------------------------------|----------------|----------------|-------------------------|--------------|
| ECMO, n (%)                             | 45 (1)         | 42 (1)         | 3 (0.51)                | 0 (0)        |
| Length of stay (d), median (IQR)        | 7 (4–12)       | 6 (3–12)       | 7 (4–13)                | 7 (4–11)     |
| Mortality rate, n died/total patients hospitalized (%) | | | | |
| March 2020                               | 414/1543 (27)  | 330/1314 (25)  | 71/186 (38)             | 13/43 (30)   |
| April 2020                               | 520/2007 (26)  | 382/1588 (24)  | 118/349 (34)            | 20/70 (29)   |
| May 2020                                 | 40/242 (17)    | 31/195 (16)    | 7/38 (18)               | 2/9 (22)     |
| June 2020                                | 9/43 (12)      | 5/33 (15)      | 0/8 (0)                 | 0/2 (0)      |
| July 2020                                | 3/49 (6)       | 2/41 (5)       | 1/5 (20)                | 0/3 (0)      |
| August 2020                              | 3/21 (14)      | 3/18 (17)      | 0/2 (0)                 | 0/1 (0)      |

IQR, interquartile range; BMI, body mass index; N/A, not available; CK, creatine kinase; CRP, C-reactive protein; ECMO, extracorporeal membrane oxygenation.

Discussion

In this observational, retrospective study we found significant rates of severe illness and mortality among patients hospitalized with COVID-19 and, to our knowledge, this is the first large-scale study comparing outcomes between those with nondialysis CKD and those with ESKD. We found that crude mortality was highest among those with nondialysis CKD, whereas patients with ESKD not only had lower crude and adjusted mortality than those with nondialysis CKD, but they also had similar crude ICU mortality compared with individuals without kidney disease. Overall, these data support the idea that the presence of ESKD does not independently increase the risk of death or COVID-19–related critical illness, and that the high reported mortality rates in this population are likely due to clustering of unfavorable demographics and comorbidities.

Although patients with nondialysis CKD and COVID-19 in this study had substantially increased crude mortality rates than those without CKD, adjustment for age and comorbidities eliminated the increased risk, highlighting the importance of age and comorbid conditions in outcomes for this group. Indeed, we found that this group was, on average, 10 years older than patients without CKD, whereas comorbidities—such as diabetes, heart disease, and chronic pulmonary disease—were roughly two to three times more prevalent.

Unexpectedly, we found that patients with ESKD had a lower crude incidence of mortality than individuals with nondialysis CKD, both in the ICU and among all admitted patients, with the latter persisting in fully adjusted models. Our overall mortality rate among admitted patients with ESKD was 27%, which is similar to other smaller cohorts from New York, Spain, and Italy, in which mortality rates were 28%–31% (22,24,25,30). Of note, the time period studied in our population was also significantly longer, and there was a clear improvement in mortality after the first 2 months, which may be more reflective of contemporary outcomes in this population. Additionally, compared with patients with nondialysis CKD, patients with ESKD in our cohort were younger and had lower obesity rates; however, the relative reduction in mortality risk versus those with nondialysis CKD persisted in models adjusting for these factors. It may be tempting to speculate that patients with ESKD, who have an impaired immune response in the setting of uremia, may have a less profound cytokine storm, but this requires further study. Finally, although patients with ESKD had higher crude overall mortality rates than patients without CKD, as with patients with nondialysis CKD, these differences were no longer significant after adjusting for confounders. Again, this underscores the importance of demographics and comorbidities as greater determinants of COVID-19 outcomes. In aggregate, our findings imply that the presence of ESKD does not increase the risk of dying among patients admitted with COVID-19, and may, in fact, be associated with reduced mortality compared with nondialysis CKD. Even in the ICU, crude mortality was similar between patients with ESKD and those without CKD. To our knowledge, other studies have not reported individual outcomes for individuals with ESKD in this setting, and the clinical implications of our findings are potentially large.
outcomes for both nondialysis CKD and ESKD in the same cohort, or compared the two directly, and it is possible that mixing these groups together in prior studies may have masked important and differential effects of these CKD stages on outcomes associated with COVID-19 illness.

This study has numerous strengths, including a large and diverse population; the capture of admissions over a much longer period (from March to August 2020), demonstrating changes in mortality over time; a more complete follow-up than other cohorts, with no patients still hospitalized at the end of the study; individual reporting of outcomes for nondialysis CKD and ESKD on a variety of characteristics and outcomes, within a single cohort; and the focus being on patients admitted primarily for COVID-19, and not those who incidentally tested positive on admission for other reasons. However, there are also several limitations, including its retrospective, electronic health record–based nature and the use of ICD-10 codes for identifying a large proportion of the patients with nondialysis CKD for whom preadmission creatinine values were not available. It is possible that patients were more likely to be labeled as having nondialysis CKD at more severe CKD stages; therefore, milder CKD could be missed and this could potentially increase the magnitude of effect of nondialysis CKD on mortality, although this would not explain our findings regarding the lack of association of ESKD with adverse outcomes. It is also possible that patients with preadmission, community-acquired AKI were also misclassified as having CKD, which would tend to bias our results, because AKI is more likely to be associated with adverse outcomes. Again, this would not affect results demonstrating a similar ICU mortality between patients with ESKD and those without CKD.

In summary, we found that crude hospital mortality from COVID-19 was highest among patients with nondialysis CKD, followed by those with ESKD, and then those without CKD. Patients with ESKD had reduced odds of mortality versus those with nondialysis CKD, whereas the risk of mortality was similar to those without CKD in fully adjusted analyses, which requires further study. Mortality, regardless of CKD status, improved significantly after the first 2 months of the pandemic.

### Table 2. Outcomes of non-CKD, nondialysis CKD, and ESKD groups, by level of care

| CKD Status       | Patients Not in ICU |         | P Value | Patients in ICU |         | P Value |
|------------------|---------------------|---------|---------|-----------------|---------|---------|
|                  | Discharged, n (%)   | Deceased or Hospice, n (%) |         | Discharged, n (%) | Deceased or Hospice, n (%) |         |
| No CKD           | 2096 (87)           | 318 (13) | <0.001  | 340 (44)        | 435 (56) | 0.27    |
| Nondialysis CKD  | 341 (76)            | 110 (24) | 0.05    | 50 (37)         | 87 (64)  | 0.27    |
| ESKD             | 79 (82)             | 17 (18)  | 0.1     | 14 (44)         | 18 (56)  | 0.1     |

ICU, intensive care unit.

### Table 3. Logistic regression models

| Outcome                               | Odds Ratio Estimate (95% CI) | P Value |
|---------------------------------------|-----------------------------|---------|
| **ICU admission**                     |                             |         |
| Nondialysis CKD versus no CKD         |                             |         |
| Unadjusted                            | 0.93 (0.75 to 1.14)         | 0.47    |
| Model 2a                              | 0.89 (0.70 to 1.12)         | 0.32    |
| Fully adjusted                        | 0.93 (0.72 to 1.18)         | 0.54    |
| ESKD versus no CKD                    |                             |         |
| Unadjusted                            | 0.99 (0.65 to 1.46)         | 0.95    |
| Model 2a                              | 0.72 (0.45 to 1.11)         | 0.14    |
| Fully adjusted                        | 0.66 (0.41 to 1.05)         | 0.09    |
| **Mortality**                         |                             |         |
| Nondialysis CKD versus no CKD         |                             |         |
| Unadjusted                            | 1.58 (1.31 to 1.91)         | <0.001  |
| Model 2a                              | 1.06 (0.85 to 1.32)         | 0.61    |
| Fully adjusted                        | 1.11 (0.88 to 1.40)         | 0.37    |
| ESKD versus no CKD                    |                             |         |
| Unadjusted                            | 1.15 (0.77 to 1.69)         | 0.48    |
| Model 2a                              | 0.79 (0.50 to 1.23)         | 0.31    |
| Fully adjusted                        | 0.83 (0.51 to 1.32)         | 0.44    |

ICU, intensive care unit.

*a*Model 2 includes adjustment for age, sex, race/ethnicity, smoking status, obesity, coronary artery disease, heart failure, hyperlipidemia, hypertension, diabetes, pulmonary, and cancer.

*b*Fully adjusted includes adjustments in model 2 and adjustments for oxygen saturation, temperature, systolic BP, D-dimer, and week of admission.
Disclosures
D.M. Charytan reports having consultancy agreements with Allena Pharmaceuticals (for serving on a data and safety monitoring board), Amgen, AstraZeneca (for serving on a data and safety monitoring board), Eli Lilly/Boehringer Ingelheim, Fresenius, Gilead, GlaxoSmithKline, Jansen (for serving on a steering committee), Medtronic, Novo Nordisk, and PLC Medical (for serving on a clinical events committee); receiving research funding from Amgen, Bioporto (for clinical trial support), Gilead, Medtronic (for clinical trial support), and Novo Nordisk; serving as a scientific advisor for, or member of, CJASN; and receiving expert witness fees related to proton pump inhibitors. S. Jones reports having ownership interest in Methods Analytics (London, United Kingdom; 1% share). All remaining authors have nothing to disclose.

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Author Contributions
J. Benstein, D.M. Charytan, L.I. Horwitz, and M. Khatri conceptualized the study; J. Benstein, L.I. Horwitz, D. Liu, J. Michael, C.M. Petrilli, and V. Tatapudi were responsible for data curation; D.M. Charytan and L.I. Horwitz were responsible for investigation and project administration; D.M. Charytan, L.I. Horwitz, and M. Khatri provided supervision and were responsible for methodology; D.M. Charytan and M. Khatri wrote the original draft; L.I. Horwitz and S. Jones were responsible for formal analysis; and all authors reviewed and edited the manuscript.

Supplemental Material
This article contains the following supplemental material online at http://kidney360.asnjournals.orglookup/suppl doi:10.34067 KID.0008520201/DSupplemental.
Supplemental Table 1. Codes used to define principal diagnosis of COVID-19, sepsis, or respiratory disease.
Supplemental Table 2. Logistic regression models for ICU mortality.
Supplemental Table 3. Logistic regression models for ESRD vs non-dialysis CKD.

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