Effect of COVID-19 on Kidney Disease Incidence and Management

Meredith McAdams, Mauricio Ostrosky-Frid, Nilum Rajora, and Susan Hedayati

Abstract
The COVID-19 outbreak has had substantial effects on the incidence and management of kidney diseases, including AKI, ESKD, GN, and kidney transplantation. Initial reports from China suggested a lower AKI incidence in patients with COVID-19, but more recent studies from North America reveal a much higher incidence, likely due to the higher prevalence of comorbid conditions, such as hypertension, diabetes, and CKD. AKI in this setting is associated with worse outcomes, including the requirement for vasopressors or mechanical ventilation and death. Performing RRT in those with AKI poses challenges, such as limiting exposure of staff, preserving PPE, coagulopathy, and hypoxemia due to acute respiratory distress syndrome. Continuous RRT is the preferred modality, with sustained low-efficiency dialysis also an option, both managed without 1:1 hemodialysis nursing support. Regional citrate is the preferred anticoagulation, but systemic unfractionated heparin may be used in patients with coagulopathy. The ultrafiltration rate has to be set carefully, taking into consideration hypotension, hypoxemia, and responsiveness to presser and ventilatory support. The chance of transmission puts in-center chronic hemodialysis and other immunosuppressed patients at particularly increased risk. Limited data show that patients with CKD are also at increased risk for more severe disease, if infected. Little is known about the virus’s effects on immunocompromised patients with glomerular diseases and kidney transplants, which introduces challenges for management of immunosuppressant regimens. Although there are no standardized guidelines regarding the management of immunosuppressant regimens, several groups recommend stopping the antimetabolite in hospitalized transplant patients and continuing a reduced dose of calcineurin inhibitors. This comprehensive review critically appraises the best available evidence regarding the effect of COVID-19 on the incidence and management of kidney diseases. Where evidence is lacking, current expert opinion and clinical guidelines are reviewed, and knowledge gaps worth investigation are identified.

KIDNEY360 2: 141–153, 2021. doi: https://doi.org/10.34067/KID.0006362020

Introduction
COVID-19, the disease caused by the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first described in Wuhan, China, but rapidly affected >40 million people worldwide (1). The clinical presentation is highly variable in symptoms, severity, and organ involvement, ranging from asymptomatic to multiorgan failure. One of the major organs involved is the kidney, which manifests as COVID-19–related AKI in hospitalized patients, especially in those requiring intensive care unit (ICU) management. Another important aspect of COVID-19 as relates to kidney disease is, given the highly infectious nature of SAR-CoV-2, patients with ESKD, kidney transplantation recipients, and those with glomerular diseases and other CKD may be at increased risk for infection and associated morbidity, especially in the light of the underlying immunocompromised state. The global COVID-19 pandemic has had a significant influence on clinical aspects and management of these patient populations. In this study, we evaluate the current evidence about the effect of COVID-19 on AKI, CKD, ESKD, renal transplantation, and GN, and address specific management challenges of these vulnerable patient populations.

AKI
Epidemiology and Outcomes
Early reports from Wuhan, China, concluded that COVID-19 does not result in significant AKI (2), with zero cases reported among 119 hospitalized patients, ranging up to 15% in other publications (2–15). Subsequent US studies reported higher incidences of 14%–69% in hospitalized patients, especially if requiring ICU and mechanical ventilation (Figure 1A) (15–23). One study reported a higher incidence of AKI among patients hospitalized for COVID-19 versus for non–COVID-19 indications (17). These differences could be explained by the varying prevalence of comorbidities among Chinese versus US cohorts, with the United States reporting a higher presence of hypertension, diabetes mellitus, and CKD, found to be risk factors for SARS-CoV-2 infection (Figure 1C and D) (3,14,24–28). Diabetes was present among 16%–49% and hypertension among 31%–74% of patients with COVID-19 (15–17,19–22,29–31) in US cohorts, but in only 7%–24% and 15%–38% in Chinese counterparts. These variations may be, in part, due to differences in racial composition, health care access, and hospitalization thresholds for disease acuity. There was also heterogeneity...
Figure 1. Differences in AKI, RRT, and comorbidities in patients with COVID-19 in the United States and in China. Percentages calculated as proportion of COVID-19-positive individuals in each study, with data from China shown in red and data from the United States in blue. (A) Incidence of AKI in patients with COVID-19 (blue for the United States and red for China), with percentage of AKI patients requiring RRT depicted in light blue for the United States and red for China. Prevalence of underlying (B) CKD, (C) hypertension, and (D) diabetes mellitus in patients with COVID-19. This figure does not include data from cohorts that only reported patients admitted to intensive care units. HTN, hypertension; DM, diabetes mellitus.

Across studies, with some comprised of all hospitalized patients, whereas others only those requiring ICU and, therefore, reporting higher AKI incidence. This is congruent with findings identifying requirement for vasopressors or mechanical ventilation as independent risk factors for COVID-19–related AKI (18). Another factor could be the lack of a standardized method for defining AKI. Most studies used standard Kidney Disease Improving Global Outcomes (32) criteria but varied in how “baseline creatinine” was established.

Reported mortality is also variable, ranging from 1% to 28% in Chinese (2,3,5,6,8–11,14,26), and 15%–24% in US studies (15–18,20–22,31). Factors implicated for heterogeneity may include case mix, socioeconomic status, hospitalization criteria, and availability and delivery of COVID-19–specific treatments. Comorbidities are also considered an important risk factor for COVID-19 disease severity and outcomes, and patients who die have a higher prevalence of hypertension and diabetes versus those who recover (24,25).

Patients with COVID-19–associated AKI have worse outcomes than those without AKI, with higher incidences of ICU admission, acute respiratory distress syndrome (ARDS), mechanical ventilation, and death (27–29). Yang and Xu et al. (27,28) reported AKI incidences of 29% and 50% in patients admitted to the ICU. AKI incidence was about 50% in a larger US multicenter cohort of >3000 ICU patients (30).

Two studies from China reported AKI occurring more frequently in patients who died than who recovered from COVID-19 (24,25). Association of AKI with poor outcomes in the setting of COVID-19 may be confounded by factors that cause or correlate with AKI and with adverse outcomes among acutely ill patients.

AKI Requiring RRT

In China, the incidence of AKI requiring RRT ranged from 0% to 7% (2,6,7,9–11,13,14,24,27). In one cohort of only ICU patients, the incidence was 17% (28). In the United States, the incidence ranged from 3.1% to 15.5% in all-comers (Figure 1A) (16–20,22) but higher at 20% in ICU patients (30). The higher utilization of RRT in the United States versus China may be due to higher AKI incidence, availability of RRT, or severity of
disease or comorbidities. Specific RRT modalities were not always reported, but acute peritoneal dialysis (PD) is utilized in some centers due to concern for lack of resources (33). Performing PD in patients who are placed in the prone position for ARDS brings up the concern for increased intra-abdominal pressures and subsequent decreased ultrafiltration. PD has been successfully used in prone position, and proning is not an absolute contraindication for PD (34). The risk of intra-abdominal hypertension and decreased ultrafiltration can be mitigated by suspension of the abdominal cavity and using low-volume continuous PD (35).

Delivering RRT in those with COVID-19 poses several challenges (Figure 2) (36–38). In addition to utilization of acute PD, various strategies were implemented to help ease the impending resource shortages. Many centers utilize continuous RRT (CRRT) or prolonged intermittent daily RRT, including sustained low efficiency dialysis, instead of intermittent hemodialysis (HD), which can be managed without 1:1 HD nursing. Other strategies included using a shorter CRRT duration, 10–12 hours, at a higher effluent rate of 40–50 ml/kg per hour, to rotate the same machine for multiple patients. Reducing the effluent dose once the patient becomes stable was recommended to preserve dialysis solutions (37–41).

The virus is easily transmitted, which raises challenges regarding safety, complicated by declining personal protective equipment (PPE). Shortages of health care workers due to illness and need to quarantine poses additional challenges. Solutions include isolation of patients in aggregate in COVID-19–only ICUs or using individual isolation rooms. Training nondialysis staff to assist with dialysis treatments has also been undertaken. Decreasing the intermittent HD length and number of weekly sessions in stable hospitalized patients is another option (38,39). Additional challenges for CRRT include an underlying hypercoagulable state, which can cause increased circuit and filter clotting. Addition of systemic unfractionated heparin to regional citrate may be required, and argatroban has also been successfully used for anticoagulation (36,42,43). To minimize catheter length, vascular access using the right internal jugular vein is preferred, anchored firmly in place, and position checked after pronation. Ultrafiltration rate has to be carefully adjusted, taking into account hypotension, ARDS, and responsiveness to presser and ventilator support.

Renal Outcomes after AKI

Limited long-term data exist regarding AKI recovery versus continued dialysis dependence. One study, median

---

Figure 2. Special challenges and strategies for RRT delivery in patients with COVID-19. Various challenges noted in the delivery of RRT and solutions that have been implemented and suggested are depicted. CRRT, continuous renal replacement therapy; SLD, sustained low efficiency dialysis; HD, hemodialysis; PPE, personal protective equipment; ICU, intensive care unit.
follow-up 12 days, reported an 18% recovery rate in patients with AKI by Kidney Disease Improving Global Outcomes criteria and 46% by expanded criteria (change in serum creatinine ≥0.3 mg/dl) (8). A multicenter US study of >3000 ICU patients reported that 63% of patients with AKI-RRT died, 34% were discharged, and 3% remained hospitalized at 17 days. Of those discharged, 34% remained RRT dependent at discharge, and 18% remained RRT dependent 60 days after ICU admission (30). More information is needed on long-term renal outcomes of patients with COVID-19.

Potential Mechanisms for AKI

Mechanisms for AKI are likely multifactorial, and usually include prerenal azotemia from intravascular volume depletion; ischemic acute tubular necrosis (ATN) from hypotension and shock; and acute interstitial nephritis from antibiotics, antivirals, and other medications (Figure 3) (19). Other mechanisms include a hypercoagulable state causing kidney ischemia (44). There is increasing evidence that much organ dysfunction is due to complement activation and cytokine release (45). Levels of IL-6 along with other inflammatory biomarkers are elevated, especially in patients with ARDS (46). The presence of SARS-CoV-2 in endomyocardial biopsies in patients with myocarditis or unexplained heart failure suggests SARS-CoV-2 can cause cardiomyopathy (47). Acute heart failure can result in type 1 cardio-renal syndrome (Figure 3).

In an autopsy series of 42 patients, ATN was the most predominant histologic finding (23). Evidence of glomerulosclerosis, myoglobin cast nephropathy, thrombotic microangiopathy, crescentic GN, cortical necrosis, and collapsing glomerulopathy were also reported. The latter was associated with presence of high-risk APOL1 genotype, suggesting that individuals with APOL1 risk alleles are at increased risk (48–52).

There is evidence that SARS-CoV-2 may exert direct cytotoxic effects on kidney tissue, although data are not consistent. This is thought to be possible due to the binding of the virus to host angiotensin-converting enzyme 2, which is expressed in the kidney (53). In 26 postmortem patients from China, all revealing ATN, coronavirus-like particles were reported by electron microscopy (EM) in podocyte foot processes and the glomerular basement membrane. There was also immunofluorescent staining for anti-SARS-CoV nucleoprotein antibody in three of seven patients (54). In biopsy findings of six deceased individuals with AKI, SARS-CoV-2 nucleocapsid protein was found in the renal tubules of all. Virus-like particles were seen by EM in two (55). Postmortem findings in another 63 patients revealed detectable SARS-CoV-2 RNA in kidney tissue of 72% of those with AKI and 43% of those without AKI (56). These findings do bring up the possibility that the virus may be causing direct tubular damage (23,57). Another case series of 10 kidney biopsies reported that staining by immunohistochemistry for SARS-CoV-2 was negative in all patients with COVID-19 and tubular injury. These disparate results may be due to viral levels being below the detection threshold in the kidney or that virus-like particles seen on EM may be intracellular components that exhibit viral-like morphology (48).

CKD-Nondialysis

Limited data exist regarding COVID-19 infection and morbidity in patients with CKD-nondialysis (CKD-ND). The prevalence of CKD-ND among patients with COVID-19 varies from 3.5% to 48% in US cohorts (15–17,19–22,29–31). Higher rates were from smaller cohorts, whereas larger samples had a prevalence ranging from 5% to 20% (16,21,30,31). Cohorts

Figure 3. | Potential mechanisms of COVID-19-related kidney injury. Diagram showing possible mechanisms of kidney injury in the setting of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). ATN, acute tubular necrosis; AIN, acute interstitial nephritis. Figure developed with BioRender.
Table 1. Summary of studies on patients with ESKD with COVID-19

| Study (Reference) | Patients, n | Sample | Dialysis Modality, n (%) | Black, n (%) | Hispanic, n (%) | Acute Respiratory Distress Syndrome / Mechanical Ventilation | Continuous Renal Replacement Therapy, n (%) | Death, n (%) | Geographic Location |
|-------------------|-------------|--------|--------------------------|--------------|----------------|-------------------------------------------------------------|---------------------------------------------|-------------|-------------------|
| Alberici et al. (70) | 21 | Hospitalized, COVID+ | 21 (100) HD | NA | NA | NA | NA | 5 (24) | Italy |
| Corbett et al. (67) | 1530 | ESKD from one large center, 300 with COVID | 290 (97) in-center HD 8 (2.7) PD 2 (0.7) home HD | 75/300 (25) | NA | NA | NA | 61/300 (20) | London |
| Fisher et al. (71) | 114 | Hospitalized, COVID+ | 114 (100) HD | 56 (49) | 45 (40) | 19 (17) | 2 (2) | 32 (28) | New York |
| Flythe et al. (61) | 143 ESKD 4121 non-ESKD | COVID+, in ICU Multicenter | 128 (90) in-center HD 9 (6) PD 2 (1) home HD 4 (3) unknown | 36 (100) HD | 71 (50) | 29 (20) | 106 (74)a | NA | 72 (50)b United States |
| Goicoechea et al. (68) | 36 | ESKD hospitalized, COVID+ | 408 (97) HD 11 (2.6) PD | 152 (36) ESKD 87 (21) | 89 (21) | NA | 0 | 11 (30.5) | Spain |
| Ng et al. (65) | 419 ESKD, 10,063 non-ESKD | ESKD and non-ESKD, all COVID+ | 41 (98) HD 1 (2) PD 57 (97) HD 2 (3) PD | 0 | 0 | NA | NA | 18 (41) | New York |
| Scarpioni et al. (72) | 42 | Hospitalized, ESKD, all COVID+ | 49 (100) HD | 0 | 0 | NA | NA | 18 (31) | New York |
| Valeri et al. (66) | 59 | Hospitalized, ESKD and non-ESKD, all COVID+ | 131 (100) HD | 0 | 0 | 16/116 (13.8) | 36 (28) | China |
| Wu et al. (63) | 49 on HD, 52 controls | ESKD and non-ESKD, all COVID+ | 237 (100) HD | NA | NA | 0 | NA | 41 (31) | China |
| Xiong et al. (69) | 131 | ESKD, all COVID+ | 237 (100) HD | NA | NA | 0 | NA | 0 | Toronto |
| Yau et al. (73) | 330 | 237 HD patients, 93 HD staff 22 COVID+ | 131 (100) HD | 0 | 0 | 16/116 (13.8) | 36 (28) | 41 (31) | Toronto |

Of studies that reported data on ESKD and non-ESKD, only values for patients with ESKD are included. HD, hemodialysis; PD, peritoneal dialysis.

aOn d 14.
bAt d 28.
from China, however, reported lower rates of pre-existing CKD-ND, 0.7% to 4.3% (Figure 1B) (3-5,7,9-14,24,26).

One Chinese meta-analysis of four studies (N=1389) found an association between CKD-ND and more severe COVID-19 disease (38). Other meta-analyses showed that CKD was associated with an increased risk of mortality in patients hospitalized with COVID-19, although it is not clear whether models were adjusted for hypertension or diabetes mellitus (59,60). A large, multi-center US study of patients in the ICU with COVID-19 also revealed that patients with pre-existing CKD-ND versus without had a higher risk of in-hospital mortality (61). Although more data are needed to confirm findings, it is important to educate patients with CKD about proper precautions to decrease risk.

ESKD

Epidemiology and Outcomes

The COVID-19 outbreak brings up increased concern for ESKD patients who are intrinsically immunocompromised and have underlying comorbidities (62). Those who receive outpatient in-center HD are in close contact with other patients and staff multiple times a week, putting them at even greater risk. Clinical presentation is atypical when compared with patients not on dialysis, with patients with ESKD presenting without typical symptoms of cough and fever but instead, fatigue and anorexia (63,64). Risk of in-hospital death is significantly higher among patients with ESKD as compared with patients without ESKD, with older age and need for mechanical ventilation increasing risk (63,65,66) (Table 1). Most early reports of mortality came from small cohorts, where mortality ranged from 14% to 30% (66-69). A more recent larger cohort reported mortality of 31.7% in patients with ESKD as compared with 25.4% in patients without ESKD (65).

Management of Outpatient Dialysis

How to best handle outpatient dialysis becomes imperative due to the propensity of COVID-19 to cause cluster outbreaks. A study from London reported cluster outbreaks at specific centers within their network (67). This and other reports illustrated a need for HD center protocols to limit transmission, and subsequently, several opinion-based editorials were published. As Wuhan saw an increase in cases in patients on dialysis and staff, preventative measures, including limiting in-person provider rounds, limiting number of patients on individual shifts, temperature and symptom checks at entry, and increased PPE utilization, were implemented. COVID-19–positive dialysis shifts were set up in designated hospitals where large numbers of patients on dialysis with the infection were treated centrally (74). If this was not feasible, then separate COVID-19–positive dialysis shifts were recommended, preferably utilizing the day’s last shift (75-77). Cohort isolation for in-center HD, screening protocols, and adequate PPE are agreed upon by many nephrologists (75,77,78). The US Centers for Disease Control has provided guidance and commented on when to transition patients who are infected to outpatient dialysis units after recovery (79). No clear correlation was found between length of illness and postrecovery shedding of virus in patients on dialysis, but recent data suggest the replication-competent virus likelihood approaches zero by 10 days of symptoms in the general population (80). Currently, the strategy for transitioning patients to outpatient dialysis is either test based, requiring two negative tests ≥24 hours apart and being symptom free; or, if testing is not available, fever free for ≥72 hours and ≥14 days since symptom onset (81).

Management of Inpatient Dialysis

In anticipation of increased numbers of affected patients on dialysis requiring hospitalization, there was concern for limited resources, for example, dialysis machines, filters, and solutions, and decreased number of available staff due to illness or quarantine. Hospital admissions will include both patients infected with COVID-19 and with AKI and patients on maintenance dialysis requiring RRT. Similar strategies were proposed to what was discussed regarding AKI, including decreasing number of weekly dialysis sessions and shortening treatments. Given mandates to defer elective nonurgent surgeries, some centers were having issues with patients not being scheduled for procedures to place or repair vascular access. This prompted the Centers for Medicare and Medicaid Services to release a statement iterating that procedures to establish dialysis access were essential and should be treated as such (82). Transitioning patients from in-center HD to home dialysis modalities, such as home HD or PD, can also be considered (Figure 3) (64).

Kidney Transplantation

Epidemiology and Outcomes

It would be logical to assume kidney transplantation recipients are at increased risk for contracting COVID-19 and having more severe disease on the basis of their immunocompromised state and common comorbidities of hypertension and diabetes. However, current evidence on the basis of several case series is unclear. Presentation of COVID-19 in transplant recipients appears to be similar to that in patients who are not immunosuppressed, with typical symptoms being cough, fever, and shortness of breath (Table 2) (39,83-85). One study of 36 patients reported a mortality rate of 28%, substantially higher than that in the general population (86). Similarly, Alberici et al. (87) described a 25% mortality rate among 20 transplant recipients, and Nair et al. a rate of 30% in 10 (39). Both groups also found an increased rate of clinical deterioration. Given small sample sizes, it is difficult to conclude whether kidney transplant recipients are at an increased risk of death from COVID-19.

Immunosuppression Management in Transplant Recipients

Although there are no standardized guidelines regarding the management of immunosuppression in patients with COVID-19, several groups recommended stopping antimetabolites in hospitalized patients, following the thought process that T-cell immunity is likely important for fighting the virus (39,83,86,90). However, there is also concern that the release of cytokines is responsible for many of the severe manifestations of COVID-19, including ARDS (83). Some form of immunosuppression could, therefore, be of benefit. In addition, new data support using corticosteroids in
Table 2. Summary of studies reporting AKI and outcomes in patients with COVID-19

| Study (Reference) | Patients, n | Sample | Black, n (%) | Hispanic, n (%) | CKD, n (%) | AKI, n (%) | AKI-RRT, n (%) | Mortality, n (%) | Geographic Location |
|-------------------|-------------|--------|--------------|----------------|------------|------------|---------------|-------------------|-------------------|
| Chen et al. (24)  | 113 deceased and 161 recovered | Hospitalized | 0 | 0 | 4 (1) | 28 (25) versus 1 (1) | 3 (1) | 113 (41.2) | China |
| Cheng et al. (3)  | 701 | Hospitalized | 0 | 0 | 14 (2) | 36 (5.1) NA | NA | 113 (16.1) | China |
| Deng et al. (25)  | 109 deceased and 116 recovered | Hospitalized | 0 | 0 | NA | 20 (18.3) versus 0 | NA | 109 (49) | China |
| Guan et al. (4)   | 1099 | Hospitalized and outpatients | 0 | 0 | 8 (0.7) | 6 (0.5) NA | NA | 15 (1.4) | China |
| Guo et al. (5)    | 701 | Hospitalized | 0 | 0 | 6 (3.2) | 18 (14.6) NA | NA | 43 (23) | China |
| Hu et al. (6)     | 41 | Hospitalized | 0 | 0 | NA | 3 (7) | 3 (7) | 6 (15) | China |
| Lei et al. (7)    | 34 | Underwent elective surgery before diagnosis | 0 | 0 | 1 (2.9) | 2 (5.9) | 1 (2.9) | 7 (20.6) | China |
| Pei et al. (8)    | 333 | Hospitalized | 0 | 0 | 0 | 35 (10.5) NA | NA | 29 (8.7) | China |
| Shi et al. (9)    | 416 | Hospitalized | 0 | 0 | 14 (3.4) | 8 (1.9) | 2 (0.5) | 57 (13.7) | China |
| Wang et al. (26)  | 107 | Hospitalized | 0 | 0 | 3 (2.8) | 14 (13.1) NA | NA | 19 (17.7) | China |
| Wang et al. (10)  | 138 | Hospitalized | 0 | 0 | 4 (2.9) | 5 (3.6) | 2 (1.45%) | 6 (4.3) | China |
| Wang et al. (2)   | 116 | Hospitalized | 0 | 0 | 5 (4.3) | 0 (0) | 0 (0) | 7 (6) | China |
| Xu et al. (27)    | 239 | ICU | 0 | 0 | NA | 119 (50) | 12 (5) | 147 (61.5) | China |
| Yang et al. (28)  | 52 | ICU | 0 | 0 | NA | 15 (29) | 9 (17) | 32 (51.5) | China |
| Zhang et al. (11) | 221 | Hospitalized | 0 | 0 | 6 (2.7) | 10 (4.5) | 5 (2.3) | 12 (5.4) | China |
| Zhang et al. (12) | 140 | Hospitalized | 0 | 0 | 2 (1.4) | NA | NA | NA | China |
| Zhang et al. (13) | 645 | Hospitalized | 0 | 0 | 6 (0.9) | 2 (0.3) | 0 (0) | NA | China |
| Zhou et al. (14)  | 191 | Hospitalized | 0 | 0 | 2 (1) | 12 (6.3) | 10 (5) | 54 (28.3) | China |
| Aggarwal et al. (15) | 16 | Hospitalized | 0 | 0 | 6 (38) | 11 (69) | NA | 3 (19) | Iowa |
| Arentz et al. (29) | 21 | ICU | NA | NA | 10 (47.6) | 4 (19.1) | NA | 11 (52.4) | Washington State |
| Argenziano et al. (16) | 1000 (850 hospitalized) | ED or hospitalized | 181 | 248 (24.8) | 137 (13.7) | 288/850 | 117/850 | 211 (21.1) | New York |
| Fisher et al. (17) | 3345 | Hospitalized | 1201 | 1247 | 409 (12.2) | 1903 (56.9) | 164 (4.9) | 775 (23.2) | New York |
| Gupta et al. (30) | 3099 | ICU | 952 | 1045 | 897 (28.9) | 1685 (54.4%) | 637 (20.6) | 350/637 (54.9%) of AKI-RRT | United States, multicenter |
| Hirsch et al. (18) | 5449 | Hospitalized | 1123 | 1145 (21) | NA | 1993 (36.6) | 285 (5.2) | 888 (16.3) | New York |
| Imam et al. (31)  | 1305 | Hospitalized | 862 | 661 | NA | 228 (17.5) | 76 (5.85) | NA | Michigan |
| Mohamed et al. (19) | 575 | Hospitalized | 414 | 9 (1.57) | 172 (29.9) | 161 (28) | 89 (15.5) | 80/161 (50) (AKI cohort) | New Orleans, Louisiana |
| Pelayo et al. (20) | 223 | Hospitalized | 152 | 14 (6) | 39 (17) | 110 (49) | 9 (4) | 44 (19) | Pennsylvania |
| Price-Haywood et al. (21) | 3481 | Hospitalized and outpatient | 2451 | 0 | 278 (8) | 197 (14.25) | NA | 326 (23.6) | Louisiana |
| Richardson et al. (22) | 5700 total, 2634 discharged or died | Hospitalized | 1230 | 1230 (23) | 186 (3.5) | 523/2634 | 81/2634 | 553/2634 (21) | New York |
| Grasselli et al. (88) | 1591 | ICU | NA | NA | 36 (3) | NA | NA | 405 (26) | Italy |
| Lim et al. (89)   | 164 | Hospitalized | 0 | 0 | Excluded | 30 (18.3) | 5 (3) | 44 (164) | South Korea |
| Kidney transplant recipients | 36 | Confirmed COVID | 14 (39) | 15 (42) | NA | NA | 6 (21) | 10 (28) | New York |
| Study (Reference) | Patients, n | Sample | Black, n (%) | Hispanic, n (%) | CKD, n (%) | AKI, n (%) | AKI-RRT, n (%) | Mortality, n (%) | Geographic Location |
|-------------------|-------------|--------|--------------|----------------|------------|------------|---------------|------------------|-------------------|
| Alberici et al. (87) | 20          | Hospitalized, confirmed COVID | NA | NA | NA | 6 (30) | 1 (5) | 5 (25) | Italy |
| Banerjee et al. (90) | 7           | Confirmed COVID | NA | NA | NA | NA | NA | 1 (14) | London |
| Columbia transplant program (85) | 15          | Confirmed COVID | NA | NA | NA | 6 (40) | 2 (13) | 2 (13) | New York |
| Husain et al. (84) | 41          | Confirmed or suspected COVID | NA | NA | NA | NA | NA | 0 | New York |
| Maritati et al. (91) | 5           | Hospitalized, confirmed COVID | NA | NA | NA | 1 (20) | 0 | 2 (60) | Italy |
| Nair et al. (39) | 10          | Confirmed COVID | 3 (30) | NA | NA | 5 (50) | NA | 3 (30) | New York |

Note that references 18,22 come from the same institution and the cohorts overlap. ICU, intensive care unit; ED, emergency department.

*aOnly looked at first 48 h.*

*bHospitalized only.*
patients who are ventilated or have increased oxygen requirements (92). Many transplant centers have practiced continuing corticosteroids and, in some patients, increasing the dose and continuing a reduced dose of calcineurin inhibitors (unless the patient is severely ill) (39,86,90). One study of 40 patients hospitalized with COVID-19 from multiple sites reported the majority were maintained on corticosteroids alone (93). Overall, it is agreed that the specific clinical scenario should guide immunosuppression, including any recent treatments for rejection, which would result in further decline in immunity. Of note, patients in many of these early case series were treated with hydroxychloroquine and azithromycin, which are no longer being recommended. More contemporary data with larger numbers are needed to determine outcomes of patients treated with other agents, including remdesivir, IL-6 inhibitors, and convalescent plasma.

As the pandemic continues, it is important to know how to manage those patients who may not need hospitalization. The transplant nephrology group at Columbia evaluated outpatients with known or suspected COVID-19, and of 41 patients, 32% required hospitalization, the remaining managed as outpatients. After a median follow-up of 12 days, 23 of 41 had resolution of symptoms. However, due to lack of testing availability at the time, not all patients were tested to confirm COVID-19 (84). The ideal outpatient management has not yet been determined, as very limited follow-up data exist on kidney transplant recipients, in particular, and patients recovering from COVID-19 in general. More information is also needed to determine the optimal timing for the reintroduction of immunosuppressants.

Performance of New Transplantations
Most transplant centers limited or temporarily stopped performing kidney transplantations during the pandemic, due risk of transmission to donors with health care contact and recipients who would be immunosuppressed. One report noted that the rate of US deceased-donor kidney transplants decreased by 50% (64). Alternatively, transplantation could mean no further need for in-center dialysis, which would reduce risk. In a recent statement, Centers for Medicare and Medicaid Services reiterated that organ transplantation is an essential procedure (82). The availability of resources is also a consideration (94). There needs to be a balance between the benefit of transplantation for individual patients and risks of nosocomial COVID-19 spread and resource utilization. Massie developed a tool using machine learning to determine the benefit versus risk of kidney transplantation and found that, in 72% of simulated scenarios, immediate transplantation provided a survival benefit to deferring transplantation and remaining on the wait list (95). This tool may be used by transplant centers to individualize transplantation decisions.

GN
Initiating or continuing immunosuppression in patients with glomerular disease is also concerning in this pandemic. There are no evidence-based recommendations, and there is very little information regarding the prevalence of COVID-19 or outcomes of patients who are infected. One group in Italy prospectively evaluated patients with nephrotic syndrome on chronic therapy with anti-CD20 antibodies, the majority of which were pediatric patients. In total, 34% were also being treated with other immunosuppressants (corticosteroids, calcineurin inhibitors, and antimetabolites). All patients had received treatment with B-cell–depleting therapy, with a median time since last treatment of 18 months. At follow-up, none developed signs of COVID-19. Six were living with an individual who was found to be COVID-19 positive. On the basis of these observations, the authors recommended not to pre-emptively alter the immunosuppression regimen in children with nephrotic syndrome, regardless of possible COVID-19 exposure (96).

To strike a balance between COVID-19 complications and kidney outcomes, the glomerular disease group at Columbia proposed recommendations on the basis of their experience in a COVID-19 hotspot (97). Initiate standard-of-care for patients with rapidly progressing glomerular disease and severe nephrotic syndrome who have decreased kidney function and/or complications of nephrotic syndrome. Defer treatment for patients who do not meet these criteria but would typically be started on immunosuppression. For those who had begun treatment before the pandemic onset, the decision to continue treatment would be made on a case-by-case basis, weighing risks and benefits. For patients started on intravenous protocols, switch to oral regimens to decrease health care visits. Consider home infusions when no equivalent oral regimen exists. For patients in remission on maintenance regimen, stop antimetabolites and avoid maintenance B-cell–depleting infusions. Tapering and discontinuing corticosteroids has also been suggested for stable patients, whereas calcineurin inhibitors are continued on the basis of experience in the transplant community. Immunosuppression adjustments for patients with confirmed COVID-19 should be on the basis of specific clinical scenarios. Other strategies to decrease exposure include limiting kidney biopsies to only those necessary for critical decision making, using home urine dipsticks versus those done at a laboratory, and utilizing telemedicine (97).

Discussion
The effect of the COVID-19 pandemic has been felt in all facets of kidney disease management. There is still much to be learned, including the long-term kidney outcomes in patients with COVID-19–related AKI. The best strategies for managing immunosuppression in kidney transplant recipients and patients with GN are unknown. Similarly, strategies on how to best manage patients with ESKD receiving outpatient in-center dialysis or patients hospitalized with COVID-19 and ESKD or AKI requiring RRT are anecdotal. As new experiences and data become available, it becomes paramount to continue sharing and publication of evidence, and to be hypervigilant in adjusting our practice to provide the best clinical care.

Disclosures
S. Hedayati reports receiving honoraria from the American College of Physicians for participation in Nephrology Medical Knowledge Self-Assessment Program, American Society of Nephrology Post-Graduate Education Program; and being a scientific advisor or member of the American Heart Association, study sections, American College of Physicians, Medical Knowledge Self-
Duer-Hestele J, Falzon L, Gitlin J, Hajizadeh N, Harvin TG, Hirschwerk DA, Kim EJ, Kozel ZM, Marrast LM, Mogavero JN, Osorio GA, Qiu M, Zanos TP; the Northwell COVID-19 Research Consortium: Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area [published correction appears in JAMA 323: 2098, 2020. 10.1001/jama.2020.7681]. JAMA 323: 2052–2059, 2020. https://doi.org/10.1001/jama.2020.6775

23. Santorinelli D, Kheirallah F, Bombard M, Xu K, Kudose S, Batal I, Barasch J, Radhakrishnan J, D’Agati V, Markowitz G: Postmortem kidney pathology findings in patients with COVID-19. J Am Soc Nephrol 31: 2151–2167, 2020. https://doi.org/10.1681/ASN.2020050744

24. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, Ma K, Xu D, Yu H, Wang H, Wang N, Bao W, Chen J, Ding C, Zhang X, Huang J, Han M, Li S, Luo X, Zhao J, Ning Q: Clinical characteristics of 113 deceased patients with coronavirus disease 2019: Retrospective study [published correction appears in BMJ 368: m1295, 2020. 10.1136/bmj.m1295]. BMJ 368: m1091, 2020. https://doi.org/10.1136/bmj.m1091

25. Deng Y, Liu W, Liu K, Fang YY, Shang J, Zhou L, Wang K, Leng F, Wei S, Chen H: Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 in Wuhan, China: A retrospective study. Chin Med J (Engl) 133: 1261–1267, 2020. https://doi.org/10.1097/CMA.0000000000000824

26. Wang D, Yin Y, Hu C, Liu X, Zhang X, Zhou S, Jian M, Xu H, Prowle J, Hu B, Li Y, Peng Z: Clinical course and outcome of 107 patients infected with the novel coronavirus: from two hospitals in Wuhan, China. Crit Care 24: 188, 2020. https://doi.org/10.1186/s13054-020-02895-6

27. Xu J, Yang X, Yang L, Zou X, Wang Y, Wu Y, Zhou T, Yuan Y, Qi H, Fu S, Liu H, Xia J, Xu Z, Yu Y, Li R, Ouyang Y, Wang R, Ren L, Hu Y, Xu D, Zhao X, Yuan S, Zhang D, Shang Y: Clinical course and predictors of 60-day mortality in 239 critically ill patients with COVID-19: A multicenter retrospective study from Wuhan, China. Crit Care 24: 394, 2020. https://doi.org/10.1186/s13054-020-03098-9

28. Yang X, Yu X, Yu J, Shu H, Xia J, Liu H, Wu Y, Zhang L, Yu Z, Fang M, Yu T, Wang Y, Pan S, Zou X, Yuan S, Shang Y: Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study [published correction appears in Lancet Respir Med 8: e26, 2020. 10.1016/S2213-2600(20)30103-X]. Lancet Respir Med 8: 475–481, 2020. https://doi.org/10.1016/S2213-2600(20)30079-5

29. Arentz M, Yim E, Klafi L, Lokhandwala S, Riedo FX, Chong M, Lee M: Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington state. JAMA 323: 1612–1614, 2020. https://doi.org/10.1001/jama.2020.6258

30. Gupta S, Hayek SS, Wang W, Chan L, Mathews KS, Metelmann LM, Brenner SK, Leonberg-Yoo A, Schenck EJ, Radbel J, Reiser J, Bansal A, Srivastava A, Zhou Y, Sutherland A, Green A, Shehata AM, Goyal N, Vijayan A, Velez JCQ, Shaeti S, Parikh CR, Arumughamani J, Athavale AM, Friedman AN, Short SAP, Kibbel JA, Ollish F, Gill J, Admon AJ, Donnelly JP, Genshengbor HB, Herman MA, Semler MW, Leaf DE; STOP-COVID Investigators: Factors associated with death in critically ill patients with coronavirus disease 2019 in the US [published correction appears in 10.1001/jama.netmed.2020.4568]. JAMA Intern Med 180: 1–12, 2020. https://doi.org/10.1001/jama.2020.3596

31. Iyavm Z, Ojinnaka C, O’Connor D, Armstrong J, Vanoond A, Iribonke O, Hanna A, Ranski A, Halalau A: Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States. J Intern Med 288: 469–476, 2020. https://doi.org/10.1111/joim.13119

32. Kellum JA, Lameire N, Aspelin P, Barsoum RS, Burdmann EA, Goldstein SD, Herzog CA, Joannidis M, Kribben A, Levey AS, MacLeod AM, Mehta RL, Naicker S, Opal SM, Gorenstein EP: COVID-19 in kidney transplant recipients. Am J Transplant 20: 1819–1825, 2020. https://doi.org/10.1111/1600-0614.15967

33. Reddy VNY, Walsensky RP, Mendu ML, Green N, Reddy KP: Estimating shortages in capacity to deliver continuous kidney replacement therapy during the COVID-19 pandemic in the United States. Am J Kidney Dis 76: 696–709.e1, 2020. https://doi.org/10.1053/j.ajkd.2020.07.005

34. American Society of Nephrology: Recommendations on the care of hospitalized patients with COVID-19 and kidney failure requiring renal replacement therapy. Available at: https://www.asn-online.org/gblast/files/AKI_COVID-19_Recommendations_Document_03.21.2020.pdf. Accessed November 13, 2020

35. Shankaranarayanan D, Mathukuman T, Barbar T, Haisan A, Geradine S, Lamba P, Lepruge L, Neupane SP, Salinas T, Shimonov D, Varma E, Liu F: Anticoagulation strategies and filter life in COVID-19 patients receiving continuous renal replacement therapy: A single-center experience. Clin J Am Soc Nephrol 16: 1246–1253, 2021. https://doi.org/10.2215/CJN.08430520

36. Wen Y, LeDoux JR, Mohamed M, Ramanand A, Scharwath K, Mundy D, Luitzk I, Velez JCQ: Dialysis filter life, anticoagulation, and inflammation in COVID-19 and acute kidney injury. Kidney360 1: 1426–1431, 2020. 10.34067/KID.00043220

37. Post A, den Deurwaarder ESG, Bakker SJL, van Meurs K, Morawietz L, Schultheiss HP: Detection of viral SARS-CoV-2 genomes and histopathological changes in endomyocardial biopsies. Nat Rev Nephrol 16: 308–310, 2020. https://doi.org/10.1038/s41581-020-0284-7

38. Escher F, Pietsch H, Alescheva G, Beck T, Baumeier C, Elsaesser A, Wenzel P, Hamm C, Westenfeld R, Schultheiss M, Gross U, Morawietz L, Schultheiss HP: Detection of viral SARS-CoV-2 genomes and histopathological changes in endomyocardial biopsies. ESC Heart Fail 7: 2440–2447, 2020. https://doi.org/10.1002/ehf2.12805

39. Sharma P, Uppal NN, Wanchoo R, Shah HH, Yang Y, Parikh R, Khaniyn Y, Madireddy V, Larsen CP, Jhaerti KD, Bijov I, Northwell Nephrology COVID-19 Research Consortium: COVID-19-Associated kidney injury: A case series of kidney biopsy findings. J Am Soc Nephrol 31: 1948–1958, 2020. https://doi.org/10.1681/ASN.2020050699
97. Centers for Disease Control: Interim additional guidance for infection prevention and Control recommendations for patients with suspected or confirmed COVID-19 in outpatient hemodialysis facilities. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/dialysis.html. Accessed August 25, 2020

98. Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, Niemeyer D, Jones TC, Vollmar P, Rothe C, Hoelscher M, Bleicker T, Brünnink S, Schneider J, Ehmann R, Zwingmaier K, Drosten C, Wendtner C: Virological assessment of hospitalized patients with COVID-2019. Nature 581: 465–469, 2020 https://doi.org/10.1038/s41586-020-2196-x

99. Centers for Disease Control: Considerations for providing hemodialysis to patients with suspected or confirmed COVID-19 in acute care settings. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/dialysis/dialysis-in-acute-care.html. Accessed August 25, 2020

100. Center for Clinical Standards and Quality/Quality SOG: Key components for continued COVID-19 management for dialysis facilities. Available at: https://www.asn-online.org/covid-19/CMS#general. Accessed August 25, 2020

101. Chen TY, Farghaly S, Cham S, Tatem LL, Sin JH, Rauda R, Ribisi M, Donati A, Perna GP, Giacometti A, Tavio M, Onesta M, Di Santa L, Ranghino A: SARS-CoV-2 infection in kidney transplant recipients: Experience of the Italian Marche region. Transplant Infect Dis 2020 10.1111/tid.13377. Available at: https://doi.org/10.1111/tid.13377

102. Horby P, Lim WS, Emberson JR, Matham M, Bell JL, Linsell S, Staplin N, Brightling C, Ustianowski A, Elmahdi E, Prudon B, Green C, Felton T, Chadwick D, Rege K, Fegan C, Chappell LC, Faust SN, Jaki T, Jeffery K, Montgomery A, Rowan K, Juszczak E, Bailie JK, Haynes R, Landray MJ: RECOVERY Collaborative Group: Dexamethasone in hospitalized patients with COVID-19: Preliminary report. N Engl J Med 2020 10.1056/NEJMoa2021436

103. Johnson KM, Belfer JJ, Peterson GR, Boekhins MR, Dumkow LE: Managing COVID-19 in renal transplant recipients: A review of recent literature and case supporting corticosteroid-sparing immunosuppression. Pharmacotherapy 40: 517–524, 2020 https://doi.org/10.1002/phar.2410

104. Stock PG, Wall A, Gardner J, Domínguez-Gil B, Chadban S, Muller E, Dittmer I, Tullius SG, TTS Ethics Committee: Ethical issues in the COVID era: Doing the right thing depends on location, resources, and disease burden. Transplantation 104: 1316–1320, 2020 https://doi.org/10.1097/TP.0000000000003291

105. Massie AB, Boyarsky BJ, Werbel WA, Bae S, Chow EK, Avery RK, Durand CM, Desai N, Brennan D, Goraznik-Wang JM, Segev DL: Identifying scenarios of benefit or harm from kidney transplantation during the COVID-19 pandemic: A stochastic simulation and machine learning study. Am J Transplant 20: 2997–3007, 2020 10.1111/ajt.16117

106. Angeletti A, Drovandi S, Sanguinieri F, Santaniello M, Ferrando DL: Identifying scenarios of benefit or harm from kidney transplantation during the COVID-19 pandemic: A stochastic simulation and machine learning study. Am J Transplant 20: 2997–3007, 2020 10.1111/ajt.16117

107. Bomback AS, Canetta PA, Ahn W, Ahmad SB, Radhakrishnan J, Appel GB: How COVID-19 has changed the management of glomerular diseases. Clin J Am Soc Nephrol 15: 876–879, 2020 https://doi.org/10.1021/CLJN.04530420

Received: October 26, 2020 Accepted: November 24, 2020