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Management of COVID-19 in special populations with kidney disease

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■ ABSTRACT

Although the literature is limited, early evidence suggests that patients with chronic kidney disease, end-stage kidney disease, and kidney transplant recipients are at increased risk for severe COVID-19 disease and death. Hence, management should focus on both infection prevention and treatment. There is currently a lack of evidence and guideline recommendations on optimal management of immunosuppression in kidney transplant recipients with COVID-19 infection. This article focuses on the prevention and management of COVID-19 in patients with chronic kidney disease, patients with end-stage kidney disease on home hemodialysis and peritoneal dialysis, and kidney transplant recipients.

■ COVID-19 AND CHRONIC KIDNEY DISEASE

The prevalence of COVID-19 in patients with chronic kidney disease (CKD) is currently unknown. However, patients with CKD may be at risk for severe COVID-19 disease.¹ Chronic kidney disease was associated with an increased risk of severe COVID-19 disease in a meta-analysis of 4 studies that included 1,389 patients with COVID-19, although individual studies did not show any association.¹ COVID-19 in patients with CKD is also associated with increased mortality.² Thus, management should focus on both infection prevention and treatment.

The most effective measures to reduce the risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection include social distancing, limiting human interaction, and prioritizing outings.

When caring for patients with stable CKD, physicians should minimize hospital and clinic visits and face-to-face encounters by performing telemedicine visits that are compliant with current Health Insurance Portability and Accountability Act regulations.³ Patients can be triaged by nursing providers before the visit to assess the need for an in-person visit. Disease prevention strategies such as the use of personal protective equipment as recommended by the Centers for Disease Control and Prevention or local authorities, physical distancing, and practicing hand hygiene should be continued in outpatient and specialty clinics.⁴

Early in the pandemic, there was concern about the use of renin-angiotensin system (RAS) inhibitors increasing patients' susceptibility to SARS-CoV-2 infection. RAS inhibitors were thought to possibly upregulate expression of angiotensin-converting enzyme 2 thus increasing susceptibility to SARS-CoV-2 infection. However, multiple studies have demonstrated that the use of RAS inhibitors are not associated with an increased risk of SARS-CoV-2 infection. Therefore, RAS inhibitors should not be discontinued when being used in patients with stable CKD.³

In May 2020, the US Food and Drug Administration issued an emergency use authorization for remdesivir, a DNA/RNA polymerase inhibitor, to treat patients with COVID-19. There is limited evidence on the use of remdesivir in patients with CKD as the clinical trials excluded patients with a glomerular filtration rate (GFR) less than 30 mL/min/1.73m². There is a concern for mitochondrial toxicity since it is a DNA/RNA polymerase inhibitor and toxicity from the accumulation of sulfobutylether-b-cyclodextrin carrier that the drug is compounded with, in patients with kidney disease.⁵ However, clinical trials for Ebola and COVID-19 did not report an increased

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risk of renal adverse events. Thus, remdesivir should not be used in patients with COVID-19 and a GFR less than 30 mL/min/1.73m² unless the benefits outweigh the risks.⁵

Dexamethasone lowered the 28-day mortality rate in hospitalized patients with COVID-19 who were on invasive mechanical ventilation or required supplemental oxygen support.⁶ Though patients with severe kidney impairment (ie, GFR less than 30 mL/min/1.73m²) were enrolled in the dexamethasone trial, a lack of subgroup analyses confirming this benefit in the CKD population is yet to be published. Despite the lack of subgroup analyses, dexamethasone can still be used in patients with CKD provided the risk-benefit ratio is taken into consideration.

■ COVID-19 AND END-STAGE KIDNEY DISEASE

Although not necessarily surprising, early evidence has emerged suggesting that patients with end-stage kidney disease (ESKD) on hemodialysis (HD) and peritoneal dialysis (PD) are more likely to develop COVID-19 complications such as acute respiratory distress syndrome, arrhythmias, shock, and acute cardiac injury along with a higher risk of mortality.^{7,8}

Patients with ESKD on home-based dialysis modalities

Data from the United Kingdom Renal Registry and Ontario Renal Network have shown that patients receiving PD and home HD have a lower risk of acquiring COVID-19 infection than patients receiving center-based HD.⁹ Thus, a robust home HD program can minimize patients' and healthcare workers' exposure to COVID-19 while still providing effective dialysis for patients with ESKD. Education of healthcare workers and patients with ESKD on advances in COVID-19, use of personal protective equipment, and infection control measures should continue to be implemented. Patients on PD should have at least 2 weeks of dialysis supplies. Home visits by healthcare workers should be avoided except for emergencies and patients with disabilities.¹⁰ For patients using automated PD systems, remote management platforms should be used to assess and monitor PD sessions. For patients on home HD, real-time monitoring of vital signs and treatment data can be performed by HD technicians who can also help patients troubleshoot or answer questions.¹¹ Thomas and colleagues showed that monthly blood sampling was not associated with a lower risk of death when compared to sampling every 6 weeks.¹² Based on this study, we recommend that the home dialysis team should work with ESKD

patients to decide if a more spaced-out surveillance blood work is appropriate.

Patients with ESKD on in-center hemodialysis

Infection control measures to reduce the risk of COVID-19 infection should be continued in all dialysis facilities. Patients must be instructed and triaged by phone calls to determine if they have been in close contact with individuals with COVID-19 or have COVID-19 symptoms before they arrive for their dialysis sessions.¹³ Although screening for COVID-19 symptoms with temperature checks is controversial, this practice continues to be implemented in our institution. Testing protocols for patients and staff at dialysis units should be implemented upon arrival at the dialysis center if it does not have the resources to triage patients beforehand. Patients with COVID-19 can be assigned to HD units dedicated only to COVID-19–positive patients.³ Routine disinfection of dialysis equipment and supplies should be implemented in all facilities. Appropriate use and preservation of personal protective equipment by providers to prevent shortage when caring for patients with and without COVID-19 is recommended in US Centers for Disease Control and Prevention guidelines. These interventions should help minimize the exposure of patients and healthcare workers in HD units to COVID-19.

COVID19 and kidney transplant recipients

Many transplant centers temporarily halted activity during the initial stages of the pandemic. However, kidney transplantation has resumed at high rates throughout the country because the competing risk of waitlist mortality outpaced the risk of COVID-19 infection as a newly transplanted patient. Screening of donors and recipients prior to kidney transplant surgery is recommended.³

Kidney transplant recipients (KTRs) are particularly vulnerable to higher morbidity and mortality in the setting of COVID-19 infection due to the higher incidence of comorbid conditions compared to the general population as well as a depressed immune state.^{3,14} In a prospective study consisting of 1,216 KTRs, the incidence of COVID-19 infection was found to be 5% with a mortality rate of 24% among COVID-19–positive patients compared to a mortality rate ranging from 1% to 5% in the general population.¹⁴ Fever is the most common reported symptom of COVID-19 in KTRs, followed by cough, dyspnea, and gastrointestinal symptoms; some patients present with mild or atypical symptoms such as conjunctivitis

and a normal white blood cell count.¹⁴⁻¹⁷ Thus, mild and atypical symptoms should prompt testing for COVID-19 in KTRs.

There is currently a lack of evidence and guideline recommendations on optimal management of COVID-19 infection in KTRs. In ambulatory recipients with COVID-19, the immunosuppression regimen is continued without any changes. For inpatient recipients with mild COVID-19 and no supplemental oxygen requirements, we recommend reducing the dose of mycophenolate mofetil while maintaining the rest of the immunosuppression regimen. If inpatient KTRs develop severe COVID-19 infection requiring supplemental oxygen, dexamethasone or remdesivir, or both, we discontinue mycophenolate mofetil while continuing the calcineurin inhibitors but targeting a lower trough level (eg, tacrolimus trough level 4–6 ng/mL). Telemedicine with remote monitoring of kidney transplant recipients should be continued to reduce exposure to COVID-19. **Table 1** summarizes the key recommendations provided throughout this article.

DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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TABLE 1
Summary of recommendations for COVID-19 in special patient populations with kidney disease

For all patients:
<ul style="list-style-type: none">• Social distancing and hand hygiene to reduce exposure to COVID-19• Use of PPE as recommended by the CDC• Education of health care workers and patients on advances in COVID-19
In addition to above, for specific populations with
Chronic kidney disease (CKD):
<ul style="list-style-type: none">• Virtual visits via telemedicine when in-person visits are not necessary• Continue RAS inhibitors in patients with stable CKD• Avoid remdesivir in patients with GFR < 30 mL/min per m² unless benefits outweigh risks
End-stage kidney disease on home-based dialysis:
<ul style="list-style-type: none">• Patients on peritoneal dialysis (PD): Maintain at least 2 weeks of PD supplies, remote management platforms to monitor PD sessions• Patients on home hemodialysis: Real-time monitoring of vital signs and treatment data• Home visits by healthcare workers should be avoided except for patients with disabilities or in cases of an emergency
End-stage kidney disease on in-center hemodialysis:
<ul style="list-style-type: none">• Screening for COVID-19 symptoms and temperature checks for patients and staff depending on institution policy• Use of dedicated HD units for patients with COVID-19• Daily disinfection of dialysis equipment and supplies
Kidney transplant recipients (KTRs):
<ul style="list-style-type: none">• Screening of donors and recipients prior to kidney transplant surgery• Ambulatory KTRs with COVID-19: continue home immunosuppression regimen• Inpatient KTRs:<ul style="list-style-type: none">• Mild COVID-19 with no supplemental oxygen use: reduce MMF while maintaining CNI and steroid therapy• Severe COVID-19 requiring supplemental oxygen, dexamethasone, or remdesivir: Discontinue MMF, target lower CNI trough levels

CDC = Centers for Disease Control and Prevention; CNI = calcineurin inhibitor; GFR = glomerular filtration rate; MMF = mycophenolate mofetil; PPE = personal protective equipment; RAS = renin-angiotensin system

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