

COVID-19 and Dialysis Patients: Unsolved Problems in Early 2021

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During the coronavirus disease 2019 (COVID-19) pandemic, as many as 20%–25% of patients on dialysis infected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may not survive the illness.^{1,2} Contributing factors may include comorbidities and inability to maintain social distancing during transportation and treatment. People of color have a higher incidence of ESKD than Whites and have a higher mortality from COVID-19.³ One early report showed that 20% of patients on hemodialysis acquired COVID-19.⁴ Case clustering among patients and staff suggested in-center spread of infection. After stringent infection prevention steps were taken, the incidence of in-center transmission fell. Across the United States, consistent use of infection prevention strategies reduced in-center virus transmission. The effectiveness of these measures to change mortality is yet to be calculated. What else must we know to help protect this highly vulnerable population?

MOST PRESSING ISSUES

The rapid deployment of several vaccines offers great hope. Should we encourage patients to be vaccinated? Although manufacturers report a high degree of safety and efficacy, the clinical studies leading the US Food and Drug Administration (FDA) to issue Emergency Use Authorization (EUA) for these vaccines did not include patients on

dialysis or patients with transplants. CKD may induce immunosuppression. Other vaccines have been studied in this population. The rates of seroprotection after influenza vaccination in patients on dialysis are reported to vary from 33% to 80%.⁵ Will patients on dialysis develop SARS-CoV-2 antibodies as dependably as healthy adults? How long do neutralizing antibodies persist after natural infection or immunization? Is cell-mediated, nonhumeral immune response important? How do natural antibodies compare with vaccine-induced antibody to mRNA to protect from infection? These are critical questions that should be addressed by post-marketing studies of patients on dialysis who received SARS-CoV-2 immunization. A related concern is the management of symptoms after vaccination. Fever and myalgia persist for up to 48 hours in >50% of those receiving the mRNA vaccines. How should dialysis facilities handle staff and patients presenting with fever within 48 hours of vaccination? Should they be treated as persons under investigation for COVID-19 and isolated? Do all need PCR tests for SARS-CoV-2? Similar questions remain for patients with kidney transplants, a population not included in vaccine trials. Will these vaccines elicit a vigorous antibody response in immunosuppressed patients? Will vaccine stimulation of their immune system result in more organ rejection or other unanticipated complications? Will patients be afraid to get vaccinated,

given these unknowns? In the midst of a devastating pandemic, it is unlikely that prospective, randomized trials can answer these questions. Nonetheless, we recommend that patients on dialysis and patients with transplants be encouraged to receive SARS-CoV-2 immunization. We believe that the clear risks of COVID-19 in this population exceed the potential risk of the vaccine. We also believe that the safety and efficacy of currently deployed vaccines for patients on dialysis and patients with transplants should be studied with carefully constructed registries for vaccine recipients. The vaccines still under development should allow inclusion of patients on dialysis and patients with transplants as targeted subgroups to assess safety and efficacy before FDA approval.

In November 2020, mAbs directed against SARS-CoV-2 received EUA. These agents are administered to reduce the viral load and the severity of COVID-19. They are indicated for patients with risk factors for poor outcomes from COVID-19, including those with CKD, but they have not been tested systematically in patients on dialysis and patients with transplants. One recent study

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shows that bamlanivimab and etesevimab in combination reduced the viral load of patients with COVID-19, whereas bamlanivimab alone did not.⁶ Although safety and efficacy questions remain in these populations, we recommend their use soon after COVID-19 has been documented. We also recommend that registries be developed to collect safety and efficacy data for patients who receive mAb treatment.

OTHER UNRESOLVED PROBLEMS

When can patients on dialysis who recover from COVID-19 return to the general outpatient dialysis population without fear of them transmitting virus to others? Many have persistently positive PCR tests weeks or even months following recovery. Because asymptomatic, nondialysis individuals do not transmit virus 10 days following first viral symptoms or positive PCR, the Centers for Disease Control and Prevention advises that asymptomatic patients can return to the general population 10 days after first infection (or 20 days if they are immunocompromised or had severe disease), without PCR testing. This guidance was on the basis of small studies showing absence of live virus in the secretions of patients recovering from COVID-19 10 days after they were first infected. The problem for patients on dialysis is that they may be more immunocompromised than healthier COVID-19 survivors. Is a prolonged positive PCR detecting lingering viral particles but not live virus? Or might patients on dialysis with altered immune systems harbor live virus longer than others? Simultaneous viral culture and serology measures might answer that question, but no well-designed studies have yet been published to answer that question. The length of time asymptomatic patients on dialysis might harbor live virus following recovery from COVID-19 remains unknown. Observational trials of patients recovering from COVID-19 should be conducted, including viral cultures, PCR, and antibody testing, to answer this question.

Many patients remain ill long after they recover from COVID-19, including fatigue and neurologic, cardiac, gastrointestinal, and respiratory symptoms. The reason for these persistent symptoms is unknown. “Long-hauler” clinics caring for and studying these patients will hopefully shed light on their pathophysiology.⁷

Coagulation abnormalities and thrombosis frequently complicate COVID-19. In the acute setting, many patients develop coagulopathy, low-grade disseminated intravascular coagulopathy, pulmonary thrombotic microangiopathy, and activation of the fibrinolytic system. Vascular wall damage seen with COVID-19 also increases the risk of thrombosis. When patients with COVID-19 require dialysis or continuous RRT, dialysis filters frequently clot and require replacement. Do these abnormalities persist after recovery from infection?⁸ Observational studies to examine vascular access patency after SARS-CoV-2 infection should be performed.

The advantages of peritoneal dialysis (PD) to treat ESKD were more evident during this pandemic. Home PD permits social distancing and limits infection exposure. Several hospitals utilized acute PD to treat AKI in patients with COVID-19. Some patients recovered from their viral illness but still required dialysis, and they wanted to continue outpatient PD. Unfortunately, Centers for Medicare and Medicaid Services regulation permits payment for AKI dialysis in a hemodialysis facility only. Thus, some had to convert to hemodialysis in-center and then, revert to PD at home after they reached ESKD. These regulations should be changed to encourage patients to continue home PD posthospitalization.⁹

Finally, an important unsolved problem concerns heroic dialysis staff members who have consistently come to work, cared for highly vulnerable patients, and risked their own health and that of their families. These nurses, technicians, dietitians, social workers, and physicians have been particularly stressed as colleagues fell ill or were forced to self-quarantine

after possible infection exposure. Long hours and high workloads became common. How can we assist dedicated staff deal with the psychologic stress and isolation of year-long hard work, reduced humanizing contact with peers, and social isolation at home? The long-term effects of this problem are yet to be well understood.¹⁰

In summary, little information is available concerning the safety and efficacy of SARS-CoV-2 vaccine and the durability of immunity in patients on dialysis. Clinical studies to answer these questions should be a priority. The safety and effectiveness of mAb treatment should be a second priority, along with a well-designed study of viral persistence in patients on dialysis recovering from COVID-19. In addition, it will be helpful to understand the source and treatment of “long-hauler” symptoms and the importance of infection-related coagulopathy. PD regulation should be updated to encourage this home-based treatment modality.

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