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COVID-19 and Dialysis Patients

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The Impact of COVID-19 on Outpatient Dialysis Facilities

Introduction

This is a point-in-time view of early pandemic. While the principles remain the same, the facts of COVID-19 care have evolved since 2020. Through August 2020, COVID-19 disease caused by the novel coronavirus SARS-CoV-2 has infected more than 30,500,000 people worldwide and caused nearly 1,000,000 deaths. The virus enters host cells via angiotensin-converting enzyme 2 (ACE-2) receptors, highly expressed in the mouth, tongue, and lower lung types I and II alveolar epithelial cells. ACE-2 receptors are expressed in target organs for SARS-CoV-2, including kidney proximal tubular cells and podocytes, cardiac endothelial cells, gut enterocytes, and blood vessels. Inhibitors of the renin-angiotensin system are common treatments for hypertension in patients with chronic kidney disease (CKD). While initial studies suggested that these agents might increase ACE-2 receptor expression, data do not support an association with COVID-19. Several possible mechanisms have been proposed for acute kidney injury (AKI) in the setting of COVID-19 infection, including prerenal injury resulting from high fever, gastrointestinal (GI) losses, and decreased oral intake; cardiac complications like cardiomyopathy or cardiorenal syndrome leading to renal hypoperfusion; toxic tubular damage due to intense production of proinflammatory cytokines leading to decreased renal perfusion and tubular injury over time; direct viral entry into kidney cells leading to tubular damage; and a hypercoagulable state leading to thrombotic microangiopathy.

Published reports document risk factors for COVID-19 infection, including hypertension (odds ratio [OR], 2.29), diabetes mellitus (OR, 2.47), and cardiovascular disease (OR, 2.93), all of which are common among patients with CKD. Increasing age, obesity, and the black race also increase the risk of infection. Minorities and older patients are disproportionately represented in the population of patients with CKD: 23% of incident patients are older than 75, 26% are black, and 15% are Hispanic. Patients requiring

maintenance dialysis have a much higher rate of infection when treated by in-center hemodialysis (HD) compared to home dialysis therapies. The risk of mortality increases as CKD progresses; 15%–40% of patients with CKD requiring maintenance dialysis who are infected by COVID-19 die. Mortality is greater in those with hypertension, diabetes mellitus, and cardiovascular disease, as well as older and black patients.

Initial symptoms of COVID-19 may be milder in patients with CKD: fatigue, cough, and dyspnea are reported less frequently; hypoxemia is less apparent because of reduced oxygen levels at baseline, and fever is less common because of reduced baseline body temperature. Diarrhea and fatigue are more common in patients with CKD. Many patients present asymptotically for HD but develop a fever during treatment and are subsequently diagnosed with COVID-19. Patients with CKD have higher levels of creatine kinase, myoglobin, troponin I, B-type natriuretic peptide, and procalcitonin than those with normal kidney function.

The impact of COVID-19 on the population of patients receiving maintenance dialysis is not yet known: will the high mortality rate be balanced by the number who initiate renal replacement therapy (RRT) as a result of AKI associated with COVID-19? Similarly, the impact of COVID-19 on the nephrology workforce is not yet known; some will retire because of the physical and emotional impact of COVID-19, but new personnel may be attracted by the opportunities the field presents to care for patients with chronic illness throughout their life cycle and the opportunity to impact the outcomes of patients with severe acute illness.

Patients

A major tool to prevent infection spread during the SARS-CoV-2 pandemic is social distancing. Maintaining at least 6 ft of separation between individuals is virtually impossible for patients receiving in-center HD, where they are often tightly clustered at the dialysis center and during transportation from home. In spite of the risk, patients must continue to receive life-sustaining dialysis treatments. Infection “hotspots” developed early during the COVID-19 pandemic in New York, Chicago, Detroit, and other cities. Hospitals

were quickly overwhelmed, precluding the possibility of sending patients with suspected or confirmed COVID-19 and mild symptoms to the hospital for dialysis management. Patients with known SARS-CoV-2 infection or those suspected to be infected (patients under investigation or PUIs) had to be treated in the outpatient setting. Some centers shortened dialysis treatments or decreased their frequency to minimize the risk of no social distancing, but concerns arose quickly about the risk of adverse outcomes of reduced dialysis adequacy. Exposure to COVID-19 was reduced by furlough of infected staff and by cohorting infected patients and PUIs in facilities treating only patients with active or suspected infection or on separate shifts caring for only infected or PUI patients. If neither option was available, the Centers for Disease Control and Prevention (CDC) advised treating such patients at the end of a row or in a corner of the dialysis facility separated from noninfected patients by at least 6 ft. Most dialysis centers adopted policies for patients to phone in before arrival if they had symptoms suggestive of infection. Patients are screened on arrival with temperature measurement and screening questions about symptoms and possible exposure. Waiting rooms are largely unused, and patients are asked to remain in their cars when possible and come directly to the dialysis station when it is ready for their arrival. Any patients who screen positive are separated from all others.

The timing of the safe return of patients to the dialysis center after SARS-CoV-2 infection symptoms are gone remains a challenge. Widespread limits on availability of reverse transcriptase-polymerase chain reaction (rt-PCR) testing for COVID-19 made it difficult to decide when patients are no longer shedding virus or viral particles. CDC guidance suggested that infected patients who have recovered from the symptoms of COVID-19 may return to the general dialysis population after two negative rt-PCR tests separated by at least 48 hours. An alternative time-based strategy permitted return 10–20 days after a positive test in the absence of symptoms. However, dialysis patients recovering from COVID-19 often continue to have positive tests for weeks or even months. Since the presence of detectable viral RNA does not necessarily indicate infectivity, these patients with persistently positive rt-PCR created confusion in this vulnerable population. While patients with normal kidney function recovering from COVID-19 are no longer infective 9–10 days after symptoms first appear, even if they have detectable viral RNA in their nasopharynx, it is not clear that the same can be said for dialysis patients, many of whom have impaired immune response systems. For this reason, the CDC eliminated its suggestion for postinfection viral testing and now advises using only the time-based method to determine when recovered patients can return to the general dialysis population. Antibody tests indicate prior exposure to the virus, but their exact meaning is not yet clear. Although some antibody tests are positive in 15%–20% of patients without known COVID-19 infection, the high prevalence of asymptomatic infection makes it difficult to interpret this finding. Vaccines against SARS-CoV-2 are

expected to be widely available in 2021. Given the impact of COVID-19 on patients with CKD, it is essential that their safety and efficacy be tested in this population. Once vaccines are proven safe and effective, patients with CKD and those caring for them must be given priority for vaccination.

Anxiety and emotional stress increased in dialysis patients during the COVID-19 pandemic. All dialysis patients, those infected, and those fearing infection may suffer from debilitating psychological distress. Tools to manage these symptoms include individual counseling and group sessions using electronic communication tools. Creative solutions, such as telehealth visits from social workers, dieticians, and for many needs, physicians, were used in outpatient dialysis centers. A waiver from the Centers for Medicare and Medicaid Services (CMS) during the public health emergency (PHE) permitted use of telehealth for monthly capitation visits. Telehealth may also be useful for patient and family education about home dialysis and transplant options and initial evaluations.

Because of the large number of patients suffering a critical illness as a result of acute respiratory distress syndrome (ARDS) associated with COVID-19 infections, attention turned to potential shortages of life-sustaining equipment like ventilators. While increasing the supply of available ventilators was the first priority, serious discussions were held about rationing them if the patient need exceeded the available supply. Policymakers considered guidelines for allocating ventilators; the State of Alabama Emergency Operations Plan stated that patients with end-stage organ failure, including anyone requiring dialysis, not receive ventilator support. The U.S. Department of Health and Human Services (HHS) Office of Civil Rights resolved a compliance review, and a revision removed this guideline. Recommendations are for a nuanced approach to rationing limited resources without arbitrarily excluding individuals.

Staff

Dedicated professionals care for patients with CKD every day; the COVID-19 pandemic changed the paradigm dramatically. Dialysis nurses and technicians are the major heroes, daily caring for in-center patients despite the risk to themselves and their families. Other staff, including physicians, social workers, dieticians, and administrators, were encouraged to have less direct patient contact and use telemedicine or telephonic contact in some instances. Strict use of hand hygiene and personal protective equipment (PPE), including gloves, masks, gowns, and eye-protective shields or goggles, proved effective in preventing viral transmission. Early pandemic reports from Europe of viral spread among patients and between staff and patients were largely eliminated after widespread measures were used to detect infection and isolate PUIs. As some staff became ill and had to stay away on sick leave, the higher workload on those remaining was particularly stressful with the restrictions imposed by screening and PPE procedures. These critical staff who remain often are faced with a very difficult decision:

to accept the risk of exposing themselves and their loved ones to a potentially fatal illness or to risk loss of salary and benefits and the psychological stress of turning away from critical needs if they decide to leave work. This dilemma places stress and anxiety on all staff and their families. Staff needs to be wary of subtle signs of COVID-19 infection while at the same time helping patients manage their physical and emotional symptoms. Staff had to learn to employ PPE and conduct their routine activities while attired with face shields, masks, gloves changed frequently, and isolation gowns.

At the same time, community-wide recognition of the valuable contributions of health care workers and enhanced relationships with colleagues and patients empowered those who worked through the pandemic. Many have shared that their self-value and confidence and pride blossomed during the pandemic, providing an opportunity to give to their community as never before. While some staff have elected early retirement, we believe that many young people may be inspired by staff heroism to choose health care professions.

Administrators

Dialysis facility administrators faced a crisis from the moment the first case of COVID-19 was diagnosed in a patient with CKD; spread mitigation had to be balanced with safety of patients and staff in the face of challenging circumstances, including national shortages of PPE. Schedules had to be retooled to allow physical distancing for patients awaiting treatment and staff during meal breaks. Community spread of COVID-19 led to staff absences for quarantine and illness, increasing the stress on the system.

Meeting social distancing requirements proved to be a substantial challenge for many administrators. While large dialysis organizations designated facilities to treat infected patients or PUIs, smaller organizations were rarely able to do so. This led to the designation of sections of a facility or shifts for patients with known or suspected infection. Using less densely crowded shifts, i.e., the last shift on Tuesday, Thursday, and Saturday allowed for the greatest separation. Some facilities were retooled to provide plexiglass shields outside the treatment area and to create greater space in other areas where patients might congregate, such as waiting areas.

At points during the COVID-19 crisis, concerns arose regarding the supply chain for PPE, dialyzers, and dialysis fluids. Fortunately, suppliers were able to keep up with demand, and shortages were addressed before crises arose. Dialyzer shortage never reached crisis proportions.

Protocols to mitigate the risk of infection spread in dialysis facilities included screening everyone entering the facility for signs of infection, known exposure, travel to areas with a high risk of community spread, fever, new cough, or shortness of breath. Everyone in the facility must wear a mask, and hand hygiene is essential. Because testing availability was limited and results were delayed, it was not practical

to test everyone on a regular basis. The CDC recommends use of standard disinfection protocols to clean the dialysis station between patients, but many facilities expanded disinfection protocols to include all touch surfaces in addition to those exposed to blood or body fluids during dialysis treatment.

Recognizing the impact of the PHE on dialysis facilities, CMS waived the requirements for data submission to the CrownWeb National ESRD Patient Registry and Quality Measure Reporting System and the ESRD Quality Incentive Program during the PHE. Facilities were permitted to opt out of the Spring 2020 In-Center Hemodialysis Consumer Assessment of Healthcare Providers and Systems because of the impact of the PHE on facilities. These waivers permitted administrators to focus attention on patient care and safety.

Home Dialysis

Compared to international rates of 30%–80%, only 10% of U.S. dialysis patients are treated by home dialysis modalities. During the COVID-19 pandemic, benefits of home dialysis increased, patients did not need treatment in dialysis facilities, and treatment prescriptions can be modified based on individual patient needs. Home dialysis patients, able to shelter at home, had lower infection rates than in-center patients.

Temporary regulatory waivers issued by CMS during the PHE provided opportunities to employ technology in unprecedented ways. CMS waived the requirement for a monthly in-person visit for home dialysis patients deemed stable by the treating nephrologist. Prior to the PHE, the first three monthly visits and one visit each quarter were required to be conducted in person; these requirements were waived during the PHE. Waivers were issued related to the requirement for initiation of telehealth. The Office of Civil Rights of the HHS notified health care providers that they would employ discretion and impose no penalties under the Health Insurance Portability and Accountability Act of 1996 as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 for the use of common electronic technologies for telehealth. These waivers greatly expanded the availability of telehealth to patients treated by home dialysis, emphasizing the benefits of home dialysis.

Coupled with the Advancing American Kidney Health Initiative announced by President Trump on July 10, 2019, the apparent benefits of home dialysis during the PHE further stimulated interest in home dialysis. Large dialysis organizations report a 10%–15% increase in the use of home modalities during the first 3 months of the pandemic. The anticipated unprecedented growth in home dialysis demands parallel growth in the workforce. Trainees must be afforded experience caring for patients managed by home dialysis; some suggest offering an additional 12 months of training dedicated to home dialysis if such programs can be funded. The COVID-19 pandemic demonstrated the inadequacy of the current nursing workforce: hospitals starting acute peritoneal dialysis (APD) programs struggled to find

nurses skilled in PD. The nationwide nursing shortage is especially acute in nephrology and more so for home dialysis therapies. Some suggest training patient care technicians to support nephrology nurses. Relatively few surgeons have experience successfully placing PD catheters; some interventional radiologists insert catheters, but payment is insufficient to induce more to learn the procedure.

Issues arose regarding home dialysis training during the PHE: patients typically spend 2–3 weeks undergoing face-to-face education about dialysis technique, monitoring of daily health, and troubleshooting before they can perform PD independently. Home HD training takes 4–8 weeks of face-to-face education. During the PHE, some programs developed virtual curricula and used telemedicine in place of hands-on training.

Some issues arose related to the delivery of supplies to home patients. Masks were in short supply, but facilities were able to reach into their own supplies to meet the demand. Some delivery services, reluctant to enter patient homes fearing exposure to infection, left supplies outside of patient homes. In some cases, dialysis facilities had to complete deliveries to permit patients to continue their dialysis treatments. These challenges were largely resolved with training and adequate PPE.

Some patients who initiate dialysis during a hospital admission are treated by PD; this number increases during the PHE. As patients recovered from their infections, they received education from hospital nurses. However, few rehabilitation facilities perform PD, and CMS regulations do not pay for PD training for patients with AKI. Thus, some patients treated in-hospital with PD for AKI were switched to HD before discharge to an outpatient dialysis facility.

The Impact of COVID-19 on Inpatient Dialysis Facilities

Acute Kidney Injury and Patient Volume

Early in the pandemic, reports from China showed that 40% of patients hospitalized with SARS-CoV-2 infection had hematuria or proteinuria, and 20% had a decline in kidney function. AKI was reported widely as the pandemic spread, affecting approximately 30% of infected patients who were hospitalized. RRT is required by about 6% of hospitalized COVID-19 patients. Among patients requiring care in intensive care units (ICUs), up to 68% require RRT. AKI and especially the need for RRT are significant predictors of mortality. Risk factors for the development of AKI include severe COVID disease, requirement for mechanical ventilation and vasopressors, increased age, male sex, black race, higher body mass index (BMI), and comorbidities including diabetes mellitus, hypertension, and cardiovascular disease. AKI is threefold more common in patients with preexisting kidney disease.

When the pandemic exploded in cities like New York, Chicago, Detroit, and New Orleans, dialysis resources were severely stressed. The volume of patients with AKI requiring

RRT and CKD requiring dialysis in the hospital required up to 5 times the usual supplies of dialysis fluid and other supplies and, in some cases, threatened to overwhelm facilities' capacity to provide dialysis. Many patients were managed in isolation settings, requiring treatments to be delivered by a dedicated nurse. Issues of risk exposure for patient care staff further complicated the administration of dialysis treatments. Dialysis personnel shortages severely stressed the system: the perfect storm of dialysis nurses who became infected or were exposed to infection required furlough from work, the increase in demand for dialysis care required working dialysis staff to increase their days and hours of work, created a personnel crisis solved by the heroic work of ICU, and dialysis nurses and additional personnel responding to a crisis call to come to hotspots and offer assistance.

While indications for initiation of RRT are no different for patients with COVID-19 with underlying AKI than for other patients with AKI, some used convective therapies and other extracorporeal therapies with a goal of removing proinflammatory cytokines from patients suffering from cytokine storm. There are inadequate data to confirm the benefits of these treatments.

Continuous Renal Replacement Therapy

Continuous RRT (CRRT) is the preferred treatment for hemodynamically unstable critically ill patients who require RRT. There are inadequate data to define an optimal CRRT prescription. Patients with COVID-19 infections, particularly those with cytokine storm, are frequently hypercoagulable. Numerous reports document higher rates of clotting of CRRT circuits in patients with COVID-19, resulting in increased nursing workload and increased replacement of CRRT filters, increasing use of potentially scarce resources. Regional citrate anticoagulation may be more efficacious in preventing clotting, but citrate may not be metabolized by patients with severe liver failure or shock. Heparin and argatroban are well-established alternative agents that improve filter life. Strategies to maintain equipment outside the patient room were employed to limit staff exposure to infection. However, this required long blood lines, causing possible cooling of circuit blood and higher return pressure leading to blood loss.

In summary, the unprecedented need for CRRT during the pandemic risked a shortage of supplies, including machines, filters, fluid, and appropriately trained staff. Care teams responded to these shortages by considering alternative renal replacement strategies, including slow, low-efficiency hemodialysis (SLED), prolonged intermittent RRT (PIRRT), and APD.

Addressing Supply Shortages

Lactate-Based Continuous Renal Replacement Therapy

In patients with AKI, metabolic acidosis, associated with poor prognosis, is treated by alkali infusion during CRRT.

Acetate or lactate can be used to provide alkali but must be metabolized to bicarbonate by the liver; data show comparable survival and acid-base control. Acetate solutions are recommended by Kidney Disease: Improving Global Outcomes (KDIGO) guidelines because of concerns regarding hyperlactatemia leading to cardiodepression, but some data show better cardiac function with lactate. During the COVID-19 pandemic, acetate-based CRRT fluids were in short supply; manufacturers offered lactate-based solutions to fill the void. Despite concerns, these fluids were used in some cases without apparent increased adverse events.

Homemade Continuous Renal Replacement Therapy Solutions

Commercially prepared sterile CRRT fluid requires careful monitoring of potassium and magnesium levels. CRRT fluid can be manufactured at the hospital level but is prone to human error, which can lead to significant electrolyte derangements. During the pandemic, when CRRT fluid shortages required creative ways to ensure adequate supplies to deliver RRT to all who needed it, several organizations manufactured their own CRRT solutions. Using standard volumetric single-pass dialysis machines with acid and bicarbonate concentrates and reverse osmosis product water, these hospitals produced fluid identical to standard dialysate used for intermittent HD. In consultation with the Food and Drug Administration (FDA), these organizations ran dialysate through a standard hemodialyzer to create ultrapure solution, which was collected into 6–8-L bags. Fluid was tested regularly to ensure it met Association for Advancement of Medical Instrumentation (AAMI) ultrapure standards for microbial counts (<0.1 CFU/mL) and endotoxin concentration (<0.03 UE/mL). These solutions were then used to provide CRRT. There were no apparent problems or complications, suggesting the safety, efficacy, and cost-effectiveness of this PHE-required process. It is important to note that FDA guidance requires that such noncommercial fluids be used as dialysate, not infusate, and be used within 4–24 hours of production. These noncommercial solutions should be used only locally and not be shipped elsewhere to avoid possible compositional deterioration.

Prolonged Intermittent Renal Replacement Therapy

Prolonged intermittent RRT (PIRRT) treatments last between 8 and 16 hours three to five times weekly. These regimens provide solute clearance and ultrafiltration intermediate between intermittent HD and CRRT. PIRRT is provided with the same equipment as CRRT. Randomized trials of patients with AKI have failed to show differences between CRRT, PIRRT, and intermittent HD in terms of mortality or recovery of kidney function. During the COVID-19 pandemic, machines capable of slow dialysis therapies were in short supply. PIRRT was used to control volume and electrolytes and to allow sharing of one machine

among two to three patients. Addressing the machine shortage required increased use of disposable dialysis supplies but allowed all patients to receive a minimum sufficient dose of dialysis.

Acute Peritoneal Dialysis

Prior to the advent of CRRT machines with blood pumps, APD was a common treatment for AKI. As intermittent HD and CRRT replaced APD treatment for AKI, fewer hospital nurses maintained competency with APD, and its popularity waned. Some data comparing APD to CRRT show better survival with APD with fewer infections, shorter ICU stay, and better renal recovery. During the COVID-19 pandemic, with shortages of CRRT machines, supplies, and trained nurses, alternative RRT modalities were required. Some turned to APD, in addition to PIRRT and standard intermittent HD, to fill the need. While many patients with AKI are good candidates for APD, others are not. Patients with abdominal scars, uncorrected hernias, high likelihood of prone ventilation, active GI issues, dual antiplatelet therapy, or BMI >30 have relative contraindications for APD. In addition, patients who are highly catabolic and those with high fluid removal requirements may be better served with hemo-based RRT. More than 25% of screened patients were deemed suitable candidates using these criteria. Double-cuff tunneled PD catheters were placed at the bedside, and APD was started within 24 hours of placement. Patients could be treated by automated or manual PD. Initial dwell volumes should start at 750 mL and increase in 500 mL increments every 48–72 hours until a goal of 2000 mL is reached. No catheter leaks or bleeding were detected, and adequate control of electrolytes and volume was achieved in all patients following this protocol.

In summary, the COVID-19 pandemic has shown that dialysis patients are particularly vulnerable to infection and have a high mortality rate. AKI among patients with and without preexisting kidney disease is surprisingly common, increasing the need for RRT. During surges in infection, care teams have demonstrated creativity in utilizing multiple RRT modalities and even by manufacturing their own dialysate solutions. Staff shortages induced by staff illness and increased demand have been major stressors on the ability to deliver RRT to all who need it, but heroic, sustained work by ICU and dialysis staff has saved thousands of lives. Mental health is stressed in patients and staff during a pandemic, and resources to help alleviate this is required. Home dialysis is particularly attractive in times of community virus transmission and social distancing. In-hospital PD has seen a resurgence for AKI and may also increase PD treatment for ESKD. Lessons learned from locations affected by COVID-19 early in the pandemic offer important lessons regarding best outpatient dialysis facility management, inpatient RRT preparedness, and best management of patients returning to the dialysis facility from the hospital after recovery from COVID-19.

Suggested Reading

- Ackerman M, Verleden SE, Kuehnel M, et al. Pulmonary vascular endothelialitis, thrombosis and angiogenesis in COVID-19. *N Engl J Med*. 2020;383(2):120–128.
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- Hirsch JS, Ng JH, Ross DW, et al. Acute kidney injury in patients hospitalized with COVID-19. *Kidney Int*. 2020;98(1):209–218.
- This paper describes AKI in patients with COVID-19 and provides information on the pathophysiology of the illness in these patients.*
- Izzedine H, Jhaveri KD. Acute kidney injury in patients with COVID-19: an update on the pathophysiology. *Nephrol Dial Transplant*. 2021;36(2):224–226.
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- This is a description from early in the COVID-19 pandemic of measures for mitigating risk of COVID-19 infection in dialysis facilities.*
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- This opinion piece addresses an approach to ensuring equitable distribution of scarce resources so that patients with CKD are not excluded simply by virtue of that diagnosis.*
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- This paper describes modalities of CRRT and their appropriate use for managing AKI in patients with critical illness.*
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