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COVID-19 and Kidney Disease

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Abstract

COVID-19 can cause acute kidney injury and may cause or exacerbate chronic kidney diseases, including glomerular diseases. SARS-CoV-2 infection of kidney cells has been reported, but it remains unclear if viral infection of kidney cells causes disease. The most important causes of kidney injury in patients with COVID-19 include impaired renal perfusion and immune dysregulation. Chronic kidney disease, especially kidney failure with kidney replacement therapy and kidney transplant, is associated with markedly increased COVID-19 mortality. Persons with severe kidney disease have been excluded from most clinical trials of COVID-19 therapies, so therapeutic approaches must be extrapolated from studies of patients without kidney disease. Some medications used to treat COVID-19 should be avoided or used at reduced dosages in patients with severe kidney disease and in kidney transplant recipients. Additional research is needed to determine the optimal strategies to prevent and treat COVID-19 in patients with kidney disease.

INTRODUCTION

Though respiratory failure is the most common cause of death in persons with COVID-19 (coronavirus disease 2019), acute kidney injury (AKI) is a frequent complication of severe COVID-19, and AKI and chronic kidney disease (CKD) are strongly associated with increased mortality in persons with COVID-19. Immune activation/dysregulation occurring in patients with COVID-19 and, rarely, after vaccination against SARS-CoV-2, can also cause kidney disease. COVID-19 disproportionately affects patients with CKD, especially those with kidney failure receiving kidney replacement therapy (KFRT) and kidney transplant recipients (KTRs). In this article, we review the mechanisms by which COVID-19 causes kidney disease, important kidney-related complications of COVID-19, and strategies to optimize the management of patients with kidney disease and COVID-19.

PATHOPHYSIOLOGY OF KIDNEY INJURY IN COVID-19

Viral Life Cycle

COVID-19 is caused by infection by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. Coronaviruses are enveloped, single-stranded RNA viruses with tropism for humans, other mammals, and nonmammalian species (1). SARS-CoV-2 primarily enters cells via binding of the viral spike (S) protein to angiotensin-converting enzyme 2 (ACE2). The S protein is then primed by cleavage by the Type 2 transmembrane serine protease (TMPRSS2) or by other proteases, which initiates formation of the fusion pore (2). Entry into host cells by SARS-CoV-2 activates innate immune responses, which can be effective in limiting viral replication and the severity of disease. However, excessive immune activation can promote cytokine storm and tissue injury, leading to tissue and organ dysfunction (3).

Does SARS-CoV-2 Infection of Kidney Cells Cause Kidney Disease?

Renal parenchymal cells, especially proximal tubular cells, express high levels of ACE2 (4). These cells also express TMPRSS2 and other proteases that may promote S protein cleavage and viral entry (2), suggesting that the kidney may be susceptible to SARS-CoV-2 infection. Several studies have reported detection of SARS-CoV-2 RNA and protein in the kidneys of patients with COVID-19 (5–7) and visualization of SARS-CoV-2 virions by electron microscopy (8, 9). However, these reports may have been confounded by false positives due to lack of specificity of assays, and normal intracellular organelles may have been misidentified as virions (10, 11). It remains controversial whether the kidney is a target of SARS-CoV-2 infection (12, 13).

Even if SARS-CoV-2 does infect kidney cells, it is unclear whether infection can cause clinically evident kidney injury. Also, since it is difficult to detect SARS-CoV-2 in the blood of patients with COVID-19, it is uncertain how kidney cells would be exposed to infectious virus. In a recent study of kidney specimens from 62 patients with COVID-19, reverse transcriptase polymerase chain reaction (RT-PCR) testing detected SARS-CoV-2 in all kidney specimens, and nucleocapsid protein was detected in 6 of 6 specimens (14). SARS-CoV-2 RNA was detected in kidney tubular cells and podocytes, and cells expressing viral RNA had increased expression of genes involved in injury, inflammation, and fibrosis (14). Though this study and others suggest a role for direct viral infection of kidney cells in the pathogenesis of kidney disease, there remains a lack of consensus regarding the prevalence of kidney infection in COVID-19 (12).

ACUTE KIDNEY INJURY

Clinical Presentation, Epidemiology, and Risk Factors

AKI is a common complication of COVID-19, particularly in hospitalized patients. In addition to acute reductions of estimated glomerular filtration rate (eGFR) and/or urine output, proteinuria and hematuria are common in patients with COVID-19 and AKI (15, 16). Studies from early in the pandemic when the rates of severe COVID-19 illness were high reported that the pooled incidence of AKI was 28.6% in studies from the United States and Europe but was much lower (5.5%) in studies from China (17, 18). Risk factors for AKI include older age, male sex, acute respiratory distress syndrome (ARDS) and/or requirement for mechanical ventilation, and comorbidities including CKD, hypertension, and diabetes mellitus (17). Higher serum levels of C-reactive protein, ferritin, and D-dimers are also associated with increased risk of COVID-19 AKI (19).

Pathogenesis of Acute Kidney Injury in Patients with COVID-19

Patients with severe COVID-19 often have multiple factors that can contribute to kidney injury, including impaired renal perfusion, exposure to nephrotoxic agents, increased systemic and local cytokine production, and endothelial injury (20, 21). Reduced renal perfusion may occur due to systemic hypotension caused by septic shock, volume depletion, or cardiac dysfunction. Acute lung injury increases systemic levels of cytokines and release of damage-associated molecular patterns (DAMPs) from injured cells. Cytokines and DAMPs can bind cytokine receptors and DAMP-sensing receptors in the kidneys, including Toll-like receptors, which then activate innate immune responses, amplifying kidney inflammation and injury (21). Major factors contributing to AKI are summarized in **Figure 1**.

In COVID-19 patients, microvascular occlusion and endothelial injury are important contributors to lung injury, and biomarkers of coagulation and endothelial injury are associated with increased kidney injury and with mortality (19, 22). There are also reports of acute renal thrombosis (23). However, histologic examination of kidney autopsy and biopsy specimens demonstrated that most patients with COVID-19 and kidney injury do not have microvascular thrombosis (13).

Treatment Considerations and Clinical Outcomes

In a large US cohort study, 20.6% of patients with COVID-19 requiring ICU admission required kidney replacement therapy (KRT) (19). The optimal modality for KRT is unknown, and the choice may be guided by provider expertise and availability of supplies. Hemodynamically unstable patients who require prone positioning may benefit from continuous KRT, whereas peritoneal dialysis may be preferable in patients with dialysis circuit clotting and/or contraindications to anticoagulation (24, 25). Fluid management can be complex in patients with COVID-19 and AKI, and clinicians should correct volume depletion while avoiding excessive volume resuscitation, which can worsen oxygenation in patients with ARDS (25, 26).

Though most patients with COVID-19 and AKI have eventual improvement in kidney function, AKI persists for >7 days in 35–40% of patients, and 30% of survivors with AKI requiring KRT remain dialysis dependent at the time of hospital discharge (16, 27). The severity of AKI is associated with risk of new and progressive CKD and with mortality (18, 25, 28, 29). Since a significant proportion of patients with COVID-19 and AKI subsequently develop CKD (30), kidney function should be monitored after AKI resolves to assess for the presence of CKD.

The severity of AKI and need for KRT in patients with COVID-19 decreased during the first year of the pandemic, even before vaccination was available, likely due to improvements in care for

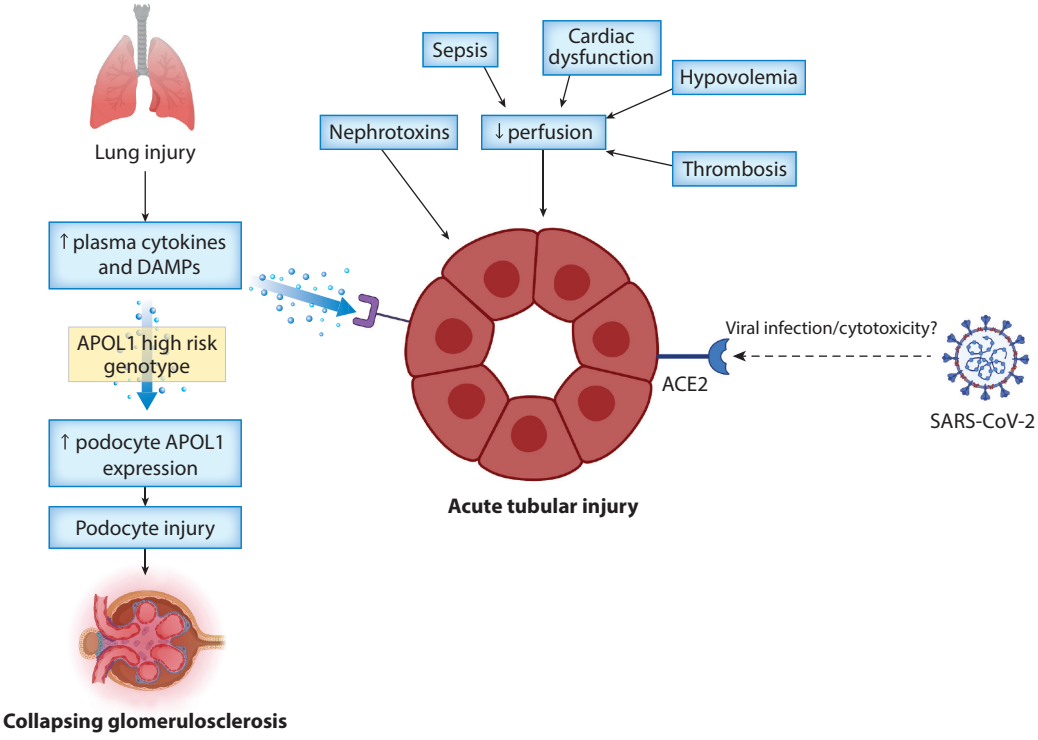

Figure 1

Schematic representation of the major factors contributing to acute kidney injury and collapsing glomerulosclerosis in patients with COVID-19. Abbreviation: DAMPs, damage-associated molecular patterns. Figure adapted from images created with BioRender.com.

patients with COVID-19 (31, 32). The incidence and severity of AKI in patients with COVID-19 will continue to evolve with increased prevalence of immunity due to vaccination and infections, emerging SARS-CoV-2 variants, and the development of new therapies.

COVID-19-ASSOCIATED GLOMERULAR DISEASES

Numerous glomerular diseases have been reported in persons with COVID-19 and/or after vaccination against SARS-CoV-2. Below, we discuss COVID-19-associated glomerular diseases manifesting primarily as proteinuria (predominant podocyte injury) and those presenting with proteinuria and hematuria of glomerular origin (glomerulonephritis).

Podocytopathies

Glomerular diseases characterized primarily by podocyte injury include focal segmental glomerulosclerosis, minimal change disease, and membranous nephropathy. Podocytopathies as reported in the context of COVID-19 disease and/or vaccination are summarized below.

Focal segmental glomerulosclerosis. Early in the pandemic, reports emerged describing a syndrome of severe proteinuria, often with AKI, in patients with COVID-19. Biopsy results revealed severe podocyte injury, often with collapse of glomerular capillary tufts [collapsing variant of focal segmental glomerulosclerosis (FSGS)] and acute tubular injury. This syndrome of acute podocytopathy occurring in the setting of COVID-19 has been termed COVID-19-associated

nephropathy (COVAN) (33–37). Another common histologic finding in COVAN is endothelial tubuloreticular inclusions, which are a hallmark of glomerular diseases associated with high systemic interferon levels, including systemic lupus erythematosus (SLE) and HIV-associated nephropathy (HIVAN). Most patients with biopsy-proven COVAN are Black, and most who have undergone genotyping have been found to have high-risk *APOL1* genotypes (34, 35, 37–39). *APOL1* high-risk genotypes are predominantly found in persons with African ancestry and are associated with markedly increased risk of collapsing glomerulopathy occurring after interferon treatment and in SLE and HIVAN, diseases associated with high systemic interferon levels (40). Since interferons increase *APOL1* expression, COVID-19 may precipitate COVAN in genetically susceptible individuals by increasing expression of toxic *APOL1* variants (**Figure 1**).

Kidney function eventually improves in most patients with COVAN, even those who are dialysis dependent at the time of diagnosis (41). However, a significant proportion progress to kidney failure requiring replacement therapy (KFRT). Though some clinicians have treated patients with COVAN with steroids, the lack of controlled studies prevents evidence-based treatment recommendations.

Rare cases of COVAN have also been reported after vaccination against SARS-CoV-2 (38, 42). Since vaccination can increase systemic interferons, it is likely that the pathogenesis of COVAN occurring after vaccination is similar to COVAN in persons with COVID-19. Though there have also been case reports of noncollapsing variants of FSGS occurring in patients with COVID-19 or after vaccination against SARS-CoV-2 (43–45), it remains unclear whether there is a causal relationship between COVID-19 or vaccination and noncollapsing variants of FSGS.

Minimal change disease. Minimal change disease (MCD) has also been reported in patients with COVID-19 (37, 46). The typical clinical presentation of MCD includes rapid onset of nephrotic range (>3.5 g/day) proteinuria, and kidney biopsy reveals normal glomeruli under light microscopy but severe podocyte injury by electron microscopy. It is unclear how COVID-19 may cause MCD, but since immune dysregulation is an important contributor to MCD, it is likely that immunologic factors are important. MCD is the most common glomerular lesion associated with SARS-CoV-2 vaccination in some series (38, 47); however, it remains unclear whether vaccination was causal in most cases.

Most patients who develop MCD during COVID-19 or after vaccination have reduced proteinuria after treatment with glucocorticoids (38, 47). However, since these studies lacked controls, it remains unclear whether treatment caused resolution of proteinuria or if it would have resolved spontaneously.

Membranous nephropathy. Membranous nephropathy (MN) is a common cause of primary nephrotic syndrome in adults and has also been reported to occur in some patients with COVID-19 (37, 48, 49). MN is caused by immunoglobulin G (IgG) deposition in the glomerular basement membrane, resulting in complement activation, which leads to podocyte injury. Though approximately 70% of cases of MN in the general population are caused by autoantibodies against the M-type phospholipase A2 receptor (50), these antibodies are variably present in patients with COVID-19 and MN (48, 49). De novo MN and relapsed MN have been reported after vaccination against SARS-CoV-2 (38, 45, 47, 51). The optimal approach to therapy for patients with MN during COVID-19 or after vaccination against SARS-CoV-2 is unknown.

Glomerulonephritis

Glomerulonephritis presents clinically as increased proteinuria, glomerular hematuria, and is often accompanied by reduced glomerular filtration, as reflected by increased serum creatinine.

Kidney biopsy reveals glomerular inflammation and injury (52). Below, we summarize the most common types of glomerulonephritis occurring during COVID-19 and/or after vaccination against SARS-CoV-2.

IgA nephropathy. Immunoglobin A nephropathy (IgAN) is diagnosed by the detection of predominantly mesangial IgA deposits in kidney biopsies. IgAN is usually a chronic and slowly progressive glomerulonephritis, but it can also manifest as a rapidly progressive GN (53). The majority of cases of IgAN reported related to COVID-19 have occurred after vaccination against SARS-CoV-2 and can also present as de novo or as relapsing disease (45, 47). The optimal treatment for IgAN occurring during COVID-19 or after vaccination is unclear, and aggressive immunosuppression has been reserved for rare cases with crescentic glomerulonephritis and AKI (47).

Systemic lupus erythematosus. Kidney disease is a common complication of SLE, and SLE can cause numerous histologic patterns of injury (54). There have been reports of exacerbations of lupus nephritis in patients with COVID-19 and several case reports of lupus nephritis (de novo or flare) after vaccination against SARS-CoV-2 (37, 38, 51, 55–57). The severity of CKD is strongly associated with clinical outcomes in patients with SLE and COVID-19 (58).

Other Glomerulopathies Related to COVID-19

De novo or relapsing ANCA (antineutrophil cytoplasmic antibody)–associated vasculitis (AAV) with rapidly progressive glomerulonephritis has been reported both during and after COVID-19 (38, 59–61). There have also been numerous case reports of AAV with glomerulonephritis occurring after vaccination against SARS-CoV-2 (38, 47, 51, 62). Patients with AAV after vaccination may have antibodies against myeloperoxidase, proteinase-3, or both antigens.

Several other forms of glomerular injury have been reported in patients with COVID-19 and/or after vaccination against SARS-CoV-2, including antiglomerular basement membrane disease (63–66) and thrombotic microangiopathy (36, 47, 67).

COVID-19 IN PATIENTS WITH KIDNEY FAILURE REQUIRING REPLACEMENT THERAPY

Epidemiology and Risk Factors

Patients with KFRT are at increased risk of acquiring COVID-19 (68). In an analysis of studies published by June 2020, the overall pooled prevalence for COVID-19 in KFRT patients from 12 countries was 22-fold higher than the average global prevalence (68). This is likely explained in part by the fact that patients receiving in-center dialysis are unable to self-isolate and must travel three or more times or more per week, often using public or group transportation to and from dialysis centers. Conversely, patients receiving KRT at home have a lower of incidence of COVID-19 than those receiving in-center KRT (69). Other risk factors for COVID-19 in patients with KFRT include living in a congregational residence, Black race, Hispanic ethnicity, lower income, and residing in more densely populated neighborhoods (70, 71). KFRT patients are also at risk of infection due to impaired innate and adaptive immunity (72). Since up to 50% of patients with KFRT develop asymptomatic infection and only 47% present with fever, compared to 90% in the general population, a high degree of clinical suspicion for COVID-19 is needed (73).

Early in the pandemic, approximately 50% of KFRT patients diagnosed with COVID-19 required hospitalization, and mortality rates were approximately 20–30% (74). Patients receiving

in-center hemodialysis were 3–4 times more likely to be hospitalized with COVID-19 than patients receiving peritoneal dialysis (75). Factors associated with increased risk of death in patients with KFRT are similar to those in the general population, but these risk factors are enriched in the KFRT population (73, 76). Though it is likely that clinical outcomes in persons with KFRT and COVID-19 have improved significantly since the widespread availability of vaccination and other advances in the care of patients with COVID-19, recent data on outcomes in persons with KFRT and COVID-19 are lacking.

Preventing COVID-19 in Patients with KFRT

Since patients receiving in-center KRT are at particularly high risk of COVID-19, infection control measures have been implemented at dialysis units to reduce the risk of exposure and spread among patients and staff. These measures include screening for symptoms and/or exposure to COVID-19, strict use of personal protective equipment, adequate spacing between patients, isolation of those with symptoms or recent exposure, and disinfection of potentially contaminated surfaces (77). Increased use of home modalities, telehealth, eliminating group travel and prolonged contact, may prevent the spread of the virus to other patients and staff.

Patients with KFRT have reduced innate and adaptive immunity, and most clinical trials testing the efficacy of vaccines against SARS-CoV-2 excluded patients with severe kidney disease. However, a systematic review reported that 41% of patients with KFRT developed antibodies after the first vaccine dose and 89% after the second dose (overall immunogenicity rate of 86%), which was lower than controls without kidney disease (78). Since evidence indicating the optimal number and timing of vaccine doses is rapidly evolving, clinicians should consult current guidelines for patients with KFRT. Vaccine hesitancy is a significant problem in persons with KFRT, especially among younger patients, women, and Black, Native American, and Pacific Islander patients, and the most stated reason for vaccine hesitancy is safety concerns (79). Vaccine education is needed to support this at-risk population.

COVID-19 IN KIDNEY TRANSPLANT RECIPIENTS

The COVID-19 pandemic has significantly impacted the community of KTRs, kidney donors, and wait-listed patients. Initial studies of KTRs with symptomatic COVID-19 reported mortality of approximately 30% (80, 81). More recent studies have reported much lower mortality (82) in KTRs but still significantly higher than in the general population. Risk factors for death in KTRs with COVID-19 are similar to those in the general population. AKI is a common complication in hospitalized patients and is strongly associated with mortality (81, 83). Early in the pandemic, up to 89% of KTRs required hospital admission, and ICU admission was associated with a twofold increase in mortality (84).

Nearly half of KTRs have minimal or no symptoms during SARS-CoV-2 infection, with evidence of prior infection detectable only by serologic testing (85). Despite impaired immune responses, most KTRs with infection detected by RT-PCR subsequently develop anti-SARS-CoV-2 antibodies (86). There is a delay in the development of anti-S IgG but no difference in development of antinucleocapsid IgG compared to normal controls (87).

Few studies have reported clinical outcomes in vaccinated KTRs with COVID-19. In one study of 55 KTRs who developed COVID-19 after receiving two doses of mRNA vaccine, 27% required hospitalization, 6 required ICU admission, and 3 died. Of the 25 with available serologic data, 24 had no detectable anti-S antibodies and 1 had weak antibody titers, strongly suggesting that poor antibody responses to vaccination may increase risk of severe COVID-19 in KTRs (88).

MANAGEMENT OF IMMUNOSUPPRESSION

Though protocols at individual transplant centers vary, changes to immunosuppressive medications largely depend upon the severity of COVID-19. Many authors recommend reducing antimetabolite dose in outpatient KTRs with mild disease and withdrawal in inpatients with moderate or severe disease. Doses of calcineurin inhibitor (CNI) and/or mechanistic target of rapamycin inhibitor (mTORi) are also often reduced in hospitalized patients with moderate–severe disease and discontinued in severely ill KTRs requiring ICU care (89–91). Clinicians must be vigilant for severe drug interactions between immunosuppressants, especially CNI, and many medications including some SARS-CoV-2 medications (reviewed below). Glucocorticoids improve clinical outcomes in patients with severe COVID-19, and most hospitalized patients receive dexamethasone as per guidelines for the general population (91, 92). Most KTRs can then be returned to their baseline glucocorticoid dose if/when appropriate.

Vaccination in Kidney Transplant Recipients

KTRs have significantly reduced antibody response to vaccination against SARS-CoV-2 (91). Only 30–54% of KTRs develop detectable antibodies after two doses of mRNA vaccine, and approximately 70% develop antibodies after a third dose. Use of antimetabolites and belatacept is associated with reduced immune response to SARS-CoV-2 vaccination (91). Guidelines therefore state that KTRs should be vaccinated with at least three doses of an mRNA vaccine at least 2 weeks prior to transplantation (92). The US Centers for Disease Control and Prevention (CDC) currently recommends immunocompromised persons receive a fourth vaccine dose least 3 months after the previous dose (**https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html**).

Though some centers temporarily ceased performing kidney transplants during periods of extremely high COVID-19 prevalence, reduced rates of community transmission, widespread availability of vaccination, and improved treatment protocols have allowed centers to safely resume kidney transplantation (93). However, additional research is needed to define optimal approaches to prevent and treat COVID-19 in KTRs.

COVID-19 Treatment in Patients with Kidney Disease

As noted above, patients with severe kidney disease were excluded from nearly all COVID-19 treatment trials, severely limiting the availability of data to support evidence-based treatment recommendations (94). Decisions regarding treatment with antiviral and immunomodulatory medications in KFRT patients and KTRs with COVID-19 depend on availability of medications; duration and degree of symptoms; and risk factors including age, comorbidities, and vaccine status. CKD patients and KTRs are defined by the CDC as persons with high-risk medical conditions and are therefore prioritized for access to COVID-19 therapeutics. Since treatment guidelines are rapidly evolving as new treatments and evidence become available, clinicians are encouraged to consult updated guidelines, including those maintained by the US National Institutes of Health (NIH) (92). Below, we highlight important information for clinicians considering the use of specific therapies for COVID-19 in KTRs and in patients with severely reduced kidney function due to AKI or CKD.

Several antiviral medications, including molnupiravir, ritonavir-boosted nirmatrelvir, and remdesivir, have been approved for use in patients with COVID-19. At this time, NIH/CDC guidelines only endorse use of molnupiravir and ritonavir-boosted nirmatrelvir in some outpatients with COVID-19 (92). Molnupiravir is a cytidine analog that inhibits viral RNA replication,

and since it is not cleared by the kidneys, no dose adjustment is necessary in patients with kidney disease (92).

Nirmatrelvir is an inhibitor of the SARS-CoV-2 M^{PRO} protease. Since nirmatrelvir is metabolized by the liver via cytochrome P450 (CYP) 3A4, it is coformulated with ritonavir, a potent CYP3A4 inhibitor, to prolong nirmatrelvir half-life. Nirmatrelvir/ritonavir dosage should be reduced by 50% in adults with eGFR 30–60 mL/min/1.73 m^2 and is not recommended for use in patients with eGFR < 30 mL/min/1.73 m^2 (92). Since CNI and mTORi are metabolized by CYP3A4, nirmatrelvir/ritonavir should be avoided in most KTRs.

Remdesivir, an adenosine analog inhibitor of the viral RNA polymerase, is currently a treatment option for selected outpatients and inpatients with COVID-19 (92). Remdesivir is administered as an intravenous infusion, and though remdesivir is not cleared by the kidneys, the vehicle formulated with it [sulfobutylether-B-cyclodextrin (SBECD)] is eliminated by the kidneys. Since high levels of SBECD can cause liver toxicity, it is recommended that clinicians use reconstituted lyophilized remdesivir (contains less SBECD), rather than the solution formulation of remdesivir, in patients with eGFR < 30 mL/min/1.73 m^2 (92). Though the US Food and Drug Administration (FDA) does not currently recommend remdesivir in patients with eGFR < 30 mL/min/1.73 m^2, the CDC recommends that clinicians consider it in patients in whom the benefits may outweigh risks (92). Recent case series have reported use of remdesivir in patients with severe kidney disease, including those with KFRT, suggesting it can be used in these patients without causing liver toxicity, but the risks and benefits of remdesivir in this population require further study (95, 96).

Several anti-S monoclonal antibody formulations have been approved for use by the FDA and other regulatory agencies around the world. Since the efficacy of these antibodies can be strongly affected by mutations in S, recommendations regarding the use of specific monoclonal antibodies for the prevention and treatment of COVID-19 change rapidly as new SARS-CoV-2 variants emerge (92). We therefore do not discuss indications for specific monoclonal antibodies, and clinicians are encouraged to review the most current guidelines in making treatment decisions. Since antibodies are not cleared by the kidneys, kidney disease is not a contraindication to monoclonal antibody treatment, and dose adjustment is not required for patients with kidney failure. It is no longer recommended to delay SARS-CoV-2 vaccination in patients who have been treated with monoclonal antibodies.

Immunomodulatory medications including tocilizumab (a monoclonal antibody inhibitor of the interleukin-6 receptor) and baricitinib (an orally available JAK1/JAK2 inhibitor) are recommended as treatment options in selected patients with COVID-19 (92). Since tocilizumab is a monoclonal antibody, no dose adjustment is necessary in patients with kidney disease. However, baricitinib is primarily cleared by the kidneys. Dose adjustment is necessary for patients with eGFR < 60 mL/min/1.73 m^2, and baricitinib is not recommended in those with eGFR < 15 mL/min/1.73 m^2 (92).

CONCLUSION

COVID-19 can cause many forms of kidney injury, which occurs primarily due to systemic immune activation and/or ischemic injury. Though kidney cells express proteins that may allow infection by SARS-CoV-2, it remains controversial how often kidney cells are infected in patients with COVID-19 and whether infection of kidney cells contributes to kidney disease. COVID-19 has had a disproportionate impact upon persons with CKD and KTRs, who are at markedly increased risk of morbidity and mortality due to COVID-19. Further research is needed to determine the optimal approach to prevent COVID-19 in persons with kidney disease and to improve clinical outcomes in persons with COVID-19 and kidney disease.

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