Review Article

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Risks and Benefits of Kidney Transplantation during the COVID-19 Pandemic: Transplant or Not Transplant?

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Abstract

COVID-19 has significantly affected the transplant community, by leading to decreased transplant activity and increased waiting list time. As expected, COVID-19 causes substantial mortality in both ESKD and kidney transplant populations. This is due to underlying CKD and a high prevalence of comorbid conditions, such as diabetes mellitus, hypertension, and cardiovascular disease in this group. Transplant programs have faced the difficult decision of weighing the risks and benefits of transplantation during the pandemic. On one hand, there is a risk of COVID-19 exposure leading to infection while patients are on maximum immunosuppression. Alternatively, there are risks of delaying transplantation, which will increase waitlist times and may lead to waitlist-associated morbidity and mortality. Cautious and thoughtful selection of both the recipient's and donor's post-transplant management has been required during the pandemic, to mitigate the risk of morbidity and mortality associated with COVID-19. In this review article, we aimed to discuss previous publications related to clinical outcomes of COVID-19 disease in kidney transplant recipients, patients with ESKD on dialysis, or on the transplant waiting list, and the precautions transplant centers should take in decision making for recipient and donor selection and immunosuppressive management during the pandemic. Nevertheless, transplantation in this milieu does seem to be the correct decision, with careful patient and donor selection and safeguard protocols for infection prevention. Each center should conduct risk assessment on the basis of the patient's age and medical comorbidities, waitlist time, degree of sensitization, cold ischemia time, status of vaccination, and severity of pandemic in their region.

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Introduction

Kidney transplantation during the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causing the coronavirus disease 2019 (COVID-19) pandemic was wrought with significant challenges worldwide. Although this crisis resulted in an unbelievable loss of life in the general community, transplant recipients were particularly susceptible (1). Transplantation is a resource-intensive endeavor, and it rapidly became clear that continuation in the face of this pandemic was fraught with unknowns because it pertained to the ability to provide unmitigated clinical care. A survey of 204 centers from 16 countries in May and June 2020 documented that 75% of responding centers held living kidney transplantation (from 67% of North American centers to 91% of European centers) (2). There was a 51% drop in transplant activity in the United States and 91% in France, which was largely driven by reductions in kidney transplantation (3). The significant decrease in kidney transplant activity during the first peak of the pandemic was due to multiple factors, including scarce hospital resources, limited testing capacity, unclear test result sensitivity, and reported poor outcomes in kidney transplant recipients with COVID-19.

Expectedly, COVID-19 causes substantial mortality in both dialysis and kidney transplant populations, due to their underlying CKD and a high prevalence of comorbid conditions such as diabetes mellitus, hypertension, and cardiovascular disease. Transplant programs have faced the difficult decision of weighing the risks and benefits of transplantation during the pandemic. Potent induction agents and higher immunosuppressive doses used early in the post-transplantation period may put patients at risk for developing COVID-19 infection. Contrastingly, the risks of delaying transplantation and increasing wait time and waitlist-associated morbidity and mortality are not without consideration. Therefore, careful and thorough selection of the recipients, donors and post-transplant management is required during the pandemic, so as not to increase the risk of morbidity and mortality associated with COVID-19. In this review article, we aimed to discuss previous publications related to clinical outcomes of COVID-19 disease in kidney transplant recipients, patients with ESKD on dialysis, or on the waiting list for transplantation. We will also examine the predictors of poor outcomes in those patients. Lastly, we aimed to discuss what precautions transplant centers should take in decision making for recipient and donor selection and immunosuppressive management during the pandemic.

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Predictors of Mortality in Kidney Transplant Recipients with COVID-19

A summary of 10 previous publications reporting mortality rates in kidney transplant recipients with COVID-19 infection are described in Table 1 (4–13). We included only publications reporting more than 100 patients because risk estimates with small sample sizes are known to suffer from inaccuracy due to random variation. Mortality rates varied between 17.9% and 32% (mean 22%) in those 2880 patients. However, most of those patients were hospitalized and thus represent patients who are more severely ill, and may not be generalizable to the broader kidney transplant recipient population. One of the initial largest single center studies from the United States was from our center, Montefiore Medical Center in New York (4,14,15). Overall mortality was 21% in 229 kidney transplant recipients and it was higher (38%) in patients who required hospitalization. However, 42% of our patients were diagnosed by SARS-CoV-2 IgG antibodies alone without significant clinical symptoms. Kates *et al*. analyzed the outcomes of 318 kidney transplant recipients from >50 transplant centers and reported that 78% of the cohort was hospitalized for COVID-19 (13). Among those hospitalized, 21% had died by 28 days after diagnosis. Similar in Europe, the European Renal Association COVID-19 Database collaboration demonstrated a hospitalization rate of 89% and mortality rate of 21% (9).

Kidney transplant recipients from the French Registry of Solid Organ Transplant were compared with a single-center cohort of patients who were nontransplant. The 30-day mortality was significantly higher in transplant recipients (18% vs 11%, respectively, $P=0.04$) (5). In a multivariate analysis for predictors of mortality in 10,926 COVID-19–related deaths in England, solid organ transplantation has the highest hazard ratio of 3.53 (95% CI, 2.77 to 4.49), and it was 2.52 (95% CI, 2.33 to 2.72) in those with GFR <30 mL/min (16).

Factors associated with higher mortality in kidney transplant recipients are summarized in Table 1. The most common risk factor, reported in almost all of the studies, was older age. Poor outcomes in the elderly were also reported in the general population. From March 1 to June 6, 2020, although the overall mortality was 1% in 205,639 New York City residents with COVID-19, it was 5% for those aged 65–74 years and 14% for those aged ≥75 years (17). The elderly, in general, are usually vulnerable to infection, mainly explained by immunosenescence. This combination of decreased production of naive T and B cells and dysfunction of innate immune cells, coupled with chronic immunosuppressive treatment, may worsen outcomes in elderly transplant recipients if they acquire COVID-19. The presence of chronic heart and lung disease, and obesity were also associated with mortality.

Predictors of Mortality in Patients with ESKD with COVID-19

According to the 2018 United States Renal Data System report, 88% of patients with ESKD receive in-center hemodialysis treatment. Undergoing this life-sustaining treatment in an enclosed facility together with other patients limits the ability of these patients to self-isolate, which in turn places them at a higher risk of contracting COVID-19. Compared with the general population, patients with ESKD are not only more susceptible to infection, but also have a higher risk of having moderate to severe disease requiring hospitalization, thereby leading to increased mortality. We have summarized previous studies reporting mortality rate and its predictors reporting in more than 100 patients with ESKD (Table 2) (9,12,15,18–29). The mortality rate was high between 20% and 32% (mean 25%) in a total of 8370 patients. Hospitalization rates ranged from 57% to 100% and intensive care unit admission rates were around 10%. The European Renal Association-European Dialysis and Transplant Association registry from seven countries involving 3285 patients receiving dialysis and 1013 kidney transplant recipients showed the mortality risk was 1.28 (1.02–1.60) times higher in transplant recipients compared with matched patients on dialysis (8). COVID-19 mortality was 44% in kidney transplant recipients >75 years of age compared with 31% in patients on dialysis. As presented in Table 2, many risk factors have been associated with increased COVID-19–related mortality in patients with ESKD, with older age being the most common. Other predictors of mortality included medical comorbidities,

Table 1. Mortality and predictors of mortality in kidney transplant recipients with coronavirus disease 2019

Study	Total Number of Patients	Overall Mortality, %	Predictors of Mortality
Ravanan *et al.* (11)	489	26	n/a
Marinaki *et al.* (10)	420	22	n/a
Kates *et al.* (13)	318	18	Older age, congestive heart failure, obesity, chronic lung disease, pneumonia on imaging, and lymphopenia (<0.5 thousand/ml)
Caillard *et al.* (6)	306	18	Age >60 years, cardiovascular disease, dyspnea, fever, and creatinine level >115 μmol/L
Hilbrands *et al.* (9)	305	21	Older age
Sánchez-Álvarez *et al.* (12)	286	19	Older age, pneumonia on imaging
Caillard *et al.* (5)	279	23	Age >60 years, cardiovascular disease, dyspnea
Azzi *et al.* (4)	229	21	Older age, deceased donor transplant recipients, lack of receipt of influenza vaccination previous year
Cravedi *et al.* (7)	144	32	Older age, respiratory rate >20 per min, low eGFR, and elevated serum IL-6 levels
Favá *et al.* (8)	104	27	Older age, acute respiratory distress syndrome, elevated lactic dehydrogenase levels on admission

Table 2. Mortality and predictors of mortality in patients with ESKD and coronavirus disease 2019

Study	Total Number of Patients	Overall Mortality, %	Predictors of Mortality
Jager *et al.* (20)	3285	21	Older age, male sex
Quintaliani *et al.* (25)	1368	33	n/a
Hilbrands *et al.* (9)	768	25	Frailty score, older age, obesity, dyspnea, high body temperature, high heart rate and elevated liver enzymes at presentation
Sánchez-Álvarez *et al.* (12)	582	25	Age, pneumonia on imaging
Ng *et al.* (24)	419	32	Older age, mechanical ventilation, vasoactive medication use, lymphopenia, elevated blood urea nitrogen and ferritin
Sosa *et al.* (27)	325	28	n/a
Weiss *et al.* (28)	306	28	Age over 65 years, longer dialysis vintage
Corbett *et al.* (18)	300	20	Older age, inactive on kidney transplant waitlist
De Meester *et al.* (19)	234	30	Male sex, diabetic nephropathy as cause of kidney disease and diabetes mellitus
Xiong *et al.* (29)	154	31	Older age, elevated D-dimer
Sim *et al.* (26)	133	23	Older age, ischemic heart disease, heart failure, diabetes mellitus
Manganaro *et al.* (23)	130	25	Male sex, cardiovascular disease
Lano *et al.* (22)	129	28	Need for oxygen therapy at presentation, lymphopenia
Keller *et al.* (21)	123	24	Fever, C-reactive protein on admission
Fisher *et al.* (15)	114	28	Elevated respiratory rate and lower oxygen saturation on admission, initial elevated procalcitonin, ferritin, lactic dehydrogenase levels and lower lymphocytes count

such as diabetes and heart disease, and longer dialysis vintage.

Comparing Patients who Are Waitlisted to Transplant Recipients with COVID-19

Outcomes for patients on the transplant waiting list with COVID-19 infection have not been as widely reported. Studying this patient population is particularly important as the waiting list frequently excludes patients with ESKD with significant frailty or severe comorbid conditions. As a result, one would expect this patient population to have better outcomes as compared with all patients on dialysis. Such studies are of interest because they would help make better informed decisions regarding whether to proceed with transplantation during the pandemic versus having the patient accrue time on the waiting list. We summarized the studies comparing patients who had received a transplant to patients who were waitlisted and had COVID-19 in Table 3 (9,11,30–35). The incidence of COVID-19 infection was much lower in the transplant recipients than in patients who were waitlisted, but this could be secondary to testing bias as waitlisted patients could be tested more often. Another explanation is the increased exposure of waitlisted patients to virus while receiving in-center hemodialysis. Most studies, which were conducted in Europe, identified a much higher COVID-19–related mortality in transplant recipients versus waitlisted patients, ranging from 20% to 37% versus 5% to 16%, respectively (9,11,31–35). The largest series came from France for the period March 1, through June 1, 2020 that identified 275 deaths among the 42,812 kidney transplant recipients and 144 deaths among the 16,210 candidates (35). This represents an excess of deaths for both populations, compared with the same period the previous 2 years, which accounted for 44% and 42% of the deaths in recipients and candidates, respectively. Although the excess risk of death due to COVID-19 was similar for recipients and candidates in high viral risk areas, it was four-fold higher for candidates in the low viral risk areas. The authors concluded that transplantation should be suspended in high viral risk areas but maintained outside those areas, both to reduce the excess of deaths of candidates and avoid wasting precious resources. The cumulative incidence rate of COVID-19 among solid organ waitlist candidates in the

Table 3. Coronavirus disease 2019 incidence and mortality in patients on the waiting list versus transplant recipients

Study	Total Number of waitlisted Patients who Are Coronavirus Disease 2019+	Incidence of Coronavirus Disease 2019 in Waitlisted Patients, %	Overall Mortality in Waitlisted Patients, %	Total Number of Coronavirus Disease 2019+ Transplant Recipients	Incidence of Coronavirus Disease 2019 in Transplant Recipients, %	Overall Mortality in Transplant Recipients, %
Thaunat *et al.* (35)	478	3	13	606	1	20
Ravanan *et al.* (11)	197	4	10	470	1	26
Hilbrands *et al.* (9)	148	n/a	5	23	n/a	30
Craig-Schapiro *et al.* (32)	56	n/a	34	80	n/a	16
Clarke *et al.* (31)	53	18	11	16	7	38
Mamode *et al.* (33)	52	4	27	121	n/a	30
Mohamed *et al.* (34)	32	10	16	28	2	32

United Kingdom was 4% through May 20, 2020, with an all-cause mortality rate of 10% among those who developed COVID-19 (11). In another center in the United Kingdom, patients who were waitlisted had a lower mortality rate (11%) compared with transplant patients (37%) with a hazard ratio (HR) of 3.36 (95% confidence interval [95% CI], 1.19 to 9.50) (31). In contrast, a study in London by Mamode *et al*. did not identify a mortality difference between both groups (27% in waitlisted patients vs 30% in transplant recipients) (33). In contrast, Craig-Schapiro *et al.* in New York detected a much higher mortality in 56 waitlisted patients at 34% versus 16% in 80 renal transplant recipients (32). In the United States, kidney waiting list mortality was higher after the national emergency declaration on March 13, 2020 (adjusted HR [aHR], 1.37; 95% CI, 1.23 to 1.52). The hazard of waitlist mortality was not significantly different for liver, pancreas, lung, and heart (36). Mortality risk was highest in New York City donation service area (aHR, 2.52) and in Black patients (aHR, 1.41 [95% CI, 1.07 to 1.86]) compared with White patients.

Differences in waitlist eligibility among transplant centers may explain the different outcomes. Some centers may accept higher-risk candidates with a higher number of comorbidities, which would increase the risk of mortality in their patients who are waitlisted. More studies comparing outcomes between these two groups are needed at this time to better inform patients of their risk of proceeding with transplant versus waiting on the list during the pandemic. Massie *et al*. built a simulation model of waitlist and post-transplant mortality in the context of COVID-19, which showed that transplantation provided survival benefit in modeled scenarios, except when the patient fatality rate of COVID-19 in transplant recipients greatly exceeded that of patients who are waitlisted (37).

Donor Assessment during Pandemics

American Society of Transplant Surgery COVID-19 Strike Force Guidance was tailored to aggressively test all donors and recipients, regardless of symptomatology (38). To date there have been innumerable protocols to assess donors for coronavirus that include donor history, RT-PCR, presence of lymphopenia, and/or axial chest imaging. Given ongoing widespread community transmission, viral testing of at least one sample from the respiratory tract by RT-PCR for SARS-CoV-2 should be performed within 3 days of procurement (Table 4). A second viral test should be performed 24 hours after the initial test, and within 24–48 hours of procurement, when feasible. Chest computed tomography findings of ground glass opacities should be assessed in the context of COVID-19 disease due to 10%–20% chance of false negative RT-PCR result. Although the risk of SARS-CoV-2 transmission through deceased donor, nonpulmonary, organs is very low (39), individuals with active RT-PCR positivity for SARS-CoV-2 should not be accepted as kidney donors. For donors previously known to have had COVID-19, it is suggested the initial COVID-19 infection occurred between 21 and 90 days before donor evaluation, irrespective of repeat nucleic acid amplification technique test results, and ≥30 days should have passed after symptom resolution.

All living donors should have viral testing of at least one sample from the respiratory tract by RT-PCR for SARS-CoV-2 within 3 days of donation. For living donors who were previously known to have had COVID-19, at least 30 days should have passed after all symptoms were resolved and should have negative chest x-ray. Living donors ideally should be vaccinated for SARS-CoV-2 before transplantation.

During the pandemic, uneasiness about surging coronavirus rates in the hemodialysis centers ushered in a desire to avoid delayed graft function (DGF) if possible. Post-transplant oliguria would relegate the patient toward an extended in-house hospital stay to avoid coronavirus exposure in a dialysis unit. As such, donor characteristics tended to favor younger ages and a lower kidney donor profile index. Moreover, consideration was given toward ensuring lower cold ischemia times to minimize DGF. This proved to be particularly challenging, because aviation disruption led to severe logistic challenges for moving organs across the country. Lastly donors after cardiac death were less favored due to their propensity for DGF.

Recipient Assessment for Transplantation during Pandemics

As discussed above, an older age has been shown to be the best predictor of mortality in multivariate analysis. For patients aged >65, especially if they have additional comorbidities such as cardiovascular disease and diabetes mellitus, transplantation was deferred at the peak of the pandemic (Table 4). Another at-risk group is comprised of highly sensitized patients with donor-specific antibodies who have an increased risk for development of acute rejection that might require augmented immunosuppressive medications, such as antithymocyte globulin and/or rituximab. Although there is scant evidence to assign coronavirus-progressive risk to antithymocyte globulin, a practice of avoidance when possible has been adopted. However, patients who are highly sensitized and have calculated panel reactive antibody >95%, receiving an offer from a donor without any donor-specific antibody, and/or mismatch could be considered for transplantation. Another important factor in decision making is the patient's time on the waiting list. Although patients at the top of the waiting list can afford to wait until the pandemic resolves, patients with an expected waiting time of >3 years on the list can be considered for transplantation if they do not have significant comorbidities. Waiting time is shorter in simultaneous kidney and pancreas transplantation, and those patients require potent induction agents so it would be advisable to defer transplant at the peak of pandemics. For simultaneous kidney and heart or liver transplantation, allocation is driven by heart and liver transplantation; the sickest patients receive the offer and transplant should not be deferred during pandemics, because survival without transplantation is limited in those patients.

Perhaps the area most rife for debate is when to transplant patients after they have been infected with, or vaccinated against, COVID-19. The American Society of Transplant Surgery Strike Force's most recent recommendation is to proceed with transplant once the patient has no evidence of active infection and has two consecutive negative PCR tests, 1 week apart, before transplantation. More importantly, the patient should wait at least 30 days after resolution of

Table 4. Clinical approach to living and deceased donor sand recipients during the coronavirus disease 2019 pandemic

Clinical Approach
Donor assessment
1. Deceased and living donor transplant activity should be assessed at each center on the basis of COVID-19 pandemic severity at their region.
2. One sample from the respiratory tract by RT-PCR for SARS-CoV-2 should be performed within 3 days of procurement. A second viral test be performed 24 hours after the initial test and within 24–48 hours of procurement when feasible.
3. For donors previously known to have had COVID-19, it is suggested the initial COVID-19 infection occurred between 21 and 90 days before donor evaluation, irrespective of repeat NAT test results, and at least 30 days passed after symptom resolution.
4. Chest computerized tomography should be negative for COVID-19 suspicious pneumonia.
5. Consideration should be given toward ensuring lower cold ischemia times to minimize delayed graft function.
6. For living donors who were previously known to have had COVID-19, ≥30 days should have passed after all symptoms were resolved.
7. Living donors should be vaccinated for SARS-CoV-2 before transplantation.
Recipient assessment
1. Patients aged >65years, especially if they have additional comorbidities such as cardiovascular disease and diabetes mellitus, transplantation could be deferred at the peak of pandemics.
2. Transplantation in patients who are highly sensitized with use of antithymocyte globulin and/or rituximab should be assessed patient by patient, considering the recipient's age and other comorbidities, degree of HLA-matching and mismatching, and severity of the pandemic at the region.
3. For recipients who were previously known to have had COVID-19, at least 30 days should have passed after all symptoms were resolved and should have an updated cardiac and pulmonary assessment before they are considered for transplantation.
4. Patients ideally should be vaccinated for SARS-CoV-2 before transplantation.

COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; NAT, nucleic acid amplification technique.

COVID-19–associated symptoms before consideration for transplantation (38). These patients should have an updated cardiac and pulmonary assessment before they are considered for transplantation due to the effects of COVID-19 on heart and lung function. Patients that have received the first dose of coronavirus vaccine (Moderna and Pfizer BioNtech), and are awaiting the second dose, can be transplanted, although there is mounting evidence that these patients do not develop an appropriate response. Initial reports documented a lower antibody response (6%–17%) to vaccination after first dose of mRNA vaccination (40–42), which is in contrast with the robust early immunogenicity observed in the general population after mRNA vaccination (43–45). However, the antibody response rate was higher in a small group of patients with ESKD (41).

Patients ideally should be vaccinated for SARS-CoV-2 before transplantation. Uncertainty sometimes arises if patients are between their first and second vaccine dose, and they receive an excellent kidney transplant offer. In this scenario, we allow the patients to decide whether to pursue transplantation, but recommend forgoing the second dose of the vaccine should they accept the organ offer. Revaccination should start 3 months after transplantation. Nevertheless, transplant center should educate fresh transplant recipients to take all precautionary measures to reduce the chance of getting infected: limiting visitors, maintaining 6 feet distance from others, wearing masks, and consider home-based blood draw, if feasible.

Immunosuppression Management during the COVID-19 Pandemic

After infection detection, lowering the immunosuppressive regimen may help recover specific immunity, which may help control viral replication. Theoretically, this may lead to lesser disease severity, especially given the documented lymphopenia and low T cell counts in these recipients (14). However, during the late phases of the disease, which is mainly considered a state of immune dysfunction, withdrawal or significant reduction of immunosuppressive drugs could hypothetically exacerbate this dysfunctional immune response. Bae *et al*. included 69,884 recipients (64,849 transplanted in the prepandemic period and 5035 in the pandemic era) and reported a decrease in the use of lymphocyte-depleting induction agents from 73% in the prepandemic era to 68% in the pandemic era (46). The use of lymphocyte-depleting agents was associated with decreased acute rejection rates, but was not associated with increased mortality. Two national registries in France reported that renal transplant recipients who died from COVID-19 were more frequently within their first year of transplantation, but there was no association between antithymocyte globulin or alemtuzumab use and death (35). A single center in New York reported a safe use of antithymocyte globulin at the peak of the pandemic (47).

Given that T cell function and proliferation is the mainstay of the immune response against generalized viral infections, withdrawal or reduction of antimetabolites such as mycophenolate mofetil of azathioprine was a practical approach in mild patients not requiring hospital admission (Table 5). A review by Marinaki *et al*. including 63 articles with 420 patients found reduction or discontinuation of immunosuppression in 58% of patients, with antimetabolite discontinued in 91% of patients and calcineurin inhibitor in 58% (10). Calcineurin inhibitor reduction or withdrawal was most frequently done in more moderate to severe disease, particularly in patients in the intensive care unit. Steroids, in contrast, were frequently left unchanged or increased in some patients. The RECOVERY trial demonstrated mortality benefit in treatment with 6 mg of dexamethasone daily for patients with COVID-19

Table 5. Management of kidney transplant recipients with coronavirus disease 2019

Management Approach
Mild patients not requiring hospital admission
1. Continuation of current immunosuppression with calcineurin inhibitor and prednisone
2. Decrease in antimetabolite dose (25%–100%)
3. Monoclonal neutralizing antibody treatment (LY-CoV555 or REGN-COV2)
Moderate patients requiring hospital admission
1. Continuation of current immunosuppression with calcineurin inhibitor treatment with 25%–50% dose reduction
2. Dexamethasone 6 mg daily for 5–10 days
3. Hold antimetabolite
Severe patients requiring intensive care unit admission
1. Holding calcineurin inhibitor and antimetabolite
2. Dexamethasone 6 mg daily for 5–10 days

REGN-COV2, casirivimab and imdevimab.

requiring oxygen. The World Health Organization consequently recommended the use of systemic corticosteroids in severe and critical patients as the standard of care (48).

Neutralizing monoclonal antibody treatment has been used successfully in mild patients not requiring hospital admission. In a randomized phase 2 trial of a single intravenous infusion of neutralizing antibody LY-CoV555 decreased the COVID-19–related hospitalization or emergency room visit (2%) compared with placebo group (6%) (49). Another randomized double-blind study using a combined cocktail (casirivimab and imdevimab) decreased the medical visit from 6% to 3% (50).

IL-6 has been shown to be the driving cytokine in severe patients and high IL-6 levels were shown to be associated with mortality. Early observational cohort studies of tocilizumab, a monoclonal antibody that blocks the IL-6 receptor, found that patients receiving tocilizumab had reduced mortality compared with standard of care (51,52). However, two randomized, double-blind, placebo-controlled, multicenter trials did not show any benefit with tocilizumab therapy (53,54). In patients who were hospitalized and had COVID-19 pneumonia, but were not receiving mechanical ventilation, tocilizumab reduced the likelihood of progression to the composite outcome of mechanical ventilation or death, but it did not improve survival (55). In a multicenter cohort study of 80 hospitalized kidney transplant recipients in Spain, tocilizumab treatment did not have an effect on outcome (56).

In a multicenter, randomized, placebo-controlled trial, patients receiving a 10-day course of remdesivir, an inhibitor of viral RNA polymerase, had a shorter time to recovery compared with placebo (11 vs 15 days, ratio for recovery, 1.32; 95% CI, 1.12 to 1.55), with the most significant improvement seen in patients who were not intubated receiving supplemental oxygen, but no mortality benefit was observed (57). Baricitinib, a Janus kinase inhibitor, plus remdesivir did not decrease mortality, but patients receiving high-flow oxygen or noninvasive ventilation at enrollment had a time to recovery of 10 days with combination treatment, and 18 days with control (58).

Passive antibody therapy through the use of convalescent plasma is another potential therapy for COVID-19, which may be effective through viral neutralization (59). A randomized trial from China revealed a trend toward clinical improvement with plasma therapy (52% vs 43%) but failed to meet statistical significance ($P=0.26$) (60). A meta-analysis of 10 studies reported that treatment with convalescent plasma compared with placebo or standard of care was not significantly associated with a decrease in all-cause mortality or with any benefit for other clinical outcomes (61). Plasma exchange has been used to remove the circulating cytokines in small case series (62,63) but also has the potential to remove antibodies to SARS-CoV-2 and could be combined with convalescent plasma.

We have reviewed the published data to answer the question of whether to "transplant or not transplant" during the pandemic. The available data do not particularly support one choice over the other. However, the higher incidence of disease observed in the waitlisted population (likely due to increased exposure during dialysis) suggests that proceeding with transplant with protocols that safeguard against infection combined with careful patient and donor selection seems most appropriate at this time. Still, each center should conduct risk assessments on the basis of the patient's age and other medical comorbidities, time on the waiting list, degree of sensitization, cold ischemia time, status of vaccination, and severity of the pandemic in their region.

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