



The impact of COVID-19 on kidney transplantation

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Management of kidney transplant recipients requires a sustainable infrastructure that can provide reliable medical care both before and after transplantation. The COVID-19 pandemic has disrupted transplant referral and listing processes, led to decreases in the numbers of transplant procedures and resulted in changes in practice for pre- and post-transplantation management and follow-up.

“Most guidelines recommend against accepting donors with active COVID-19”

The landscape of solid organ transplantation has dramatically changed since the COVID-19 pandemic unfolded. The transplant workforce has implemented several changes in response to rapidly changing circumstances with the aims of preserving personal protective equipment, maintaining hospital capacity during an anticipated surge in COVID-19 cases and minimizing the risk of virus transmission. There is immense uncertainty about the adequacy of available SARS-CoV-2 testing and concerns about the potential risk of transmitting a virulent disease to heavily immunosuppressed transplant recipients and otherwise healthy live donors.

Impact on kidney transplant programmes

Although the Centers for Medicare and Medicaid Services categorized solid organ transplantation as a Tier 3b procedure, meaning that it should not be postponed, the majority of transplant centres in the USA have reduced their numbers of kidney transplant procedures in response to the COVID-19 pandemic. In late March 2020, a survey of 88 US transplant institutions reported that 71.8% had completely suspended live donor kidney transplantation and 84% had implemented restrictions for deceased donor kidney transplantation¹. Such restrictions include transplanting only highly sensitized patients, higher acuity patients and those who do not have access to dialysis. Another study reported 51% and 90% reductions in solid organ transplant procedures in the USA and France, respectively, mostly driven by reductions in kidney transplantation². An analysis of US registry data showed that between 15 March and 30 April 2020, the numbers of deceased donor and live donor kidney transplant procedures were, respectively, 24% and 87% lower than would be expected based on pre-epidemic data³. A 2.2-fold increase in mortality was observed among wait-listed patients in states with the highest COVID-19 burdens. In addition, the number of new registrants for the deceased donor kidney transplant waiting list decreased by 18%, likely reflective of delays in the evaluation of kidney transplant candidates³. These statistics demonstrate the devastating effect of the pandemic on patients awaiting kidney transplantation.

With the goal of assisting transplant centres in making difficult decisions, researchers have developed a simulation calculator that uses the characteristics of transplant candidates and regional COVID-19 parameters to identify those who could potentially benefit the most from kidney transplantation during the pandemic⁴. In most scenarios, the simulations showed potential immediate survival benefits of kidney transplantation, particularly in areas where the case fatality rate from COVID-19 among the general population was low.

Donor testing

The risk of donor-transmitted COVID-19 infection in kidney transplant recipients remains unknown. The lack of reports of such transmission suggests that the risk has been mitigated by the decreased number of transplants and rapid implementation of donor screening protocols by organ procurement organizations (OPOs). These protocols have evolved as the pandemic unfolded and more data became available. In their updated guidelines from 8 July 2020, the American Society of Transplantation (AST) recommended epidemiological, clinical and laboratory assessment of potential deceased donors⁵. Epidemiological assessment includes identification of factors such as residence in or travel to high incidence areas and recent exposure to individuals with COVID-19. Clinical assessment includes assessment of COVID-19 symptoms and laboratory assessment comprises nucleic acid testing of at least one sample from the upper or lower respiratory tract for SARS-CoV-2 within 3 days of organ procurement. Most guidelines recommend against accepting donors with active COVID-19. Donors with recent COVID-19 might be considered for donation if they had repeated negative nucleic acid testing at least 24 h apart and resolution of symptoms more than 28 days before organ procurement⁵. Similar guidelines were issued for live donors with the addition of providing counselling about infection prevention. In addition, the AST recommends temporary suspension of living donor kidney transplantation during periods of high local transmission of COVID-19 to minimize infection risk for live donors⁵.

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COVID-19 in transplant recipients

Multiple published case series and preliminary data from a multinational, multicentre registry of >400 solid organ transplant recipients that were presented at the American Transplant Congress 2020 have provided information on the clinical features of COVID-19 in this population⁶. In these studies, COVID-19 mortality among recipients of solid organ transplants varied but was generally 6–30%. Similar to non-transplant patients, solid organ transplant recipients often have a biphasic illness, with a flu-like inflammatory phase followed by an inflammatory cytokine release syndrome; however, some transplant recipients are only mildly symptomatic or asymptomatic. A US case series of 90 solid organ transplant recipients (including 46 kidney recipients) with COVID-19 reported fever in 70%, cough in 59% and dyspnoea in 43% (REF.⁷). Many patients had comorbidities that are associated with COVID-19 severity, such as obesity, cardiovascular disease and chronic kidney disease; 76% required hospitalization and 35% required mechanical ventilation. Overall mortality was 18%; 24% of hospitalized patients and 52% of those who were admitted to the intensive care unit died during the 3 week study period⁷.

Protracted nucleic acid testing positivity has been observed in some solid organ transplant recipients and could pose problems for their return to laboratory or clinic sites⁸.

The effectiveness of therapies such as remdesivir, convalescent plasma and immunomodulators in solid organ transplant recipients with COVID-19 is still being evaluated. A marked response to the IL-6 receptor inhibitor tocilizumab was reported in a liver transplant recipient with COVID-19 but further studies of this treatment approach are needed⁹. The optimal management of immunosuppressive agents in kidney transplant recipients with COVID-19 is also not yet clear. Although some immunosuppressants such as mycophenolate could have a deleterious effect on infection outcomes, others such as calcineurin inhibitors (CNIs) could potentially mitigate the risk of COVID-19 inflammation. Evidence from the pre-COVID-19 era suggests that tacrolimus might inhibit the in vitro replication of coronaviruses¹⁰. Many centres have elected to discontinue or reduce antime-tabolite therapies such as mycophenolate, which is a common approach to viral infections in transplant recipients, but maintain CNI therapy in solid organ transplant recipients with COVID-19.

Minimizing infection risk in recipients

Conducting adequate screening of kidney transplant candidates is crucial given their anticipated burden of immunosuppression. Such assessment should take into account local disease activity, and should include screening for COVID-19 symptoms as well as laboratory testing. The AST recommends nucleic acid testing of at least one sample from the respiratory tract for SARS-CoV-2. Chest imaging can be helpful as an adjunct to rule out asymptomatic infection. In addition, transplant centres have been restricting visitation and unnecessary interactions with staff to prevent transmission from asymptomatic individuals.

Some transplant centres have revised their induction and maintenance immunosuppression regimens to

reduce infection risk. A US study found that patients who were transplanted in the first 7 weeks of the pandemic had approximately half the odds of receiving lymphocyte-depleting induction as those who were transplanted in the pre-pandemic era (S. Bae, unpublished work). Data are as yet insufficient to make definitive recommendations regarding empirical modification of immunosuppression for non-infected kidney transplant recipients, but some experts recommend pre-emptively minimizing therapy as feasible based on individual immunological risk.

The long-term management of kidney transplant recipients requires ongoing evaluation of the tolerability of immunosuppressants as well as frequent laboratory assessment of drug levels and allograft function. Most transplant centres have implemented policies to obviate physical interaction of kidney transplant recipients with the public and health-care workers, and such policies should continue in the reopening phases. Examples include converting clinic visits into telemedicine and minimizing unnecessary laboratory testing. In addition, protocol biopsies should be deferred and the risks and benefits of performing for-cause kidney transplant biopsies should be carefully weighed. In some cases, protocol biopsies could potentially be replaced with noninvasive diagnostics such as quantification of donor-derived cell-free DNA and genomic tools.

Future perspectives

In a few short months, the COVID-19 pandemic has wrought profound changes in kidney transplantation. This impact has been felt at the levels of individual patient care, transplant centres, OPOs and national policies. Consequences such as excess mortality on the waiting list and decreased referrals for transplant evaluation will continue to have an impact long after the pandemic has subsided. We hope that lessons learned from this pandemic will allow us to protect our patients more effectively, devise rational policies for transplant decisions and establish systems of care in the event of another such crisis.

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Competing interests

The authors declare no competing interests.