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Ethical Issues in Kidney Transplant and Donation During COVID-19 Pandemic

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Summary
The coronavirus disease-19 pandemic caused by the severe acute respiratory syndrome coronavirus has faced the transplant community with unprecedented clinical challenges in a highly vulnerable patient category. These were associated with many uncertainties for patients and health care professionals and prompted many ethical debates regarding the safe delivery of kidney transplantation. In this article, we highlight some of the most important ethical questions that were raised during the pandemic and attempt to analyze ethical arguments in light of core principles of medical ethics to either suspend or continue kidney transplantation, and to mandate vaccination in transplant patients, transplant candidates, and, finally, health care providers. We have come up with frameworks to deal responsibly with these ethical challenges, and formulated recommendations to cope with the issues imposed on patients and transplant professionals. Semin Nephrol 42:151272 © 2022 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)

Keywords: Autonomy, beneficence, ethics, kidney transplant, vaccination

The coronavirus disease-2019 (Covid-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been causing disruptions of an unprecedented magnitude in clinical practice in all areas including organ transplantation. The public health emergency poses ethical challenges for organ donation and transplantation health care professionals. As in other areas of health care, the Covid-19 crisis calls into question how to maintain the welfare of patients based on the ethical principles of justice, autonomy, beneficence, nonmaleficence, and accountability.

This article summarizes ethical issues associated with kidney transplantation during the Covid-19 pandemic. An ethical framework to address different questions is provided. Key issues for kidney transplantation during the time of Covid-19 include keeping kidney transplant patients safe, the need to ration scarce medical resources and make recommendations for suspending or continuing transplant activity, and recommendations toward advising or mandating vaccination.

ETHICAL CHALLENGES

The challenging issues of kidney transplant patients and those on the waiting list for kidney transplantation have surfaced since the first Covid-19 wave before availability of the vaccine, but remain critical after the delta and omicron waves.

Data from the Scientific Registry of Transplant Recipients have illustrated the magnitude of impact. During the early part of the pandemic, there was a 2.2-fold increase in mortality for patients on the kidney transplantation waitlist in the United States. At the same time, the total mortality rate observed in kidney transplant recipients during the Covid-19 era also has been shown to exceed the expected deaths by 1.4-fold according to the Scientific Registry of Transplant Recipients data. The ratio of observed to expected deaths varied substantially by race or ethnicity even within the national study of the United States, being highest (82% greater than expected) among Hispanic solid organ transplant recipients.

Based on meta-analyses of observational studies, the 30-day mortality rate of Covid-19 was 19% among kidney transplant recipients. There was a trend toward lower mortality rates with time, approaching 14% during the second half of 2020 and as low as 2% during the omicron surge in 2022. The mortality of kidney transplant recipients from Covid-19 in low- and middle-income countries, such as Latin America, was higher, ranging from 14.3% to 35.4%. Although Covid-19 vaccines are effective in curtailing cases and reducing

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Financial disclosure and conflict of interest statements: none.
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https://doi.org/10.1016/j.semnephrol.2022.07.006

Seminars in Nephrology, Vol 42, No 4, July 2022, 151272
mortality, ethical challenges come from the issue of vaccine equity. In many low-resource countries, the critical shortage of the vaccine made it impossible to achieve herd immunity to allow preparedness for sustaining kidney transplantation activity, or even dialysis service. Such an ongoing mismatch between demand and supply of vaccines likely would cause controversy and divide opinion whether booster dosing should wait until global distribution of vaccines is better achieved.\textsuperscript{19}

**Challenge 1: Should Kidney Transplantation Be Continued or Suspended During the Pandemic?**

Of note, the pandemic has imposed significant stress on health care systems, requiring a shift of resources to combat the infection and temporary cessation of elective clinical activities.\textsuperscript{10} A substantial reduction in organ donation and transplantation has been reported worldwide,\textsuperscript{11-13} and not necessarily restricted to regions with the highest infection rates. Based on a nationwide analysis in the United States, there was a reduction of more than 50\% in deceased donor transplantation since the Covid-19 outbreak, mostly driven by reduced kidney transplantation.\textsuperscript{12} Another survey in the United States reported that 72\% of transplant institutions had completely suspended living donor kidney transplantation in early 2020, where restrictions to deceased donor kidney transplantation was imposed in 84\% of centers.\textsuperscript{13} A decrease in kidney retrieval also was evident in regions with low caseloads, indicative of a global and nationwide effect beyond the local Covid-19 incidence and prevalence.\textsuperscript{12} To quantify the impact of Covid-19 on solid organ transplantation, international data should be collected. The most comprehensive international data leverage the transplant activity from 22 countries, starting from the onset of the 100th cumulative Covid-19 cases through the end of 2020.\textsuperscript{14} Despite variation between countries, the most pronounced reduction was in kidney transplantation, with an overall decrease of 19\%. Deceased and living kidney donor transplantation was decreased by 12\% and 40\%, respectively.\textsuperscript{14} The trend of reduced transplantation after 2020, including burnout in transplant workforces and the impact of increase in the incidence of infection in kidney transplant recipients secondary to the omicron variant, remains to be evaluated and monitored.\textsuperscript{15,16}

Deferring elective surgical or medical procedures during the Covid-19 crisis is justified ethically to protect patients and health care workers (nonmaleficence and distributive justice because resources and staff were not available for elective and even many emergency services). There was an unknown risk in the beginning of Covid-19 infection (prevaccination era) for immunosuppressed patients. We could not ascertain if Covid-19 could be transmitted from donors to recipients. The fact that many hospitals were overwhelmed and operating rooms were converted to intensive care unit beds had substantial consequences. Anesthetists and many other specialists had been deployed to work in intensive care units, dialysis units, or areas other than the transplant program. This could have had implications for the decision to keep or suspend the transplant program, and in many cases was dictated by hospital directors.

The rationale underscores the need to balance individual patients’ needs and those of the community (again, distributive justice). We have a duty to the communities, hospital employees, and patients, in addition to a responsibility to individual waitlisted kidney transplant candidates. It amounts to an estimation of the reserve of personal protective equipment (PPE) availability and the utilization of PPE for kidney transplantation surgery and perioperative transplant care. Other factors include the population density and incidence of Covid-19 cases in the community, hospital bed and intensive care unit bed surge capacity, in addition to staffing availability. When high-filtration N-95 masks are in short supply, suspending elective surgery or endoscopy is considered more appropriate than contingency measures such as reusing masks or downgrading protective gear requirements. Blood product availability is not a major concern for kidney transplantation (but still needs to be reserved for every case even though there rarely is a need to transfuse), as opposed to liver transplantation. Although the blood donation rate is expected to be reduced during a pandemic (because of the fear of being infected while donating blood and restricted freedom of blood collection teams to attend public places), the demand for blood products may well turn out to be lower because the number of trauma patients decreases secondary to lockdown-related travel restrictions. The same applies to the consideration of ventilator capacity, which should not be affected too much by kidney transplantation; most kidney transplant recipients do not require ventilator support postoperatively, although we might argue that there always should be an intensive care bed for ventilation standby.

To aid in the decision making as to whether deceased and living donor kidney transplantation should be deferred/suspended during a region or hospital’s Covid-19 response, there are several consequences to be considered. The first and foremost factor is the patients who need and benefit from kidney transplantation. That ethical principle is to strike a balance between equity and clinical results. Although ethical values might inform the choice, one should distinguish between the situations when the position of a center is at the peak of the incidence curve versus those at the downslope stage,\textsuperscript{18} and between the prevaccination and postvaccination era. Transplant programs definitely also should include patient factors regarding clinical risk. The question to address, in other words, is whether—and how long—the end-stage kidney disease patients can wait without...
transplantation. The waitlisted kidney transplant patients’ views should be given a prominent place in the decision-making process because we learned that communication with kidney transplant candidates is of the utmost importance. The majority of surveyed patients favor receiving a kidney transplant despite the ongoing Covid-19 pandemic. Reactivation of candidates on the waitlist cannot be assumed, however, and should take an individualized approach, incorporating clinical risk with patient perspectives.

Given the imbalance between supply and demand for medical resources, the pertinent question is not whether to set priorities, but how to do so ethically and consistently. The need to be consistent by no means implies a fixed answer because the risk—benefit ratio can be highly dynamic during different stages of kidney disease and the varying Covid-19 incidence in the community and disease burden. The best framework for pandemic resource allocation during Covid-19 has been constructed by medical ethicists previously (Table 1). In essence, four fundamental pillars appear in the proposed ethical considerations: maximizing the benefits produced by scarce resources, treating people equally, promoting and rewarding instrumental value, and giving priority to the sickest patients.

Intuitively, one of the reasons for kidney transplantation to be the most affected by the Covid-19 pandemic among all solid organ transplantation is the perceived effective alternative to transplantation for managing kidney failure. Although dialysis is perceived as a reasonable alternative, it is important to note that there is an exceptionally high SARS-CoV-2 infection attack rate (the proportion of patients who become infected) among hemodialysis patients. Because of the difficulty for dialysis patients to self-isolate and practical challenges of implementing social distancing in the dialysis units, hemodialysis patients are subjected to an exceptionally high likelihood of infection. Furthermore, the urgency of kidney transplantation varies between patients. Many patients can afford to wait longer when transplantation has to be suspended, whereas less-lucky patients need a kidney transplant within a short time to survive. Examples are those who have limited access to dialysis, who have exhaustion or imminent lack of vascular access, and either have absolute contraindications to or technique failure of peritoneal dialysis. Highly sensitized patients with a high percentage panel of reactive antibodies and impending dialysis technique failure also could be given priority status for kidney transplantation. Adoption of a broad-brush approach stopping all kidney transplantation could have significantly disadvantaged these high-priority waitlisted transplant candidates who will have the lowest life expectancy in the absence of a kidney transplant. Instead, priority setting is a more reasonable approach, even though priority-setting also entails trade-offs to be made. While acknowledging that priority is inherently a value-laden process, we should make decisions on the premise that fair and transparent priority setting would address both population health needs and an individual patient’s urgency. As outlined in Table 1, it is highly justified to give priority to maximizing the number of patients who survive treatment with a reasonable life expectancy. If we simply consider save the most lives, we should always save five lives rather than one. However, prognosis allocation is relevant, too. That means incorporating estimated life-years into benefit estimation. The concept or metric of life-years, as initially introduced as an epidemiologic and economic indicator of disease burden, now often is used by bioethicists to assign priority. In other words, we should not simply aim to save the most lives and should aim to save the most life-years. Although not all

| Table 1. Ethical Framework for Guiding Kidney Transplantation Management During the Covid-19 Pandemic |
| --- |
| Ethical Values and Guiding Principles | Application to Kidney Transplantation and Covid-19 Pandemic |
| Maximize total benefits: utilitarianism | Receives the highest priority |
| Save the most lives | Receives the highest priority |
| Save the most life-years—maximize prognosis | Should not be used |
| Treat people equally: egalitarianism | Used for selecting transplant recipients with similar HLA matching to donor |
| First-come, first-served | Gives priority to vaccinated patients when other factors such as maximizing benefits are equal |
| Random selection | Gives priority to previous organ donors when other factors such as maximizing benefits are equal |
| Promote and reward social usefulness (reciprocity or benefit to others) | Used when it aligns with maximizing benefits |
| Retrospective—priority to those who have made relevant contributions | Used when it aligns with maximizing benefits such as preventing spread of the virus |
| Prospective—priority to those who are likely to make relevant contributions | |
| Give priority to the worst off: prioritarianism | |
| Sickest first | |
| Youngest first | |

Abbreviations: Covid-19, coronavirus disease-2019; HLA, human leukocyte antigen. Reprinted with permission from Emanuel et al and Luyckx and Moosa.
appear to champion the life-year approach, this approach is receiving the most support from a prognosis-based allocation perspective. Based on the estimation of reduced transplant activity during the Covid-19 pandemic compared with 2019, it has translated into a negative effect of 37,664 life-years lost for patients waitlisted for a kidney, much higher than the 7,370 life-years lost for patients waitlisted for a liver.

There is a certain logic to have different policies for kidney transplantation program suspension and resumption. Within the domain of kidney transplantation, most patients with end-stage kidney disease can wait until an organ becomes available. However, some patients cannot wait too long. Live kidney donation can be rescheduled, whereas deceased donor kidneys will be wasted (because they also likely will not be retrieved, not just discarded) if transplant services are suspended. Should a deceased donor kidney be considered suitable for an immunologically high-risk patient awaiting transplant, that kidney could have been the one and only chance for this challenging cohort of often long-waiting patients. Outcome studies of highly sensitized kidney transplant candidates further argues for prioritizing the transplant for them despite the pressures of the Covid-19 pandemic. A key finding of safety in using lymphocyte-depleting agents (associated with a decrease in rejection and without an increase in mortality) even during the pandemic era supports the argument to prioritize highly sensitized transplant candidates. The policy of complete cessation of transplant surgery for highly sensitized patients would have precluded the precious chance of getting a compatible kidney; these patients may not get a another suitable offer. Consideration of relevant factors in deciding the policy should include the supply-to-demand gap of organs. That means we should evaluate the impact of stopping kidney donation and transplantation. When stratifying urgency of resuming transplantation, it is reasonable to give higher priority to regions with lower organ donation rates.

In the face of ethical dilemmas surrounding decision conundrums regarding deferring versus maintaining transplantation, a simulation of the outcomes using a Markov decision process model and probabilities can provide additional information. That means an estimation of risks and benefits for different phenotype patients in different geographies, the latter referring to Covid-19 acquisition risks and case fatality rates. In addition to the characteristics of the pandemic, the length of delay should be factored in, because the length of the pandemic could influence the waitlist and post-transplant mortality rate. According to a simulation calculator developed for this purpose (http://www.transplantmodels.com/covid_sim), the best immediate survival benefits of kidney transplantation occur in areas where the case fatality rate from Covid-19 among the general population is low. On the other hand, kidney transplantation will result in harm only when case fatality rates are substantially higher for kidney transplant recipients (ie, ≥50%) than for waitlist patients (ie, ≤30%), and when the community risk of Covid-19 acquisition is medium or high. When the survival probability is assessed for waitlist patients, we also have to consider the survival benefit for patients receiving home dialysis.

Increasingly concerned that patient autonomy should be respected, surveys should be conducted to assess transplant waitlisted patients’ attitudes and concerns toward transplantation during different periods of Covid-19. During the peak of Covid-19 and before the availability of vaccination in Singapore, when safe distancing measures were strictly enforced and activities around the country were limited to essential activities only, a standardized telephone survey of patients awaiting transplant was conducted. Nearly half of the respondents were waiting for a kidney transplant. Although most patients initially responded that transplantation services should continue despite Covid-19, their opinion changed after the series of questions designed to introduce thoughts on the risk of infection to a transplanted patient. Careful consideration on the pretransplant and post-transplant care and the potential harm from donor-derived infection had influenced the willingness of patients to proceed with transplantation; the proportion of patients keen to proceed decreased by half. A similar survey conducted in the United Kingdom, also before the era of a SARS-CoV-2 vaccine, showed that the majority of kidney transplant candidates would like to be reactivated immediately on the transplant waitlist when transplant activity is resumed.

Ideally, centers should decide the pragmatism and prioritizing of living versus deceased donor transplantation. Some transplant centers tend to defer deceased donor transplantation because the hospitalization tends to be lengthier than for living donor transplant patients, and even more so if extended criteria donor kidneys are accepted. Resource utilization and demands for deceased donor kidney transplant are also of concern when the recipient hospitals are heavily affected by the shortage of manpower, including nursing staff, PPE, beds, and testing capacity. These key considerations for proceeding with living donor kidney transplantation are particularly relevant in regions where dialysis capacity is constrained or not affordable.

Last but not least, we need to consider the ethical principle of accountability and safety of health care professionals, in addition to the benefit to society and the transplant candidates. Even when a waitlisted candidate accepts the risk of infection and transplant, we have to be considerate of the risk to the medical team. This is even more relevant in situations when PPE shortage occurs and there is a lack of resources to conduct universal screening. Under such constraints, the rate of contagion among health care workers has been reported to...
increase, leading to a vicious circle of in-hospital nosocomial spread to patients and staff.38

All in all, the ethical considerations would favor a phased approach rather than all-or-none approach.39 This could be either a stepwise decreasing or stepwise ramping up of transplant activity according to (clinical) risk assessments (Table 2). The varying degrees of reduction therefore would depend on risk stratification, namely, resource availability and medical urgency (Fig. 1). In the United Kingdom, National Health Service Blood and Transplant has supported organ donation and transplantation with up-to-date national guidance and data collection.

**Challenge 2: Should Vaccination of Kidney Transplant Candidates Be Mandatory During the Covid-19 Pandemic?**

The concern about pandemic spread and transmission risk from donor to recipient and nosocomial transmission has been calling into question whether or not mandating Covid-19 vaccination was justified. Are there ethical,

| Kidney Transplant Activity Level | Priority Level Description | Examples, Including but Not Limited To the Following |
|---------------------------------|----------------------------|-----------------------------------------------------|
| 25% reduction in transplant activity | Elective cases: patients whose conditions are not life-threatening or can be managed with dialysis and for whom services can be deferred until the end of a pandemic wave (approximately 6-8 wk) | No living donor activity, deceased donor activity allowed |
| 50% reduction in transplant activity | Urgent cases: patients who are deemed urgent and who need service within 14 days Services can be deferred for a few days, but not for the length of a pandemic wave | No activity except highly sensitized cases (such as panel reactive antibody of ≥95% with suitable donor offer and negative donor-specific antibody) |
| 75% reduction in transplant activity | Emergency cases: patients who are deemed critical, whose condition is immediately life-threatening | No activity unless for medically urgent status (such as lack of dialysis access, uremic cardiomyopathy) Combined kidney–pancreas transplant is not suggested |
| 100% reduction in transplant activity | Health system is overwhelmed with Covid-19 No intensive care unit or other capacity available Severe shortage of health personnel | Complete cessation of all living and deceased donor transplant activity |

Abbreviation: Covid-19, coronavirus disease-2019. Reprinted with permission from Kumar et al.39

**Figure 1.** Schematic diagram of factors in favor or against maintaining kidney transplantation during the coronavirus disease-2019 (Covid-19) pandemic.
Table 3. Ethical Arguments for or Against Mandatory Vaccination Before Transplant Waitlisting

| Arguments for Mandating Vaccination in Transplant Waitlisted Candidates | Arguments Against Mandating Vaccination in Transplant Waitlisted Candidates |
|---|---|
| Duty to protect patients: first do no harm |
| High mortality of Covid-19 in transplant recipients |
| Additional risk of mortality in immediate post-transplant period |
| Potential harm to others |
| Ensure safety of others and the hospital as a whole |
| Inappropriate use of a scarce resource |
| Maximize the benefit derived from the scarce resource of donated organs |
| Damage to public perceptions of organ donation |
| Possible precedents |
| Predicating transplantation listing on aspects of patient choice or behavior such as abstinence from alcohol for liver transplant |
| Poor compliance behavior before transplantation as a predictor for nonadherence after kidney transplant |
| Autonomy and human rights |
| Respect patient decision |
| Clear difference between vaccination passport for tourism and access to life-saving transplantation |
| Unfairness to less-educated or health-illiterate populations who are more likely to be misinformed by fake news |
| Equity of access |
| Damage to trust in medical profession |
| Practical uncertainties |
| Efficacy of SARS-CoV-2 vaccine |
| Uncertain efficacy to limit infectivity and virus transmission, especially new virus variants |

Abbreviations: Covid-19, coronavirus disease-2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2. Reprinted with permission from Gokmen et al.47 and Hurst et al.48

legal, and scientific reasons for mandatory vaccination before candidates can be waitlisted or accepted for kidney transplantation? One important factor that should caution the decision is that vaccine-resistant populations often are hard hit by Covid-19 itself in terms of ethnicity, socioeconomic background, and comorbidities, and, in other words, are a vulnerable group. By mandating vaccines, we would have fueled an act of discrimination.

Before the spread of the delta variant of SARS-CoV-2, there were optimistic indications that vaccines could eliminate transmission of the virus. With more data and experience with the vaccine efficacy, especially in kidney patients and transplant patients, as well as the parade of variants, their transmissibility, and antigenic changes affecting protection by vaccination, the vaccination landscape has changed. It now is believed that SARS-CoV-2 vaccines should be relied on to prevent symptomatic infection and reduce Covid-19–associated morbidity and mortality, rather than a panacea.40 As compared with previous variants, the omicron variant shows substantial immune-evasion capability, and more so among kidney transplant recipients.41 That being said, vaccination still can provide a reasonably satisfactory reduction in viral shedding and infectivity, especially in vulnerable populations in hospitals42 and elderly care facilities.43,44

For the sake of protecting transplant candidates from Covid-19 infection, vaccinations preferably should be administered before transplantation. To draw the analogy with seasonal influenza vaccination, vaccination before kidney transplantation would confer better protection to patients than those who do not receive a vaccine (or defer vaccination until after transplantation). The same phenomenon is even more pronounced for a humoral response to the SARS-CoV-2 vaccine.45 A pooled estimate of antibody response after two doses of messenger RNA vaccines was 35% for transplant recipients, which is much lower than that of 89% for dialysis patients.46

A detailed ethical framework to argue for or against mandating vaccination in kidney patients before activation or reactivation on a transplant waiting list has been published previously (Table 3).47,48 One of the arguments against mandating vaccination is the uncertain vaccine efficacy, especially in transplant candidates or transplant recipients on immunosuppression.47 On the other hand, this is exactly the reason to strongly recommend for vaccination before and not after kidney transplantation, to ensure optimal protection. Registry data have suggested reduced mortality risk from Covid-19 infection for vaccinated kidney transplant recipients when compared with unvaccinated patients.49,50 Furthermore, the protection conferred by vaccination among transplant candidates and recipients can be enhanced by accelerated or fourth booster doses of messenger RNA vaccines,51,52 even a fifth dose,53 and ring vaccination54 (priority and booster dosing of close household contacts of kidney transplant recipients).

The controversy of a vaccine mandate55,56 was shown in an electronic survey of 141 transplant centers in the United States,57 where mandatory vaccination before solid organ transplant was implemented in only 36% of the centers. The most commonly cited justifications for a mandate included stewardship (64%), public health obligations (52%), and a desire to reduce transmission risks to health care personnel (40%), other patients, and family members (40%).57 Almost none of the centers required clinical evidence showing vaccine responsiveness such as measurement of anti-SARS-CoV-2 spike
protein antibodies (although measurement is not universally available and not easy to interpret). To a certain extent, these results suggest that the predominant view is a strong recommendation for vaccination as opposed to a mandatory policy. Most bioethicists oppose mandatory vaccination as eligibility for transplant waitlisting; this is to uphold patient autonomy and avoid forced medical treatment. To align with the principle of informed consent, waitlisted transplant candidates should be allowed time and room for decision, even when the current evidence favors vaccination. There is no doubt that when mentally competent patients decline to receive a vaccine, compulsory vaccination before allowing kidney transplant violates the principle of autonomy. Although vaccination is in line with the principle of beneficence, denying transplantation has been considered to be in conflict with the principle of nonmaleficence toward an individual transplant candidate who does not want to receive vaccination. Respect for autonomy requires holding patients responsible for the consequences of their conscientious choice, which occasionally conflicts with other important ethical principles such as public interest and other patient safety concerns. The imperative to respect a transplant candidate’s right to informed consent, however, is not necessarily violating public interest. In fact, patients can opt for regular surveillance to be allowed hospitalization for transplant surgery. Part of the problem for this argument justifying equal candidacy for organ transplantation irrespective of SARS-CoV-2 vaccination status, of course, is the lack of evidence to support that regular surveillance can mitigate risk of infection to the hospital. Because the level of protection and optimal frequency of surveillance remains unknown, vaccination remains the safest and primary strategy to prevent SARS-CoV-2 (poor clinical outcomes of) infections from patients awaiting transplantation. In that case, respecting the personal choice to forego vaccination could have violated the principle of nonmaleficence because of the potential harm to other patients.

To turn the decision making from transplant centers to a transplant candidate: should he or she decline a kidney transplant offer and delay the transplantation to allow time for pretransplant vaccination optimization? A similar strategy of deferring rituximab B-cell–depletion therapy for 4 weeks after SARS-CoV-2 vaccination has been proposed. As opposed to drug therapy, a kidney transplantation will be more complicated. To assess the benefit or harm of delays in transplantation to facilitate pretransplant vaccination, a Markov microsimulation model has been created. In general, scenario analysis suggested a benefit to short delays in deceased donor transplants to receive the SARS-CoV-2 vaccine in waitlisted patients older than 55 years. In fact, delaying transplants for 6 months before a living donor transplant is estimated to yield effectiveness of 22.83 quality-adjusted life-years. However, caution should be exercised when delay to access of transplantation is expected to exceed 3 years (as in the case for deceased donor transplantation), or with a high Kidney Donor Risk Index of the eventual deceased donor transplantation. Notably, this Markov model included unadjusted probability of Covid-19 deaths (when the probability of dying from Covid-19 is more than two times higher in transplant recipients compared with dialysis patients). Another major criticism for the study is the (inappropriate) assumption that the probability of Covid-19 death in transplant recipients does not change according to vaccination status. In other words, the model could have underestimated the mortality in non-vaccinated transplant recipients.

Another argument against a vaccine mandate for kidney transplant candidates, as a result of recent drug development, is the emergence of therapeutic monoclonal antibodies. The current monoclonal antibodies (casirivimab and imdevimab, cilgavimab, and tixagevimab), however, have limited neutralizing activity against BA.1 and BA.2 omicron variants after administration to immunocompromised patients. Based on the suboptimal protection to protect kidney transplant recipients against infection, the arguments of moving from vaccine to monoclonal antibody as pre-exposure prophylaxis remain speculative. Regarding the use of monoclonal antibody such as cilgavimab and tixagevimab, another ethical issue would be the controversy of granting these drugs for transplant candidates who decline vaccination. Policy makers, transplant pharmacists, and doctors need to make decisions concerning the appropriate prevention measures. In other words, should transplant candidates get priority for the monoclonal antibody treatment if they decline SARS-CoV-2 vaccines? To address this issue, consideration should be given to the supply of monoclonal antibodies, effectiveness of the monoclonal antibodies for the predominant variants circulating in the community, and immune response of the patients to vaccines. From the standpoint of distributive justice, the weight assigned to the fair distribution of monoclonal antibodies to transplant candidates should be given due consideration of the inequalities that already existed among this cohort of patients who have higher infection rates, higher mortality rates, and less access to the health care. According to the National Institutes of Health guidelines in the United States, however, the monoclonal antibodies should not be considered a substitute for Covid-19 vaccination and, in particular, should not be used in unvaccinated individuals in whom Covid-19 vaccination is recommended and who are anticipated to have an adequate response. On the other hand, many transplant candidates face significant emotional and existential threats; emotional support and dedicated pretransplant patient education are fundamental to prepare and equip them with knowledge.
One ultimate and useful solution would be moving away from the language of mandated treatments and, instead, aiming to assess the risks and benefits on an individual basis.\textsuperscript{47} That would entail exploration and understanding the reasons behind any transplant candidates’ vaccine hesitancy. Vaccine acceptance has been found to decrease with financial hardship, younger age, less education, and among those with suspected past Covid-19 infection.\textsuperscript{66} Rather than a blanket policy of mandatory vaccination, doctors and transplant health care workers should aim to encourage, and not enforce, vaccination. In tandem with respect for autonomy, mutual trust plays a key role in the doctor–patient relationship, and more so in long-term dialysis or transplant care. An increasing body of literature suggests that one of the most effective means of communicating vaccine information to parents is through sharing anecdotes and nudging, in contrast to coercion.\textsuperscript{67,68} A more caring approach has been proposed. This approach, called the patient-centered trauma-informed approach,\textsuperscript{58} refers to the need to acknowledge a patient’s past trauma and its impact on patient interactions and treatment decision making. Instead of informing patients in terse letters that they are ineligible to receive a kidney transplant until they are vaccinated, the patient-centered trauma-informed approach calls for compassion, trustworthiness, collaboration, and dignity.\textsuperscript{75} As such, transplant health care workers and health authorities should work to improve the health literacy of kidney transplant candidates, and should listen actively to patients regarding their concerns and vaccine hesitancy.\textsuperscript{69} The bottom line is for the patients to meet trained clinicians and discuss their concerns. Other measures of protecting against infection, including proper hygiene and social distancing, also should be encouraged.

**Challenge 3: Should Vaccination of Transplant Health Care Workers Be Mandatory During Pandemic?**

The issue of mandating Covid-19 vaccination is less controversial for health care workers than patients, although such a policy could have been in tension with health care workers’ autonomy.\textsuperscript{70} As previously signed by more than 80 organizations, a joint statement representing physicians, nurses, pharmacists, physician assistants, nurse practitioners, epidemiologists, public health workers, and long-term care workers has called for universal vaccination of health workers.\textsuperscript{71} The rationale for such a mandate is based on three important reasons.\textsuperscript{71,72} First, it is considered a general ethical duty of health care workers to protect others. Second, getting vaccinated is considered a special duty to achieve professional objectives and be committed to putting patients first. Mandating health workers to have the vaccine, in short, implies a policy of mandatory assignment to different tasks within the hospital. Whether it is ethically acceptable to dismiss the health workers because they refuse vaccination is another issue. Third, this is not new but an extension of well-established and historical practices such as getting vaccinated against influenza, hepatitis B, and other infectious diseases. Indeed, large-scale longitudinal analysis of national data over 23 years recently showed that state laws promoting influenza vaccination for hospital workers were associated with reductions in annual pneumonia and influenza mortality by 1.92 deaths per 100,000 persons in the general population.\textsuperscript{73} The magnitude of population mortality reduction was especially obvious among elderly persons. Mandating SARS-CoV-2 vaccination for transplant health care workers is expected to protect the lives of vulnerable populations and build trust with the public. Genomic and epidemiologic investigations previously confirmed rapid nosocomial outbreaks of SARS-CoV-2 dissemination within the hospital setting triggered by asymptomatic health care workers, amplified by health care worker transmission to health care workers and patients.\textsuperscript{74} Health care workers have been shown repeatedly to be the previously hidden link between contact clusters in hospital environments.\textsuperscript{75}

In addition to the earlier-mentioned argument for health care workers to receive vaccination to protect patients, we also should be mindful of the workers’ autonomy and concerns. Efforts should be made to address the vaccine hesitancy (and more so when this overlaps with other disadvantages in the workplace). Flexibility of implementation, including the time frame for different types of employees (clinical staff versus clerical staff), a grace period before enhanced education and vaccine acceptance, and redeployment of employees, could be considered and subjected to the difference in cultural and legal settings.

**CONCLUSIONS**

The guiding principles for resource allocation including the delivery of kidney transplantation during the Covid-19 pandemic are relatively well established and supported by an ethical framework (Table 1). The dichotomy of continuation versus suspension of transplant activity should best be replaced by a stepwise approach (Table 2). The decision to continue or suspend transplant activity during the Covid-19 pandemic requires a risk-stratified approach strongly incorporating patient views. The decision on mandatory vaccination for kidney transplant candidates (Table 3) is much more controversial, partly owing to concerns regarding autonomy and violation of human rights. Arguments to mandate vaccination before transplant waiting lists are outweighed by arguments in favor of strongly recommending vaccination to patients but respecting their autonomous choices. We recommend moving away from coercion to encouragement of vaccination. After documented risk–benefit
discussions are held, based on trusted patient–clinician relationships, and on individual risk assessment of morbidity and mortality risk after transplantation, kidney transplantation should not be declined for people who do not wish to be vaccinated. In contrast, we found a stronger, but not necessarily agreed upon by all, ground for mandatory vaccination for transplant health care workers. The mandate for health care workers seems indisputable given the need to protect themselves and others. The debate is contentious, however, if this is associated with loss of jobs and when perceived as coercion and loss of autonomy.

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