Received: 4 May 2021 | Revised: 17 June 2021 | Accepted: 4 July 2021

DOI: 10.1111/ctr.14421

Clinical TRANSPLANTATION
The Journal of Clinical and Translational Research
WILEY

BRIEF COMMUNICATION

Ethical considerations regarding COVID-19 vaccination for transplant candidates and recipients

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Abstract

Solid organ transplant (SOT) candidates and recipients were not included in the COVID-19 vaccine trials that have justified vaccine administration to millions worldwide and will be critical to ending the pandemic. The risks of COVID-19 for SOT candidates and recipients combined with data about this population's response to other vaccines has led to transplant centers recommending vaccination for their candidates and recipients in accordance with guidance from major transplant organizations. Relevant ethics considerations include: weighing the low risk of vaccination causing transplant complications against potentially limited antibody response of vaccines for transplant recipients; the equitable distribution of vaccines among vulnerable populations; the duty to steward and respect organs as limited resources; the duty to support vaccination; and patient autonomy. Vaccinated transplant patients and candidates should also consider participating in research studies to better understand the efficacy and potential long-term risks in this patient population. There are difficult scenarios, like timing transplant after second vaccine dose, when to administer the second dose to a partially vaccinated candidate who gets an organ match, whether to vaccinate a recent transplant recipient with low exposure risk and which vaccine to use. Here we provide ethics considerations for vaccinating different groups within the transplant population.

KEYWORDS
COVID-19 vaccine, ethics, health policy, transplantation

Solid organ transplant (SOT) recipients were not included in the COVID-19 vaccine trials that have justified their administration to millions worldwide and will be critical to ending the pandemic. Many transplant centers are now recommending vaccination to their candidates and recipients in accordance with guidance from major transplant organizations because of the severe risks of COVID-19 for SOT recipients combined with data about this population's response to other vaccines. Yet several questions remain. What are the risks of COVID-19 vaccination for graft survival? Do transplant recipients develop adequate immune responses from vaccination? How should transplantation be timed with candidate vaccination schedule? What is the right course of action to protect the recipient, steward organs, and promote vaccination generally? Here we will discuss the latest data on vaccine risks and effectiveness for transplant recipients, United States policy approaches, and different ethics approaches to decision making for vaccinating different groups within the transplant population.

While trials demonstrated that the Pfizer and Moderna vaccines are 94.1–95% effective at preventing severe illness in immunocompetent people, transplant patients generally demonstrate a less robust response to most vaccines[1,2] due to the use of T-cell and B-cell depleting agents used in induction and maintenance immunosuppression regimens after transplantation as well as those used for the treatment of

rejection. There has also been concern expressed that vaccines might contribute to organ rejection, though this has not been confirmed with prior vaccines.[3] However, the mRNA mechanism employed by two of the vaccines currently approved for emergency use is different from all other previously licensed vaccines, so it is difficult to make any strict inferences about mechanistic risks for these vaccines. The Johnson and Johnson vaccine uses a more traditional vaccine platform, and previously approved vaccines demonstrate very low risk of associated rejection episodes.[4]

Johns Hopkins researchers recently published preliminary data from close to 200 transplant recipients suggesting the Pfizer and Moderna COVID-19 vaccines have not caused early signs of rejection and that the reactogenicity profile for this population is mild, similar to older adults.[5] The study also suggests that antibody response to vaccines is lower for this population, but this does not necessarily mean lack of benefit. Because both mRNA vaccines demonstrate significant protection in studied populations only 7 days after complete vaccination, it is likely that protection is conferred at least in part from cellular immunity regardless of humoral immunity.[6] This means it is critical to study antibody and cellular responses in transplant recipients further. Although there is reason to believe that transplant recipients might have impaired immune responses after vaccination, the risks of being vaccinated appear low and the risks of COVID-19 are, for many, high. Further, while vaccination may not prevent COVID-19 entirely, studies have demonstrated significant prevention of severe COVID-19 in the general population, which is an important consideration for decreasing risk of morbidity and mortality in transplant patients. For transplant candidates, prevention of severe COVID-19 can also help prevent significant delays in timing of their transplantation.

Accordingly, current guidance from the American Society of Transplantation, the International Society of Heart and Lung Transplantation, and the American Society of Transplant Surgeons, all generally recommend vaccinating transplant recipients because of their higher risk of severe illness and death from COVID-19.[7–9] Ideally, the vaccine regimen should be completed at least 2 weeks prior to transplant, and if not possible, administered after an interval of at least 1 month following transplant.

Each state in the United States took a different approach to prioritizing transplant recipients and candidates. Some explicitly included recipients in early phases, some explicitly included dialysis patients, some implicitly included them by prioritizing immunosuppressed patients or those at high risk of severe illness due to underlying conditions. Few guidelines mention families or intimate caregivers. At this point in the pandemic, all adult transplant recipients and candidates in the United States are eligible to receive the vaccine.

From a utilitarian approach, weighing the risks and benefits of vaccinating this population requires consideration of many variables: (1) Likelihood and severity of COVID-19; (2) Likelihood and severity of side-effects from vaccination; and (3) Likelihood and strength of benefits from vaccination. For most transplant recipients and candidates, the likelihood and severity of infection are both high. Studies suggest transplant recipients are at greater risk of severe illness and death from COVID-19 than the general population,[10] and their compromised immune systems might mean they are more likely to contract the virus. Data so far suggests low risk from actual vaccination for this population.[5] It is unclear how variants of concern impact vaccine efficacy in immunocompromised people; however, some vaccines confer significant protection against some variants for the general population.[11] While the degree of benefit conferred by a vaccine is not known and could be lower than for the general population, the likelihood of at least partial response, higher risk of severe disease, and risk of spreading SARS-CoV-2 variants strongly lean in favor of vaccination.

From a deontological or duty-based approach, vaccinating transplant recipients and candidates will also contribute more information to the understanding of risks and benefits, which is critical, as long as this data can be systematically tracked. To the extent that vaccination might confer benefit and is low risk, transplant recipients should pursue vaccination out of respect for the gift of life that organ donation confers. There is also a duty to demonstrate strong support for vaccination across all populations for whom it will not create undue risk. For vaccinated transplant recipients, the burden of agreeing to monitored outcomes through research is low and the benefits of understanding vaccine effectiveness for future transplant recipients is immense. There is also potential direct benefit for vaccinated transplant recipients for participating in research that may inform the need for booster vaccine doses for themselves. Accordingly, all vaccinated transplant candidates and recipients should consider participating in vaccination studies. These approaches will hopefully also have some impact on high levels of vaccine hesitancy.

There will be a number of situations for which this guidance might need modification. The United States now has adequate supply to vaccinate those who are willing whereas other countries still face significant supply shortage. Emerging data regarding low risk to transplant recipients should favor granting this population priority status, but perhaps slightly lower than for populations with high risk of severe disease who also demonstrate strong antibody responses. Other modification scenarios could concern timing of transplant in relation to vaccination, and different platforms of vaccines or booster doses. This includes determining when to give the second dose to transplant candidates who have been partially vaccinated with an mRNA vaccine but then receive an organ offer, and when to transplant candidates after completing a vaccine series. Clearly, the duty to promote the patient's health is preeminent. Patients should be transplanted as soon as safe and feasible, and should be protected from COVID-19 risk to the greatest extent possible regardless of vaccination status. Generally, the opportunity to transplant should not be forgone in favor of vaccination. Timing might be more flexible for transplant recipients with living donors.

These decisions will need to be individualized based on each patient's clinical acuity and underlying illness. Patients with severe end-stage organ disease often have poor vaccine responses.[1,2,12] Transplant patients with very low exposure risk might not need to consider vaccination as strongly. An example might be individuals living in isolated settings with exposure only to vaccinated individuals who have very low outside interaction in communities with low disease incidence. At least one vaccine has now been authorized for younger pop-

ulations, but to date children and adolescents tend to be at lower risk for severe COVID-19. There are significant knowledge gaps regarding utility and safety for vaccines for other diseases in the pediatric transplant population.[13] These patients should only be offered vaccines approved for their age group, and further research should lead to pediatric COVID-19 vaccination guidelines.

We must also consider how hard to urge vaccine-hesitant transplant candidates to proceed with vaccination. Part of prioritizing patient health is promoting patient trust. Vaccine-hesitant patients should be provided with sufficient information about vaccine safety and COVID-19 risk without force or judgment, and they should be allowed to make their own decisions.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Brendan Parent drafted article. Sapna A. Mehta provided concept for article and critical revision. Arthur Caplan provided critical revision and approval of article.

DISCLOSURES

Brendan Parent receives salary support in the form of a gift from United Therapeutics.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this as no new data were created or analyzed in this study.

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REFERENCES

1. Aggeletopoulou I, Davoulou P, Konstantakis C, Thomopoulos K, Triantos C. Response to hepatitis B vaccination in patients with liver cirrhosis. *Rev Med Virol*. 2017;27(6):e1942.
2. Krueger KM, Ison MG, Ghossein C. Practical guide to vaccination in all stages of CKD, including patients treated by dialysis or kidney transplantation. *Am J Kidney Dis*. 2020;75(3):417-425.
3. Schaffer SA, Husain S, Delgado DH, Kavanaugh L, Ross HJ. Impact of adjuvanted H1N1 vaccine on cell-mediated rejection in heart transplant recipients. *Am J Transplant*. 2011;11(12):2751-2754.
4. Mulley WR, Dendle C, Ling JEH, Knight SR. Does vaccination in solid-organ transplant recipients result in adverse immunologic sequelae? A systematic review and meta-analysis. *J Heart Lung Transplant*. 2018;37:844-852.
5. Boyarsky BJ, Ou MT, Greenberg RS, Teles AT, Werbel WA, Avery RK, Massie AB, Segev DL, Garonzik-Wang JM. Safety of the first dose of SARS-CoV-2 vaccination in solid organ transplant recipients. *Transplantation*. 2021;105(5):e56-7.
6. Hartzell S, Bin S, Benedetti C, et al. Evidence of potent humoral immune activity in COVID-19-infected kidney transplant recipients. *Am J Transplant*. 2020;20(11):3149-3161.
7. COVID-19 vaccine FAQ sheet. American Society of Transplantation. https://www.myast.org/sites/default/files/Education/2021%2003%2002%20COVID19%20VACCINE%20FAQS_update%20v4%20FINAL%20%281%29.pdf. Published March 2, 2021. Accessed March 5, 2021.
8. Guidance from the International Society of heart and lung transplantation regarding the SARS CoV-2 pandemic. The International Society of Heart and Lung Transplantation. https://ishlt.org/ishlt/media/documents/SARS-CoV-2_Guidance-for-Cardiothoracic-Transplant-and-VAD-center.pdf. Published March 5, 2021. Accessed February 1, 2021.
9. Transplant capacity in the COVID-19 era and early vaccine recommendations. American society of transplant surgeons. https://asts.org/advocacy/covid-19-resources/asts-covid-19-strike-force/transplant-capacity-in-the-covid-19-era#.YEKAXI1Kgc8. Published December 3, 2020. Accessed March 5, 2021.
10. Pereira MR, Mohan S, Cohen DJ, et al. COVID-19 in solid organ transplant recipients: initial report from the US epicenter. *Am J Transplant*. 2020;20(7):1800-1808.
11. Bian L, Gao F, Zhang J, et al. Effects of SARS-CoV-2 variants on vaccine efficacy and response strategies. *Expert Rev Vaccines*. 2021;20(4):365-373.
12. Mastalerz-Migas A, Gwiazda E, Brydak LB. Effectiveness of influenza vaccine in patients on hemodialysis–a review. *Med Sci Monit*. 2013;19:1013-1018.
13. Dulek DE, De St Maurice A, Halasa NB. Vaccines in pediatric transplant recipients—past, present, and future. *Pediatr transplant*. 2018;22(7):e13282.

How to cite this article: Brendan Parent, Arthur Caplan, Sapna A. Mehta. Ethical considerations regarding COVID-19 vaccination for transplant candidates and recipients. *Clin Transplant*. 2021;35:e14421.
https://doi.org/10.1111/ctr.14421