

COVID-19 vaccination timing and kidney transplant waitlist management: An international perspective

Yasar Caliskan¹  | David Axelrod²  | Alexis Guenette¹  | Ngan N. Lam³  |
Vivek Kute⁴  | Tarek Alhamad⁵  | Mark A. Schnitzler¹  | Krista L. Lentine¹ 

¹ Saint Louis University Center for Abdominal Transplantation, St. Louis, Missouri, USA

² University of Iowa/Transplant Institute, Iowa City, Iowa, USA

³ Division of Nephrology, Cumming School of Medicine, University of Calgary, Calgary, Canada

⁴ Sciences, Institute of Kidney Diseases and Research Center and Dr. H L Trivedi Institute of Transplantation, Ahmedabad, India

⁵ Washington University in St. Louis, St. Louis, Missouri, USA

Correspondence

Krista L. Lentine, Saint Louis University Transplant Center, 1201 S. Grand Blvd., St. Louis, MO 63104, USA.

Email: krista.lentine@health.slu.edu

Funding information

National Institutes of Health, Grant/Award Number: R01DK120518

Abstract

Background: The coronavirus disease 2019 (COVID-19) pandemic has created unprecedented challenges for solid organ transplant programs worldwide. The aim of this study is to assess an international perspective on challenges faced by kidney transplant programs.

Methods: We administered an electronic survey instrument from January 3, 2021 to June 8, 2021 to staff at transplant programs outside the United States that comprised of 10 questions addressing the management of kidney transplant candidates with asymptomatic COVID-19 infection or unvaccinated who receive an organ offer.

Results: Respondents ($n = 62$) represented 19 countries in five continents. Overall, 90.3% of respondents encourage vaccination on the waiting list and prior to planned living donor transplant. Twelve percent of respondents reported that they have decided to inactivate unsensitized candidates (calculated panel reactive antibody, cPRA <80%) until they received the two doses of vaccination, and 7% report inactivating candidates who have received their first vaccine dose pending receipt of their second dose. The majority (88.5%) of international respondents declined organs for asymptomatic, nucleic acid testing (NAT)+ patients during admission without documented prior infection. However, 22.9% of international respondents proceeded with kidney transplant in NAT+ patients who were at least 30 days from initial diagnosis with negative chest imaging.

Conclusions: Practitioners in some countries are less willing to accept deceased donor organs for waitlist candidates with incomplete COVID-19 vaccination status and to wait longer before scheduling living donor transplant, compared to United States practices. Access to vaccinations and other resources may contribute to these differences. More research is needed to guide the optimal approach to vaccination before and after transplant.

KEYWORDS

COVID-19, kidney transplantation, offer acceptance, pandemic, practices, vaccination, waitlist management

1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic is a global challenge that requires an international response.¹ We recently conducted a national survey of United States (U.S.) kidney transplant programs and found that despite recommendations,^{2,3} very few U.S. centers are requiring pretransplant COVID-19 vaccination. In contrast to immunocompetent participants in vaccine trials,^{4,5} solid organ transplant recipients have low immunization rates after receiving two doses of messenger RNA (mRNA)-based vaccines.^{1,6} Immunosuppressive drugs appear to attenuate the immune response to vaccination in kidney transplant recipients.⁶ Many centers are proceeding with transplant in patients with persistently positive COVID-19 tests after clinically resolved infection, based on presumption that sustained positive tests reflect prolonged viral shedding rather than active infection, although uncertainty remains.⁷ The landscape of practice continues to evolve with emerging data on the benefits of vaccine boosters in the immunosuppressed population.^{8–10} These complex considerations have created operational challenges for decision-making related to the timing of transplantation in relation to vaccination and recovery from COVID-19 infection. To capture a broadened perspective from practitioners in other parts of the world, we designed and administered the electronic survey successfully used among U.S. programs,⁷ to staff (nephrologists, surgeons, coordinators, other staff) at kidney transplant programs outside the U.S. from January 3, 2021 to June 8, 2021.

2 | METHODS

2.1 | Survey design

The survey instrument comprised of 10 questions addressing the management of kidney transplant candidates with asymptomatic COVID-19 infection who receive an organ offer as well as deceased donor transplant candidates who are not yet vaccinated (Table 1). The survey also queried information on the participant role (nephrologist, transplant surgeon, clinical coordinator, social worker, administrator, or other) at the transplant center. This study was approved by the Saint Louis University Institutional Review Board (Protocol # 31284).

2.2 | Survey administration

The target population was healthcare providers at active international kidney transplant centers. U.S. results were collected first and reported separately.⁷ International participants were recruited from kidney transplant programs in Africa, Asia, Europe, North and South America. Potential participants were derived from the investigators' professional connections and the survey was emailed through the Qualtrics Survey Software. Opportunity for self-elected participation through a Qualtrics link was also posted to professional society list serves including that of the American Society of Transplantation (AST) Outstanding Questions in Transplantation (which includes international mem-

bership), the Turkish Society of Nephrology, and the Canadian Blood Services Living Donation Advisory Committee.

2.3 | Statistical analysis

Each program was represented only once in the analysis. For programs with multiple respondents, we selected a single participant to represent the program using our algorithm in previous studies.⁷ Responses to each survey question were described with percentages and frequencies. To obtain rates, we divided the number of program responses by the total number of programs who responded to the question, such that percentages reflect proportions of respondents, as per previous methods.^{1,7} For questions where participants were asked to "select all that apply," the denominator for calculating percentages was the number of participants responding to that question. All analyses were performed using R for windows version 1.2.5042 (RStudio Inc., Boston, MA, USA).

3 | RESULTS

Respondents ($n = 62$) represented 19 countries in five continents. The majority of the participants were transplant nephrologists (75.8%), followed by transplant surgeons (8.1%), coordinators (3.2%), and pharmacists (3.2%), while 9.7% were other transplant professionals.

Overall, 90.3% of respondents at international centers encourage vaccination for all patients on the waiting list and prior to planned living donor transplants (Table 1). Twelve percent of respondents reported that they have decided to inactivate unsensitized candidates (calculated panel reactive antibody, cPRA <80%) until they received the two doses of vaccination, and 7% report inactivating candidates who have received their first vaccine dose pending receipt of their second dose. Management of organ offers for asymptomatic patients who were found to be COVID-19+ with and without prior infection are similar in U.S.⁷ and international survey responses. International participants appeared more conservative for deceased donor acceptance among waitlisted patients in the context of the pandemic. Inactivation of patients with cPRA <80% until they receive a complete two-dose vaccine course was higher in international participants compared to U.S. participants (11.7% vs. 1.1%) (Figure 1A). Acceptance of organs for unvaccinated patients who are not highly sensitized, followed by vaccination 4–12 weeks after transplant, was also a less common practice in international compared to U.S. centers (66.7% vs. 83.7%). Although none of the U.S. centers reported inactivating highly sensitized patients with cPRA \geq 80% until they receive complete two-dose vaccine course, 16.9% of international participants inactivate these highly sensitized patients pending complete vaccination (Figure 1B). More than half of the international respondents (52.5%) wait >4 weeks after completion of a recipient candidate's vaccination to schedule a living donor kidney transplant, while 35.8% of U.S. respondents wait >4 weeks. Regarding deceased donor transplants, most of the international respondents (87.5%) recommend recipients to wait

TABLE 1 Transplant practices related to vaccination status

	% (n)
How do you educate your kidney transplant candidates regarding acceptance of COVID-19 vaccine, when available? (N = 62)	
We encourage vaccination on the waiting list and prior to planned living donor transplant	90.3% (56)
We counsel that benefits and risks are uncertain in the transplant population and defer to patient preference	17.7% (11)
We request that patients contact the transplant center after receiving the vaccine	12.9% (8)
Other	3.2% (2)
How are you tracking vaccination status of candidates on your waiting list? (N = 59)	
Asking patient at time of organ offer	45.8% (27)
Asking all listed patients to update their coordinator after vaccination	42.4% (25)
Directed inquires by program staff	28.8% (17)
Other	10.2% (6)
How long is your center waiting after completion of a recipient's vaccination to schedule a living donor kidney transplant (N = 61)	
0–2 weeks	11.5% (7)
>2–4 weeks	36.1% (22)
>4–8 weeks	37.7% (23)
>8 weeks	14.8% (9)
For those not vaccinated prior to transplant, how long after deceased donor transplant do you recommend recipients wait to receive their first dose of COVID-19 vaccination? (N = 59)	
0–2 weeks	1.7% (1)
>2–4 weeks	11.9% (7)
>4–8 weeks	46.8% (27)
>8 weeks	40.7% (24)
For asymptomatic patients called in for deceased donor transplant without prior documented COVID-19 infection and positive nasopharyngeal swabs, which of the following best describes your current practice? (N = 61)	
Decline the organ, inactive and delay transplant until the patient has negative COVID-19 screens	70.5% (43)
Decline the organ, inactive and delay transplant for at least 30 days, without rescreening	18.0% (11)
Obtain pulmonary imaging (e.g., CT scan) and if clear, proceed with transplant after informed consent and counseling of the recipient	6.6% (4)
Check antibody levels and if antibodies are present (suggesting immunity), proceed with transplant	6.6% (4)
Other	8.2% (5)
For asymptomatic patients called in for deceased donor transplant with prior documented COVID-19 infection (>30 days) and positive nasopharyngeal swabs, which of the following best describes your current practice? (N = 61)	
Decline the organ, inactivate and delay transplant until the patient has negative COVID-19 screens	60.7% (37)
Obtain pulmonary imaging (e.g., CT scan) and if clear, proceed with transplant after informed consent and counseling of the recipient	22.9% (14)
Check antibody levels and if antibodies are present (suggesting immunity), proceed with transplant	16.4% (10)
Other	13.1% (8)

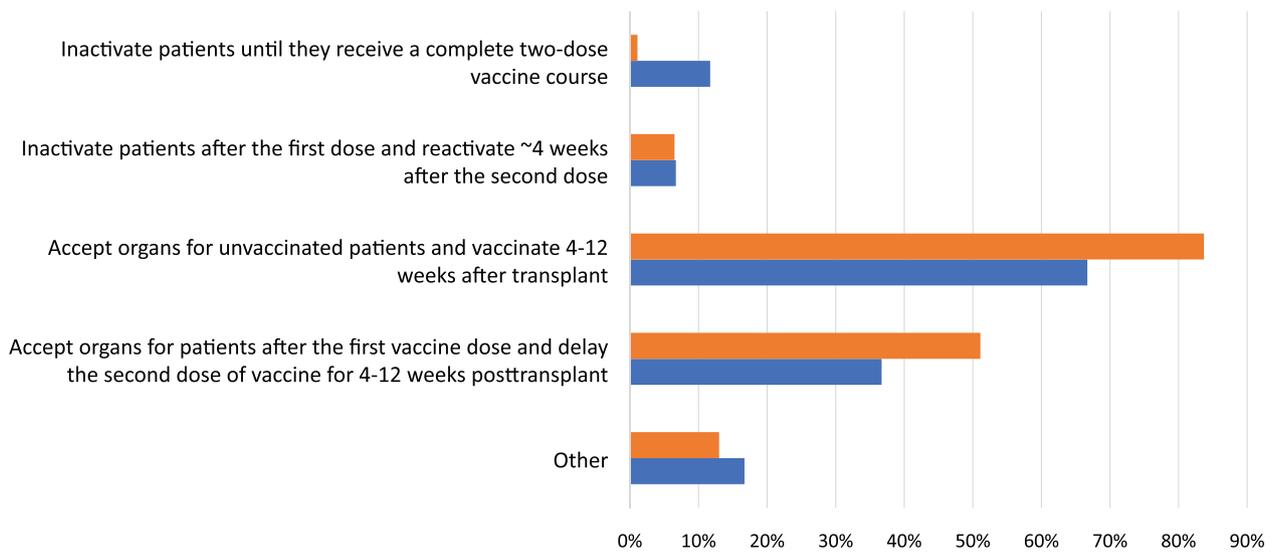
Note: 'N=' indicates the item denominator, based on number of respondents, and accounting for contingent responses. Abbreviations: COVID-19, coronavirus disease 2019; CT, computed tomography scan.

>4 weeks after deceased donor transplant to receive their first dose of COVID-19 vaccination. The majority (88.5%) of international respondents declined organs for asymptomatic patients without documented prior infection who were found to have positive nasopharyngeal swab nucleic acid testing (NAT)+ during admission for transplant. However, 22.9% of international respondents proceeded with kidney transplant in NAT+ patients on admission who were at least 30 days from initial diagnosis with negative chest imaging (Table 1).

4 | DISCUSSION

COVID-19 pandemic has been a global concern for public health and has overwhelming impacts on organ transplantation.^{1,5,7} During the initial pandemic period, transplantation volume in the majority of the countries including U.S., France, and Spain were reduced as 51%, 90%, and 87%, respectively.^{11,12} This profound impact of COVID-19 on transplantation may have potentially devastating effects on patients

A. Patients on deceased donor waiting list who are **not highly sensitized (cPRA <80%)**



B. Patients on deceased donor waiting list who are **highly sensitized (cPRA ≥80%)**

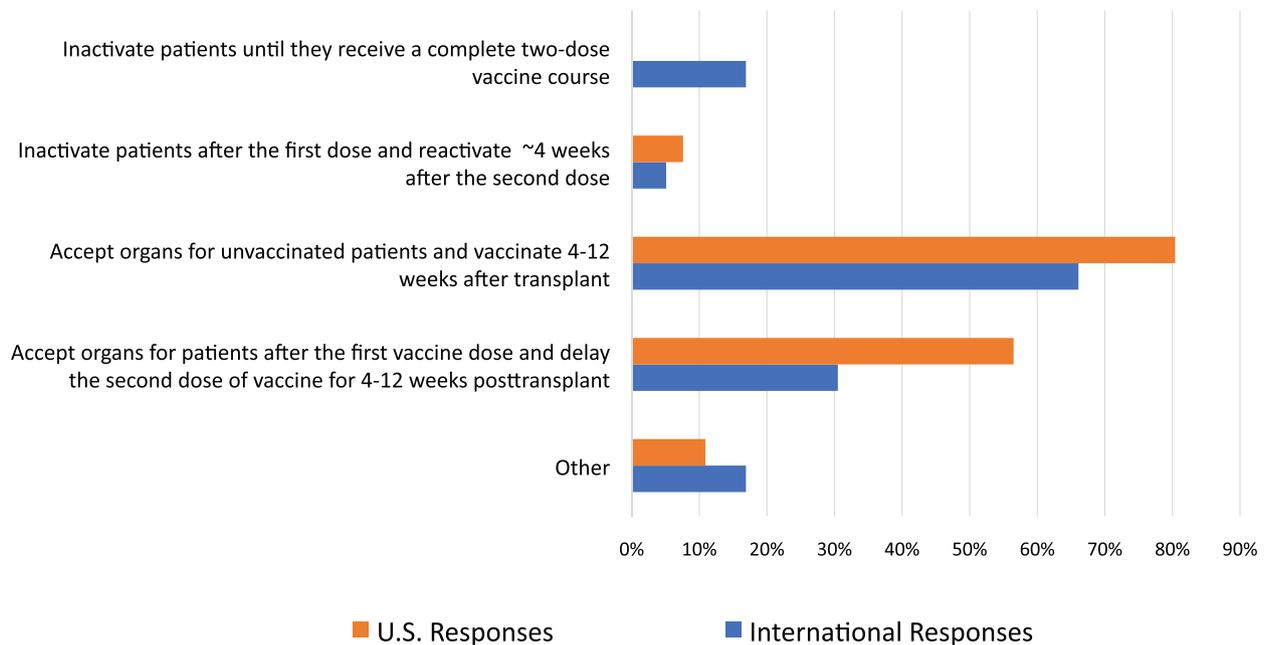


FIGURE 1 (A) International versus United States responses for management of candidate vaccination status with regard to transplant acceptance for non-highly sensitized (calculated panel reactive antibody, cPRA <80%) patients on deceased donor waiting list. (B) International versus United States responses for management of candidate vaccination status with regard to transplant acceptance for highly sensitized (cPRA ≥80%) patients on deceased donor waiting list. Respondents to the international survey ($n = 62$) included practitioners in: Turkey ($n = 18$; 29%), Canada ($n = 14$; 22.6%), India ($n = 12$; 19.4%), Morocco ($n = 2$; 3.2%), Spain ($n = 2$; 3.2%), Argentina ($n = 1$; 1.6%), Bolivia ($n = 1$; 1.6%), Egypt ($n = 1$; 1.6%), Germany ($n = 1$; 1.6%), Guatemala ($n = 1$; 1.6%), Italy ($n = 1$; 1.6%), Mauritania ($n = 1$; 1.6%), Norway ($n = 1$; 1.6%), Poland ($n = 1$; 1.6%), Portugal ($n = 1$; 1.6%), Saudi Arabia ($n = 1$; 1.6%), Ukraine ($n = 1$; 1.6%), United Kingdom ($n = 1$; 1.6%), and Vietnam ($n = 1$; 1.6%)

on transplant waitlist. The results of this international survey suggest that practitioners in some countries are less willing to accept deceased donor organs for waitlist candidates with incomplete COVID-19 vaccination status and to wait longer before scheduling living donor transplant, compared to U.S. practices. These practice differences may be impacted by lower COVID-19 vaccination rates compared to U.S. in the participant countries and differences in access to supportive care in the event that a patient contracts COVID-19 after transplantation.¹³

While the number of respondents was limited, a broadened perspective can be drawn from this survey results. Patients with end stage kidney disease may have more a robust response to vaccines before rather than after kidney transplant,¹⁴ and when possible, SARS-CoV-2 vaccines should be given before transplantation.¹⁴ In ideal way, transplant candidates should be tried to be completely vaccinated while they are awaiting transplant. In general, vaccines are recommended for completion at least 2 weeks prior to transplantation or starting at 1 month after transplantation.¹⁴ Despite this recommendation even acceptance of organs for unvaccinated candidates followed by vaccination 4–12 weeks after transplant, was also a less common practice in international compared to U.S. centers. One-sixth of international participants inactivate highly sensitized patients pending complete vaccination. More than half of the international respondents wait more than a month after completion of a recipient candidate's vaccination to schedule a living donor kidney transplant. Access to vaccinations and other resources may contribute to these differences. Reliable access to timely, accurate information on the status of deceased donor viral infection is also essential to inform decisions on organ acceptance and ensure optimal organ utilization.¹⁵

Vaccine mandate and management of patients who refuse vaccination is a timely and controversial topic. Our U.S. study found that in Spring 2021, most U.S. transplant programs were encouraging vaccination but were not routinely delaying deceased donor transplant to complete a full vaccination.⁷ Updated surveys focused directly on this topic in current practice are underway. Antibody testing of patients with a history of COVID-19 infection or vaccination is another important topic. Currently, the Transplant Infectious Disease (TID) section of The Transplantation Society (TTS) does not recommend serologic antibody testing given the level of protective antibody and duration of serologic protection have not yet been defined, particularly in the transplant population.³ There are a range of assays with different targets, not all detect neutralizing antibodies, and most do not provide results with titers. The presence of antibodies may also represent reaction to vaccine but not protection from infection. The Organ Procurement and Transplantation Network (OPTN) concluded that at this time, there is insufficient evidence to support the use of SARS-CoV-2 antibody donor testing as a marker for assessing safety or potential transmission risk to recipients.¹⁶

Our study has limitations. Respondents were identified by online outreach to limited transplant professionals in limited number of countries, and not all programs are represented. These survey data reflect the opinions and experiences of the respondents at the time of completion, and given the rapidly dynamic nature of the COVID-19 pandemic, may not be reflective of subsequent practice and when COVID-

19 vaccines are more widely available particularly the management of patients who receive the three-dose vaccination regimen.

In conclusion, transplant practitioners in some countries are less willing to accept deceased donor organs for waitlist candidates with incomplete COVID-19 vaccination status and to wait longer before scheduling living donor transplant, compared to U.S. practices. More research is needed to inform the risks and benefits of these practices, guide the optimal approach to vaccination before and after transplant including the emerging use of vaccine boosters, and the timing of transplantation in patients with recovered COVID-19 in all practice settings.^{8–10}

ACKNOWLEDGMENTS

The authors thank survey respondents, including members of the Turkish Society of Nephrology (TSN), Canadian Society of Transplantation (CST), CST Kidney Transplant Group, Indian Society of Organ Transplantation (ISOT), and the American Society of Transplantation (AST) Outstanding Questions in Transplantation list serves. We also thank the AST Education Committee for review of the survey instrument. K.L.L. is supported by the Mid-America Transplant/Jane A. Beckman Endowed Chair in Transplantation. M.A.S. and K.L.L. receive research support related to kidney transplantation from the National Institutes of Health (R01DK120518).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Y.C., D.A., and K.L.L. participated in study design, analysis, interpretation, and writing of the manuscript. A.G., N.N.L., V.K., T.A., and M.A.S. participated in interpretation, and manuscript review/critical editing.

ORCID

Yasar Caliskan  <https://orcid.org/0000-0003-3816-8047>

David Axelrod  <https://orcid.org/0000-0001-5684-0613>

Alexis Guenette  <https://orcid.org/0000-0001-5804-4506>

Ngan N. Lam  <https://orcid.org/0000-0002-0129-7091>

Vivek Kute  <https://orcid.org/0000-0002-0002-2854>

Tarek Alhamad  <https://orcid.org/0000-0003-4289-0817>

Mark A. Schnitzler  <https://orcid.org/0000-0001-8547-5643>

Krista L. Lentine  <https://orcid.org/0000-0002-9423-4849>

REFERENCES

1. Salvalaggio PR, Ferreira GF, Caliskan Y, et al. An international survey on living kidney donation and transplant practices during the COVID-19 pandemic. *Transpl Infect Dis*. 2021;23(2):e13526.
2. AST. American Society of Transplantation. *Statement on COVID-19 vaccination in solid organ transplant recipients*. 2021. Accessed September 3, 2021. <https://www.myast.org/sites/default/files/06.2-21%20ISHLT%20AST%20COVID-19%20vaccine%20statement%20v10%20CLEAN.pdf>
3. TTS. The Transplantation Society Transplant Infectious Disease Section. *Guidance on coronavirus disease 2019 (COVID-19) for transplant clinicians*. 2021. Accessed September 3, 2021. https://tts.org/index.php?option=com_content&view=article&id=749&Itemid=140

4. Walsh EE, Frenck RW, Falsey AR, et al. Safety and immunogenicity of two RNA-based Covid-19 vaccine candidates. *N Engl J Med*. 2020;383(25):2439-2450.
5. Lentine KL, Vest LS, Schnitzler MA, et al. Survey of US living kidney donation and transplantation practices in the COVID-19 era. *Kidney Int Rep*. 2020;5(11):1894-1905.
6. Boyarsky BJ, Werbel WA, Avery RK, et al. Antibody response to 2-dose SARS-CoV-2 mRNA vaccine series in solid organ transplant recipients. *JAMA*. 2021;325(21):2204-2206.
7. Axelrod DA, Ince D, Harhay MN, et al. Operational challenges in the COVID era: asymptomatic infections and vaccination timing. *Clin Transplant*. 2021:e14437.
8. Hall VG, Ferreira VH, Ku T, et al. Randomized trial of a third dose of mRNA-1273 vaccine in transplant recipients. *N Engl J Med*. 2021;385:1244-1246.
9. Kamar N, Abravanel F, Marion O, Couat C, Izopet J, Del Bello A. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. *N Engl J Med*. 2021;385(7):661-662.
10. Ducloux D, Colladant M, Chabannes M, Yannaraki M, Courivaud C. Humoral response after 3 doses of the BNT162b2 mRNA COVID-19 vaccine in patients on hemodialysis. *Kidney Int*. 2021;100(3):702-704.
11. Loupy A, Aubert O, Reese PP, Bastien O, Bayer F, Jacquelinet C. Organ procurement and transplantation during the COVID-19 pandemic. *Lancet*. 2020;395(10237):e95-e96.
12. Rodrigo E, Minambres E, Gutierrez-Banos JL, Valero R, Belmar L, Ruiz JC. COVID-19-related collapse of transplantation systems: a heterogeneous recovery? *Am J Transplant*. 2020;20(11):3265-3266.
13. Mathieu E, Ritchie H, Ortiz-Ospina E, et al. A global database of COVID-19 vaccinations. *Nat Hum Behav*. 2021;5(7):947-953.
14. Danziger-Isakov L, Kumar D, AST ID Community of Practice. Vaccination of solid organ transplant candidates and recipients: guidelines from the American society of transplantation infectious diseases community of practice. *Clin Transplant*. 2019;33(9):e13563.
15. Lentine KL, Singh N, Woodside KJ, et al. COVID-19 test result reporting for deceased donors: emergent policies, logistical challenges, and future directions. *Clin Transplant*. 2021;35(5):e14280.
16. OPTN (Organ Procurement and Transplantation Network) summary of current evidence and information – donor SARS-CoV-2 testing & organ recovery from donors with a history of COVID-19. 2021. Accessed October 19, 2021. <https://optn.transplant.hrsa.gov/media/kkhn1wah/sars-cov-2-summary-of-evidence.pdf>

How to cite this article: Caliskan Y, Axelrod D, Guenette A, et al. COVID-19 vaccination timing and kidney transplant waitlist management: An international perspective. *Transpl Infect Dis*. 2022;24:e13763. <https://doi.org/10.1111/tid.13763>