Solid Organ Transplantation From Donors With COVID-19 Infection

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Solid organ transplantation (SOT) has suffered since the beginning of the COVID-19 pandemic, chiefly through a reduction in transplant activity and the high mortality in SARS-CoV-2–infected SOT candidates and recipients.[1] It was inferred that COVID-19 infection immediately after SOT acquired from an infected donor would have mortality rates higher than 5% to 50% reported in unvaccinated SOT recipients infected at various durations posttransplant.[1] In an effort to reduce the likelihood of donor-derived infection, the initial policy of most jurisdictions was routine SARS-CoV-2 polymerase chain reaction (PCR) testing for all solid organ donors at least from an upper respiratory tract swab, with advice to consider transplantation with organs from SARS-CoV-2–infected donors only if donors were many weeks after symptom onset, had clinically recovered, and had negative PCR tests.[2] These policies effectively prevented SARS-CoV-2 donor-derived infection,[3] apart from documented instances of transmission through lung transplantation where upper respiratory tract PCR was negative and lower respiratory tract (LRT) PCR had not been prospectively performed but was positive when tested retrospectively.[4,5]

Concurrently, transplantation activity reduced dramatically through the pandemic, driven by factors such as a reduced number of donors, reduced intensive care unit capacity, and suspension of transplant activity.[1] The transplant community was encouraged by the lack of SARS-CoV-2 transmission and generally good organ function from initial reports of 68 transplants from 58 donors with prior SARS-CoV-2 infection and negative PCR tests at procurement.[6] Transplant physicians are familiar with risk–benefit analysis and regularly need to push clinical boundaries for unstable waitlisted patients in the context of organ shortages, leading to nonlung SOT from donors infected with SARS-CoV-2 earlier from symptom onset and with positive PCR tests. Reassuringly, SARS-CoV-2 transmission did not occur in 25 nonlung transplants from 15 donors with positive PCR tests at the time of procurement.[6] Some of these recipients may have had immunity from prior infection or vaccination, and some received prophylactic monoclonal antibodies or remdesivir.[7] Regardless of the recipient's immunity status, SARS-CoV-2 has not been definitively transmitted through nonlung organs or blood products despite the presence in such organs of SARS-CoV-2 RNA, virus-like particles, positive immunohistochemistry against SARS-CoV-2 antigens, and, in a small number of instances, markers of viral infectivity.[8] Although SARS-CoV-2 viral load or PCR cycle threshold (Ct) values have some association with positive SARS-CoV-2 culture as a potential marker of infectivity,[9] these results demonstrate high interindividual variability in persons recovering from COVID-19.[9,10] As such, quantitative SARS-CoV-2 results are not emphasized in the conditions for release from isolation in public health guidelines[11] and are of uncertain utility in determining suitability for organ donation. An additional concern with transplanting organs from an infected donor is the ability of COVID-19 to damage organs other than lungs.[12] Organs from SARS-CoV-2–infected donors have generally functioned well through short-term follow-up, acknowledging the donor COVID-19 disease was generally mild or asymptomatic.[6]

The evolving evidence of a lack of SARS-CoV-2 transmission and good short-term organ function has led to increasing support by organizations guiding SOT for utilizing nonlung organs from COVID-19–recovered donors even in the setting of persistent respiratory tract SARS-CoV-2 PCR positivity. The Organ Procurement and Transplantation Network suggests nonlung organ donation may be considered from donors with a history of mild COVID-19 infection as early as 11 d after symptom onset,[13] and the Transplantation Society of Australia and New Zealand suggests nonlung organ donation may be considered when donors are deemed noninfectious according to public health guidelines,[14] which at the earliest

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TABLE 1.

Management by transplantation societies of Australia, United States, United Kingdom, and Canada of factors related to solid organ donation from donors with COVID-19 infection

	TSANZ[14]	OPTN[13]	NHSBT[15]	CST[16]
Require LRT SARS-CoV-2 PCR test for nonlung donation	No	No	Yes	Yes
Minimum duration from symptom onset (d)	7	10	28	28
Require symptom resolution	No	Yes	Yes	Yes
Require negative SARS-CoV-2 PCR	No	No	Yes	Yes
Analysis of organ quality	Yes	Yes	Yes	No
Recipient vaccine requirement	No	No	No	No
Post exposure prophylaxis suggested	No	No	No	No
Alteration in immunosuppression suggested	No	No	No	No

COVID-19, coronavirus disease 19; CST, Canadian Society of Transplantation; LRT, lower respiratory tract; NHSBT, National Health Service Blood and Transplant; OPTN, organ procurement and transplantation network; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TSANZ, The Transplantation Society of Australia and New Zealand.

occurs 8 d after symptom onset.[11] Consideration of lung donation requires negative donor bronchoalveolar lavage SARS-CoV-2 PCR.[14] Other guidelines, such as those of NHS Blood and Transplant and Canadian Society of Transplantation, are currently more conservative, requiring negative SARS-CoV-2 PCR to consider proceeding to SOT (Table 1).[15,16] Guidelines emphasize the requirement for recipient informed consent.[13-16]

Lack of SARS-CoV-2 transmission through nonlung organ donation may also relax requirements for LRT PCR testing in all donors currently suggested, for example, in NHS Blood and Transplant and Canadian Society of Transplantation guidelines.[15,16] In this regard, the Transplantation Society of Australia and New Zealand has altered the routine requirement of LRT SARS-CoV-2 PCR in deceased organ donor assessment to a suggestion in nonlung donation and a requirement in lung donation (Table 1).[14]

As SARS-CoV-2 evolves with the emergence of new variants of concern, so must our understanding of this virus and its impact on organ transplantation. Although future variants may have increased severity and will predictably have ecological advantages due to immune evasion or increased transmissibility through the respiratory tract, it is not expected that they will develop enhanced transmission through the nonrespiratory route to make the donation and transplant communities more concerned about SARS-CoV-2 transmission through nonlung SOT.

The long-acting monoclonal antibody combination tixagevimab with cilgavimab has recently received Emergency Use Authorization in the United States as pre-exposure prophylaxis for those who may not mount an adequate immune response to COVID-19 vaccination. Molnupiravir has been approved for use in early COVID-19 infection in the United Kingdom, and Paxlovid is being assessed by regulatory bodies for use in early COVID-19 infection. These and other new therapeutics will allow better prevention and treatment of COVID-19, and these agents may be incorporated into the management of transplantation from a SARS-CoV-2–infected donor, particularly for recipients who are have not mounted an immune response after vaccination, or if lung donation is considered.

Organ donation surveillance bodies, such as the Disease Transmission Advisory Committee, NOTIFY LIBRARY, and the Australian Vigilance and Surveillance System for Organ Donation for Transplantation of the Organ and Tissue Authority, have an important role in documenting the safety and outcomes of organ transplantation from donors with COVID-19 infection, relying on prompt and complete reporting of outcomes from donation and transplant clinicians. With progressive policies allowing donation earlier after donor SARS-CoV-2 acquisition, we will gather further information to inform future practice regarding donor, recipient, viral, or treatment factors associated with transmission or organ dysfunction. In many respects, the COVID-19 pandemic has been a lesson in learning in real time, which has been borne out in our continually evolving management of COVID-19 related to solid organ donation and transplantation, including utilizing organs from SARS-CoV-2–infected donors.

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