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EDITORIAL

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The pandemic provides a pathway: What we know and what we need to know about using COVID positive donors

Already challenged by organ shortages and high waitlist mortality, the field of organ transplantation has suffered considerably from the COVID-19 pandemic. Questions surrounding the safety of transplanting organs from COVID-19 positive donors have surfaced. In five clinical correspondences in this edition of *Transplant Infectious Disease*, 13 cases of solid organ transplantation from SARS-COV-2 infected donors into non-infected recipients are described, including nine kidneys, two livers, and two hearts. Of the recipients, three had positive pretransplant SARS-CoV-2 antibodies, two had been fully vaccinated, and one was partially vaccinated prior to transplant. None of the 13 transplant recipients developed COVID-19.[1–5] The authors are to be commended for sharing their experiences and contributing vital data to the existing sparse literature (Table 1) on organ transplantation from COVID-19 positive donors.

To date, three cases of donor derived COVID-19 infection have been reported, each occurring in lung transplant recipients[6,7] (personal communication). In each of these cases, the donor had a negative COVID-19 nasopharyngeal swab at the time of organ procurement, but was later found to have SARS-CoV-2 on bronchoalveolar lavage. All three recipients developed critical COVID-19 infection, and one died.[6] No other cases of donor derived COVID-19 have been reported among other types of solid organ transplant recipients.

In light of a national shortage of organs, patients with end stage organ disease need an expanded donor pool. Centers interested in exploring organ transplantation from COVID-19-positive donors should carefully assess the donor and recipient to minimize the risk of adverse outcomes. Only kidney, liver, heart, or pancreas donations should be considered; lung donation should not be performed outside of extreme circumstances, due to risk of viral transmission and subsequent poor outcomes. Cases of pancreas transplantation from a COVID-19 positive donor have not been reported, but in theory are unlikely to pose any greater risk COVID transmission than kidney, liver, or heart transplantation.

Initially, many centers only considered COVID-19 positive donors with previous known COVID-19 that appeared to have persistent positive testing likely representing resolved infection. However, even non-lung donors with unknown time since infection but without severe disease have been used without transmission. While a high cycle threshold value (indicating a low viral load) would be potentially valuable information, this information is only variably available. Donors dying with critical COVID-19 may have separate organ quality issues and should be considered cautiously, likely with preimplantation biopsy to evaluate for microvascular disease. As with transplantation of hepatitis B and hepatitis C positive organs, the immediacy of donor need for transplantation should be considered. Waitlisted patients in urgent need of an organ, such as patients with end stage heart disease or fulminant liver failure, may be considered for organ transplant from a COVID-19 positive donor. Waitlisted patients with high morbidity but who are not imminently positioned to receive an organ may also be good candidates. Preferably, recipients who have been fully vaccinated or who have documented serologic evidence of immunity from prior infection should be considered for such transplant. Therefore, in order to be considered for this expanded donor organ pool, providers should strongly encourage patients get vaccinated while awaiting transplant. As with all recognized donor infections, recipient informed consent should be obtained well in advance of transplant.

In order to minimize risk for healthcare personnel, surgical teams should consider SARS-CoV-2 personal protective equipment (PPE) at the time of organ procurement, especially for thoracic procurements and lung implantation (currently there is no evidence to suggest risk of disease transmission to transplant teams implanting a non-pulmonary organ). Non-lung transplant recipients may safely be placed on standard contact precautions.

While SARS-COV-2 RNA has been detected in the heart, kidney, and liver of deceased patients,[8] to our knowledge, viable, transmissible virus may not exist in organs other than the lung. Even if viable virus exists in these organs, the experience with other respiratory viruses—and with COVID-19 to date—suggests that transplantation may not result in productive clinically relevant infection in the recipient.[9] To establish the safety of COVID-19 positive organ transplantation, transplant centers must continue to publish their experience with COVID-19 organ donation. Creation of a formal registry through the United Network for Organ Sharing (UNOS) recording recipient outcomes from COVID-19 positive organ donation would be of substantial benefit to the transplant community. Additionally, studies prospectively analyzing viral viability such as with culture or sub-genomic RNA in plasma and donor organ tissue could help determine whether viable virus exists in non-respiratory tissue.

The role of empiric treatment of COVID-19 in the recipient is another important question to consider. Of the cases reviewed in our editorial, seven of the recipients underwent empiric treatment for COVID-19 with either Remdesivir, casirivimab/ imdevimab, or both. We recognize that patients with chronic organ disease (e.g., patients on immunosuppression, patients with end stage renal disease, and patients with cirrhosis) have impaired humoral immunity which may result in decreased effectiveness of the COVID-19 vaccine in prevent-

TABLE 1 Summary of existing literature on solid organ transplantation from COVID-19 positive organ donors

Reference	Donor information	Organ transplanted	Recipient fully vaccinated	Recipient with prior COVID-19 infection	Recipient serostatus at the time of transplant	Recipient develop COVID-19?	Recipient receive COVID-19 therapy?	Graft outcome
Puodziukaite[1]	Mild symptoms, NPS+ CT values* = 32.0; 33.8	Kidney	No	Yes	IgG +	No	No	Good
		Kidney	No	Yes	IgG+	No	No	Good
Meshram[2]	Donor with critical COVID-19 infection: NPS – at the time of organ procurement	Kidney	No	No	NR	No	No	Good
		Kidney	No	Yes	NR	No	No	Good
de la Villa[3]	Mild COVID infection 2 months prior NPS+ CT value† = 30, Plasma PCR –	Heart	NR	No	IgG–	No	No	NR
		Liver	NR	Yes	IgG+	No	No	NR
Frattaroli[4]	No history of COVID-19 symptoms NPS+ CT value‡ = 40.2	Kidney	No	NR	NR	No	No	Good
		Kidney	No	NR	NR	No	No	Good
	COVID-19 infection during terminal hospitalization; NPS – at the time of organ procurement	Kidney	No	NR	NR	No	No	Good
		Liver	Yes	NR	NR	No	No	Good
Sigler[5]	NPS+ CT values† = 29.45, 31	Heart	No	No	IgG–	No	Remdesivir + casirivimab/imdevimab	Good
		Kidney	No	NR	IgG–	No	Remdesivir	Good
		Kidney	Yes	NR	IgG–	No	Remdesivir	Good
Koval[11]	NPS+ IgG+	Kidney	No	No	NR	No	No	Good
		Kidney	No	No	NR	No	No	Good
	NPS+ CT values† = 40; 38	Kidney	No	Yes	NR	No	No	Good
		Kidney	No	No	NR	No	No	Good
	NPS+	Kidney	No	No	NR	No	No	Good

(Continues)

TABLE 1 (Continued)

Reference	Donor information	Organ transplanted	Recipient fully vaccinated	Recipient with prior COVID-19 infection	Recipient serostatus at the time of transplant	Recipient develop COVID-19?	Recipient receive COVID-19 therapy?	Graft outcome
		Kidney	No	Yes	NR	No	No	Good
	NPS+	Kidney	No	Yes	NR	No	No	Good
		Kidney	No	No	NR	No	No	Good
	NPS+, CT values[†] = 31, 41	Kidney	No	No	NR	No	No	Good
		Kidney	No	No	NR	No	No	Good
Hong[12]	Mild symptoms NPS4.2 log copies/ml	Partial Liver	No	No	NR	No	Lopinavir + ritonavir followed by hydroxychloroquine	Not reported
Manzia[13]	No known symptoms BAL+, CT values[§] = 24; 27; 24	Liver	No	Yes: Recipient+ on BAL and NP swab	IgG+	Recipient already NPS+ at the time of transplant	No	Good
Dhand[14]	Early mild-moderate COVID-19, NPS+ CT value[*]: 38.5; 40.5	Heart	NR	NR	NR	No	casirivimab/imdevimab	Good
		Liver	Yes	NR	NR	No	casirivimab/imdevimab	Good
Kaul[6]	NPS− BAL+ CT values[¶] = 8.5; 9.5	Lung	NR	NR	NR	Yes	Remdesivir and convalescent plasma	Attributable death
Perlin[15]	NPS+	Kidney	NR	NR	IgG−	No	No	Delayed graft function
		Kidney	NR	NR	IgG−	No	No	Good
Ngueyn[16]	NPS+	Partial Liver	NR	NR	IgG−	No	Convalescent plasma	Good
Kumar[7]	NPS− BAL+	Lung	NR	NR	NR	Yes	Two courses Remdesivir + methylprednisolone	Prolonged stay in intensive care unit with new oxygen requirement
		Liver	NR	NR	NR	No	No	Good
		Kidney	NR	NR	NR	No	No	Non-attributable mortality
		Kidney	NR	NR	NR	No	No	Good
	NPS− BAL+	Kidney	NR	NR	NR	No	No	Good

Abbreviations: BAL, bronchoalveolar lavage; CT, cycle threshold; IgG, SARS-CoV-2 immunoglobulin G; NPS, nasopharyngeal swab; NR, not reported.

*GeneXpert SARS-COV-2 Cepheid platform.

[†]Platform not specified.

[‡]Labcorp.

[§]Allplex SARS-CoV-2 assay Seegene.

[¶]DiaSorin molecular.

ing disease. There is now an emergency use authorization approving emergency use of casirivimab and imdevimab for post exposure prophylaxis for COVID-19.[10] We need to establish whether there is a role for preemptively boosting the humoral response with a long acting monoclonal antibody at the time of transplant. Once again, understanding if viable virus is present in the transplanted organ would help guide clinicians on the need for antiviral or antibody therapy posttransplant.

In conclusion, the use of extra-pulmonary organs from COVID-positive donors may present a viable pathway to transplant for selected patients who would benefit from an expanded donor pool. More data are urgently needed, especially as we face resurgent cases of the delta variant, in order to establish the safety of this practice.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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