

EDITORIAL

Low risk high reward: What should we worry about with coronavirus disease 2019 positive donors?

As the coronavirus disease 2019 (COVID-19) pandemic evolves, transplant centers are successfully exploring avenues to safely utilize organs from donors testing positive for COVID-19. In this edition of *Transplant Infectious Disease*, Sanchez-Vivaldi et al report on the short-term outcomes of nine kidney transplant recipients who received organs from donors testing positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on the lower respiratory tract nucleic acid test (NAT). One of the donors died from SARS-CoV-2 pneumonia but had preserved renal function at the time of procurement. All nine kidney recipients received standard induction immunosuppression therapy. None of the recipients received post-exposure SARS-CoV-2 therapy, and none developed COVID-19. Two of the recipients had delayed graft function, but all recipients had satisfactory allograft function at 30-days post-transplant. Although longer-term graft outcomes are not yet available, the authors are to be commended for sharing their experience and contributing to the existing limited literature.

In our previous correspondence,¹ we summarized 13 articles describing 36 transplants using organs from donors testing positive for COVID-19. Since our commentary, 10 additional reports have emerged from centers describing the transplantation of organs from donors testing positive for COVID-19 (Table 1). In each of the reviewed cases, no documented transmission of COVID-19 occurred, and short-term graft function, when reported, was satisfactory. Further, we are aware of other transplant centers using large numbers of COVID-19 positive donors without documented transmission, though full details and recipient outcomes have not been published. Collectively, the published reports provide very encouraging evidence that transplantation of hearts, livers, and kidneys from COVID-19 positive donors is unlikely to transmit COVID-19 infection to recipients, even when donors test positive on lower respiratory tract specimens. SARS-CoV-2 RNA, sub-genomic RNA, and the culturable virus has been identified in multiple tissues,^{2,3} but thus far no clinically apparent transmission of COVID-19 has occurred outside of the setting of lung transplantation.

While routine transplantation of lungs from donors with active COVID-19 infection or positive lower respiratory tract NAT should not be performed, we have experience transplanting lungs from COVID-19-positive donors under restricted circumstances.⁴ Specifically, if the donor's first positive COVID-19 test is greater than 20 days prior to death and the lower respiratory tract NAT is negative, we believe the lungs are unlikely to transmit infection.

A careful assessment of donor history and organ quality is needed prior to accepting an organ from a COVID-19 positive donor. Donors presenting with hypercoagulability or dying from severe

hyperinflammatory COVID-19 may have organ quality concerns. Further, it remains unknown if even donors with the mild disease might have a hypercoagulable state that could manifest with clinically impactful venous or arterial thrombosis, particularly in liver transplant recipients. Understanding the donor's vaccination status, when available, may also lend insight into the donor's risk for COVID-related complications.

The utility of cycle threshold (CT) values to assess organ eligibility for transplant is not proven. While higher CT values appear to correlate with negative viral cultures, CT values vary by testing platform and collection technique. Moreover, CT values are not uniformly reported by performing laboratories nor routinely available during organ assessment.

The urgency with which a recipient requires an organ should be considered. Waitlisted patients with a high risk of mortality or those with high morbidity who are not imminently positioned to receive an organ may be particularly suited to a COVID-19 positive donor even if some questions about organ quality and transmission of a hypercoagulable state exist. While 15 recipients in the referenced literature were unvaccinated for COVID-19 prior to transplant, we continue to recommend all waitlisted recipients receive the COVID-19 vaccination series to provide greater protection against complications from post-transplant exposures.

We should not forget our duty of care to our colleagues in health-care. It remains prudent for procurement teams to don personal protective equipment in accordance with donor hospital policy. This may be especially true for thoracic organs, where exposure to open airways may occur. However, because we presume hearts, livers, kidneys, and pancreases to be non-infectious regardless of the donor's timeline of infection, surgical teams managing implantation may wear standard operating room attire during organ transplantation, and recipients may be managed with routine contact precautions after implantation.

COVID-19-directed therapeutics for the recipient are unnecessary given the negligible risk of transmission for non-lung organs. In the current report, most recipients received no directed therapeutics post-transplant, and all recipients remained free from donor-derived COVID-19 transmission. Similarly, we recommend routine induction and maintenance immunosuppression given the current state of the evidence.

There are scenarios in which we recommend against transplanting COVID-19 positive donors. First, in keeping with our above recommendations, BAL-positive lungs should not be routinely used for transplants. Additionally, we caution against small intestine

**TABLE 1** Summary of experience transplanting organs from donors testing positive for coronavirus disease (COVID-19)

Reference	Donor		Recipient				Develop COVID-19?	COVID-19 therapy post-transplant	Change in immunosuppression	Outcome
	Donor information	Organ	SARS-CoV-2 RNA detected in organ tissue?	Fully Vaccinated?	Prior COVID-19 Infection	Serostatus Pre-Transplant				
Sanchez-vivaldi et al*	All seven donors with LRT SARS-CoV-2 NAT+ test. One donor with COVID-19 related cause of death	Nine kidneys	NR	Seven fully vaccinated 2: not vaccinated	Two recipients, yes	NR	No	No	All alive with satisfactory allograft function at 30-days	
Romagnoli ⁵	First + test 5 days prior to organ recovery. LRT- upon organ recovery	Liver	No	No	Yes	IgG-	No	No	Alive	
	First + test at organ recovery, LRT+	Liver	No	No	Yes	IgG+	No	No	Alive	
	First + test 10 days prior to organ recovery; LRT+ at recovery	Liver	No	No	Yes	IgG+	No	No	Alive	
	First + test 1 day prior to organ recovery; LRT+ at organ recovery	Liver	No	No	Yes	IgG+	No	No	Alive	
	First + test at organ recovery, LRT+	Liver	No	No	Yes	IgG+	No	No	Alive	
	First + test 3 days prior to organ recovery; LRT- at organ recovery	Liver	No	No	Yes	IgG+	No	No	Alive	
	First + test 2 days prior to organ recovery	Liver	No	No	Yes	IgG+	No	No	Alive	
	First + test 6 days prior to organ recovery; LRT+ at organ recovery	Liver	No	No	Yes	IgG-	No	No	Alive	

(Continues)

TABLE 1 (Continued)

Reference	Donor		Recipient					Develop COVID-19?	COVID-19 therapy post-transplant	Change in immunosuppression	Outcome
	Donor information	Organ	SARS-CoV-2 RNA detected in organ tissue?	Fully Vaccinated?	Prior COVID-19 Infection	Serostatus Pre-Transplant					
	First + test 1 day prior to organ recovery; LRT+ at organ recovery	Liver	NR	No	Yes (first + 30 days prior to transplant, remained positive at transplant)	IgG+	No [†]	No	No	Deceased at 75 days post-transplant due to MDR <i>Acinetobacter</i> infection	
Yetmar ⁶	First + test at organ recovery, LRT+	Liver	No	No	Yes	IgG+	No	No	No	Alive	
	NP+ on screening	Liver	NR	No	Yes, active infection at the time of transplant	NR	No, already infected at the time of transplant	Remdesivir ⁵	No	Alive	
Barros ⁷	NP+, CT = 12	Liver	No	NR	Yes, active infection at transplant	IgG+	No	No	No	Alive, satisfactory graft function	
Lee ⁸	Died from severe COVID-19 respiratory failure, COVID-19 test - at organ recovery	Kidney	No	NR	NR	NR	No	No	NR	Alive, satisfactory graft function	
La Hoz ⁹	Unvaccinated donor; LRT + N1 gene CT = 37.8 N2 gene-	Liver	NR	No	No	NR	No	No	No induction immunosuppression Standard maintenance immunosuppression	Alive, satisfactory graft function	
	LRT + N1 gene CT = 32.8 N2 gene CT = 32.9	Liver	NR	Yes	No	NR	No	No	No induction immunosuppression; Standard maintenance immunosuppression	Alive, satisfactory graft function	

(Continues)



TABLE 1 (Continued)

Reference	Donor information	Organ	Recipient				Serostatus Pre-Transplant	Develop COVID-19?	COVID-19 therapy post-transplant	Change in immunosuppression	Outcome
			SARS-CoV-2 RNA detected in organ tissue?	Fully Vaccinated?	Prior COVID-19 Infection	COVID-19?					
Molnar ¹⁰	Death from severe COVID-19, NP+, CT = 38	Kidney	NR	Yes	No	igG+	No	No	No	Alive, satisfactory graft function	
Wall ¹¹	Mild symptoms, NP+	Kidney	NR	No	No	igG+	No	No	No	Alive, satisfactory graft function	
Royo-Villanova Reparaz ¹²	Mild symptoms, NP+, CT = 33.1	Heart	NR	NR	NR	igG-	No	No	NR	Alive	
Eichenberger ⁴	LRT+, CT = 38.14	Heart	NR	NR	NR	NR	No	No	No	Alive, satisfactory graft function	
	NP+, CT = 34	Heart	No	Yes	NR	NR	No	No	No	Alive, satisfactory graft function	
	Asymptomatic, NP+, CT = 16.1;	Heart	No	Yes	NR	NR	No	Yes, monoclonal antibody for post-exposure prophylaxis	No	Alive, satisfactory graft function	
	Mild symptoms; NP+, CT = 41.9; LRT-	Heart	No	Yes	NR	NR	No	No	No	Deceased**	
	NP+ and LRT+ CT ranged 20–39 on multiple specimens;	Heart	NR				No	No	No		
	NP+, CT = 40	Heart	No	Yes	NR	NR	No	No	No	Alive, satisfactory graft function	
	NP+, CT = 23	Heart	NR	Yes	NR	NR	No	No	No	Alive, satisfactory graft function	
	NP+, CT = 40.2; LRT-	Heart	NR	Yes	NR	NR	No	No	No	Alive, satisfactory graft function	
	Mild symptoms, NP+	Heart	NR	Yes	NR	NR	No	No	No	Alive, satisfactory graft function	

(Continues)

TABLE 1 (Continued)

Reference	Donor		Recipient					Outcome		
	Donor information	Organ	SARS-CoV-2 RNA detected in organ tissue?	Fully Vaccinated?	Prior COVID-19 Infection	Serostatus Pre-Transplant	Develop COVID-19?		COVID-19 therapy post-transplant	Change in immunosuppression
	Asymptomatic; First NP+, 38 days prior to death; LRT-	Lung	NR	Yes	Yes	NR	No	No	No	Alive, satisfactory graft function
	Mild symptoms; NP+, LRT-	Heart	NR	Incomplete vaccination series	Yes	NR	No	No	No	Alive, satisfactory graft function
	Asymptomatic First NP+, 30 days prior to death; LRT-	Lung	NR	Yes	NR	NR	No	No	No	Alive, satisfactory graft function
	NP+, CT = 28.1; LRT+ CT = 27.97	Heart	NR	Yes	NR	NR	No	No	No	Alive, satisfactory graft function
	NP+, CT = 34.6; LRT-	Heart	NR	Yes	NR	NR	No	No	No	Alive, satisfactory graft function

Abbreviations: CT, cycle threshold; d, day; lower respiratory tract; NP, nasopharyngeal; LRT; NR, not reported.

*Authors report an additional eight transplants (two kidneys, six livers) from COVID-positive patients but do not describe outcomes.

[†]Recipient remained + at time of transplant.

[§]Received casirivimab and imdevimab 3 days prior to transplant (while awaiting organ) and then remdesivir post-transplant.

^{***}intraoperative complications requiring re-do heart transplant, underwent second heart transplant using another COVID-19 positive donor. Death due to post-surgical complications on day 88.



transplantation given limited experience and higher levels of SARS-CoV-2 in the intestine. Organs from COVID-19-positive immunosuppressed hosts may have higher viral loads and theoretically pose a greater risk of transmission, though this has not yet been demonstrated in the literature. Finally, organs from donors dying due to severe COVID-19 may have organ quality concerns such as thromboses or inflammatory changes. In such cases, we caution that the recipient's urgency for transplant is carefully weighed against potential organ quality concerns prior to proceeding with transplantation.

It is important to emphasize that while growing evidence supports that transplantation of non-pulmonary organs from COVID-19 infected donors is a safe practice, this remains a nascent field with incompletely understood risks. It is difficult with the current literature to exclude an increase in rare events, such as thrombosis or shorter time to graft failure. Long-term outcomes beyond 1-year post-transplant remain unknown. Finally, given the recognized donor-derived transmission of COVID-19 in lung recipients, the use of BAL positive covid organs should still be discouraged in the absence of dire recipient needs. As the SARS-CoV2 virus becomes endemic, donors will continue to test positive for COVID-19, and transplant centers need to understand how to assess these donors and safely utilize these organs. Large registry data particularly focused on outcomes such as venous or arterial thrombosis, would be extremely valuable. The Organ Procurement and Transplantation Network maintains a data review that is regularly updated as a potential source of additional information.¹³ We commend transplant centers for sharing their experiences transplanting organs from COVID-positive recipients and urge others to do the same.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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