Low Risk High Reward: What Should We Worry About with COVID-19 Positive Donors?

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As the 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 SARS-CoV-2 on 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 transplantation of organs from donors testing positive for COVID-19 [Table]. 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 culturable virus has been identified in multiple tissues,[2,3] but thus far no clinically apparent transmission of COVID-19 has occurred outside of 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 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 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 healthcare. 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 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 transplant. Additionally, we caution against small intestine 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 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 be 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 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 need. 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 (OPTN) maintains a data review that it 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.

Table: Summary of experience transplanting organs from donors testing positive for COVID-19	**DONOR**			**RECIPIENT**						
Reference	**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 immuno-suppression**	**Outcome**
Sanchez-vivaldi et al*	All 7 donors with LRT SARS-CoV-2 NAT + test 1 donor with	9 Kidneys	NR	7 fully vaccinated 2: not vaccinated	2 recipients yes	NR	No	No	No	All alive with satisfactory allograft function at 30-days

	COVID-19 related cause of death									
Romagnoli[5]	First + test 5d prior to organ recovery. LRT- upon organ recovery	Liver	No	No	Yes	IgG -	No	No	No	Alive
	First + test at organ recovery, LRT +	Liver	No	No	Yes	IgG +	No	No	No	Alive
	First + test 10d prior to organ recovery; LRT + at recovery	Liver	No	No	Yes	IgG +	No	No	No	Alive
	First + test 1d prior to organ recovery; LRT + at organ recovery	Liver	No	No	Yes	IgG +	No	No	No	Alive
	First + test at organ recovery, LRT +	Liver	No	No	Yes	IgG +	No	No	No	Alive
	First + test 3d prior to organ recovery; LRT – at	Liver	No	No	Yes	IgG +	No	No	No	Alive

	organ recovery									
	First + test 2d prior to organ recovery	Liver	No	No	Yes	IgG +	No	No	No	Alive
	First + test 6d prior to organ recovery; LRT + at organ recovery	Liver	No	No	Yes	IgG -	No	No	No	Alive
	First + test 1d prior to organ recovery; LRT + at organ recovery	Liver	NR	No	Yes (first + 30d prior to transplant, remained positive at transplant)	IgG +	No[†]	No	No	Deceased at d75 post-transplant due to MDR *Acinetobacter infection*
	First + test at organ recovery, LRT +	Liver	No	No	Yes	IgG +	No	No	No	Alive
Yetmar[6]	NP + on screening	Liver	NR	No	Yes, active infection at time of transplant	NR	No, already infected at time of transplant	Remdesivir[§]	No	Alive
Barros[7]	NP + CT = 12	Liver	No	NR	Yes, active infection at transp	IgG +	No	No	No	Alive, satisfactory graft

					lant					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 immuno-suppression 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 immuno-suppression; Standard maintenance immunosuppression	Alive, satisfactory graft function
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-Villanov	Mild symptom	Hear	NR	NR	NR	IgG -	No	No	NR	Alive

a Reparaz [12]	s, NP+, CT = 33.1	t								
	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
Eichenberger [4]	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
	Asymptomatic; First NP + 38d 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 + 30d 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;	Heart	NR	Yes	NR	NR	No	No	No	Alive, satisfactory graft

	LRT-									function

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

*Authors report an additional 8 transplants (2 kidneys, 6 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.

References

1. Eichenberger EM, Kaul DR, Wolfe CR. The pandemic provides a pathway: What we know and what we need to know about using COVID positive donors. *Transpl Infect Dis*. Oct 6 2021:e13727. doi:10.1111/tid.13727
2. Gaussen A, Hornby L, Rockl G, et al. Evidence of SARS-CoV-2 Infection in Cells, Tissues, and Organs and the Risk of Transmission Through Transplantation. *Transplantation*. Jul 1 2021;105(7):1405-1422. doi:10.1097/tp.0000000000003744
3. Chertow D, Stein S, Ramelli S, et al. SARS-CoV-2 infection and persistence throughout the human body and brain. *Research Square [preprint]*. 2021;doi:10.21203/rs.3.rs-1139035/v1
4. Eichenberger E, Coniglio A, Milano C, et al. Transplanting Thoracic COVID-19 Positive Donors: Overcoming the Pandemic. *Oral Presentation at Proceedings of the 42nd International Society for Heart and Lung Transplantation*. 2022 Apr 27-30; Boston, MA.
5. Romagnoli R, Gruttadauria S, Tisone G, et al. Liver transplantation from active COVID-19 donors: A lifesaving opportunity worth grasping? *Am J Transplant*. Dec 2021;21(12):3919-3925. doi:10.1111/ajt.16823
6. Yetmar ZA, Ranganath N, Huebert RC, Rosen CB, Razonable RR, Beam E. Successful Liver Transplantation From a SARS-CoV-2 Positive Donor to a Positive Recipient: Potential Role of Monoclonal Antibodies. *Transplantation*. Mar 1 2022;106(3):e181-e182. doi:10.1097/tp.0000000000004032
7. Barros N, Ermel A, Mihaylov P, Lacerda M, Fridell J, Kubal C. Deceased Donor Liver Transplantation from a SARS-CoV-2-Positive Donor to a SARS-CoV-2-Positive Recipient. *Liver Transpl*. Dec 2021;27(12):1849-1851. doi:10.1002/lt.26253
8. Lee K, Desai NM, Resnick J, et al. Successful kidney transplantation from a deceased donor with severe COVID-19 respiratory illness with undetectable SARS-CoV-2 in donor kidney and aorta. *Am J Transplant*. Jan 13 2022;doi:10.1111/ajt.16956
9. La Hoz RM, Mufti AR, Vagefi PA. Short-term liver transplant outcomes from SARS-CoV-2 lower respiratory tract NAT positive donors. *Transpl Infect Dis*. Feb 2022;24(1):e13757. doi:10.1111/tid.13757
10. Molnar MZ, Hall IE, Raghavan D, et al. Kidney transplantation from SARS-CoV-2-positive deceased donor. *Am J Transplant*. Apr 2022;22(4):1280-1282. doi:10.1111/ajt.16905
11. Wall AE, McKenna GJ, Onaca N, et al. Utilization of a SARS-CoV-2-positive donor for liver transplantation. *Proc (Bayl Univ Med Cent)*. 2022;35(1):62-63. doi:10.1080/08998280.2021.1985888
12. Royo-Villanova Reparaz M, Dominguez-Gil B, Moreno Docón A, Cánovas López SJ, Pastor Pérez FJ, Ortín Freire AJ. Organ donor with PCR positive for SARS-CoV-2, it has been always no? *Med Intensiva (Engl Ed)*. Apr 2022;46(4):225-226. doi:10.1016/j.medine.2022.02.003

13. OPTN, Summary of Current Evidence and Information– Donor SARS-CoV-2 Testing & Organ Recovery from Donors with a History of COVID-19. Available at: https://optn.transplant.hrsa.gov/media/kkhnlwah/sars-cov-2-summary-of-evidence.pdf , Last accessed on May 25, 2022