Received: 4 March 2022 | Revised: 19 April 2022 | Accepted: 20 May 2022

DOI: 10.1111/tid.13890

TRANSPLANT INFECTIOUS DISEASE

BRIEF COMMUNICATION

Short-term kidney transplant outcomes from severe acute respiratory syndrome coronavirus 2 lower respiratory tract positive donors

Jorge A. Sanchez-Vivaldi[1] | **Madhukar S. Patel**[1] | **Jigesh A. Shah**[1] | **Benjamin K. Wang**[1] | **Juan D. Salcedo-Betancourt**[2] | **Christine S. Hwang**[1] | **David Wojciechowski**[2] | **Ricardo M. La Hoz**[3,*] | **Parsia A. Vagefi**[1,*]

[1]Division of Surgical Transplantation, Department of Surgery, University of Texas Southwestern Medical Center, Dallas, Texas, USA

[2]Department of Medicine, University of Texas Southwestern Medical Center, Dallas, Texas, USA

[3]Division of Infectious Diseases and Geographic Medicine, Department of Medicine, University of Texas Southwestern Medical Center, Dallas, Texas, USA

Correspondence
Ricardo M. La Hoz, Division of Infectious Diseases and Geographic Medicine, Department of Medicine, University of Texas Southwestern Medical Center, Dallas, Texas, USA.
Email: Ricardo.LaHoz@UTSouthwestern.edu

Parsia A. Vagefi, 5959 Harry Hines Blvd, HP04.102, Dallas, TX 75390–8567, USA.
Email: Parsia.vagefi@utsouthwestern.edu

Abstract

Objective: In this study, we aim to assess short-term allograft outcomes following deceased donor kidney transplantation from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) lower respiratory tract (LRT) nucleic acid testing (NAT) positive donors.

Methods: From September to December 2021, SARS-CoV-2 NAT positive organ donors, whose solid abdominal organs were transplanted at our academic medical center were identified. Donors were stratified into having tested positive for SARS-CoV-2 in an upper respiratory tract (URT) or LRT sample. For this study, the SARS-CoV-2 LRT NAT positive deceased kidney donors and their respective recipients were examined. Donor and recipient demographic data, coronavirus disease 2019 (COVID-19)-related history, patient outcomes, as well as postoperative graft function were evaluated.

Results: Thirteen SARS-CoV-2 positive deceased donors were identified. Of these, eight were LRT NAT positive and yielded nine kidneys. These allografts were successfully transplanted into vaccinated and unvaccinated recipients. All recipients received standard induction immunosuppression and did not receive any prophylactic therapy for SARS-CoV-2. Two recipients had delayed graft function. At 1-month post-transplant, there was no clinical evidence of donor-derived COVID-19 or graft loss, and all recipients were free from dialysis.

Conclusion: We describe the first case series of SARS-CoV-2 LRT NAT positive deceased kidney donors for vaccinated and unvaccinated recipients with excellent short-term allograft outcomes and no clinical evidence of donor-derived COVID-19 post-transplantation. Given the increasing prevalence of SARS-CoV-2 in the population, utilization of SARS-CoV-2 LRT NAT positive deceased donors could be considered

Abbreviations: AKI, acute kidney injury; CDC, Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; DGF, delayed graft function; DTAC, Ad Hoc Disease Transmission Advisory Committee; LRT, lower respiratory tract; NAT, nucleic acid testing; OPTN, Organ Procurement and Transplantation Network; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

*These authors contributed equally to this work.

an acceptable source of organs for renal transplantation, especially as multi-center experiences and longer-term follow-up emerge.

KEYWORDS
COVID-19 deceased donors, lower respiratory tract positive donors, renal transplant, SARS-CoV-2

1 | INTRODUCTION

Given persistent disparities between organ supply and demand, the solid organ transplant community continues to explore opportunities for expansion of the donor pool. Recent studies describe the use of organs from donors testing positive for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by nucleic acid testing (NAT) in an upper respiratory tract (URT) sample.[1,2] In April 2021, the Organ Procurement and Transplantation (OPTN) Executive Committee approved the "Lower Respiratory SARS-CoV-2 Testing for Lung Donors" policy which requires all potential lung donors to be tested for SARS-CoV-2 in a lower respiratory tract (LRT) specimen by NAT.[3] An additional outcome of this policy was the emergence of a new population of potential donors- the SARS-CoV-2 LRT NAT positive donors.

To date, there are no reports on the use of SARS-CoV-2 LRT NAT positive donors for kidney transplantation, and limited case reports have evaluated the safety of using liver allografts from these donors.[4,5] The weight of the evidence including the absence of proven cases of SARS-CoV-2 transmission from positive non-lung donors suggests that the risk of transmission is low.[1,4–6] From May 27 through November 30, 2021, 178 non-lung organs were transplanted from donors with a positive lower respiratory tract SARS-CoV-2 test.[6] The safety of using organs in this scenario remains unknown. In this report, we provide the first description of short-term allograft outcomes following deceased donor kidney transplantation from SARS-CoV-2 LRT NAT positive donors.

2 | METHODS

From September to December 2021, all coronavirus disease 2019 (COVID-19) positive organ donors, defined by SARS-CoV-2 NAT positive result during Organ Procurement Organization evaluation, whose solid abdominal organs were transplanted at our academic medical center were identified. Donors were stratified into having tested positive for URT (nasopharyngeal swab) or lower respiratory tract (LRT; tracheal aspirate or bronchoalveolar lavage) infection (Figure 1). For this study, SARS-CoV-2 LRT NAT positive deceased kidney donors and their respective recipients were examined, as we have previously described our experience with SARS-CoV-2 LRT NAT positive deceased liver donors.[4] The pre-donation status of COVID-19 infection was assessed using the United Network for Organ Sharing donor history and the donor risk assessment interview (DRAI). The DRAI asks specific questions about recent travel, exposure, or documented COVID-19 infection. Donor and recipient demographic data, COVID-19-related history (i.e., donor clinical history of infection and imaging findings as well as recipient clinical history, vaccination status, and testing upon admission), patient outcomes, as well as postoperative graft function (occurrence of delayed graft function (DGF), serum creatinine at 14- and 30-days from transplant) were examined. Cycle threshold values were not readily available for donors at the time of organ offer. Delayed graft function was defined as the need for dialysis within the first week of transplant. Major complications were those with Clavien Dindo ≥ Grade III requiring surgical, endoscopic, or radiologic intervention.

Numerical analyses were performed using Stata 16/MP4 (StataCorp LP, College Station, TX). Donor and recipient characteristics were described using the median (interquartile range) for continuous variables. Categorial characteristics were described as frequencies.

3 | RESULTS

During the study period, 13 SARS-CoV-2 positive deceased donors were utilized. Of these thirteen donors, five tested positive for isolated LRT NAT, three tested positive for both URT and LRT NAT, and five tested positive for isolated URT NAT. The eight LRT NAT positive yielded nine kidneys and three livers for transplantation (Figure 1). Only one of the donors died from severe SARS-CoV-2 pneumonia. Of the other six, one had recovered from mild COVID-19 (symptom resolution > 28 days; no hospitalization required) and died from bacterial meningitis, with the remainder having expired from other causes. In this latter group, even after having reviewed the available histories, we are unable to state with certainty whether other causes of death may have been related to COVID-19. The median donor age was 39 years old with a kidney donor profile index of 35 (Table 1). Of note, the recipient whose allograft was from the donor that died from SARS-CoV-2 pneumonia was a zero-HLA-mismatch and the donor's renal function was preserved (terminal creatinine 0.59 mg/dl and urine output of 200cc/hr) at the time of procurement. Five LRT NAT positive donors had a preoperative chest computed tomography available. Three of them were positive, defined as the presence of pulmonary ground-glass opacities, patchy opacities, or consolidations on radiologist read. All donors had satisfactory urine output (> 30cc/h) at the time of procurement and the median terminal creatinine was 2.26 mg/dl (Table 1). Data regarding donor vaccination status was not available.

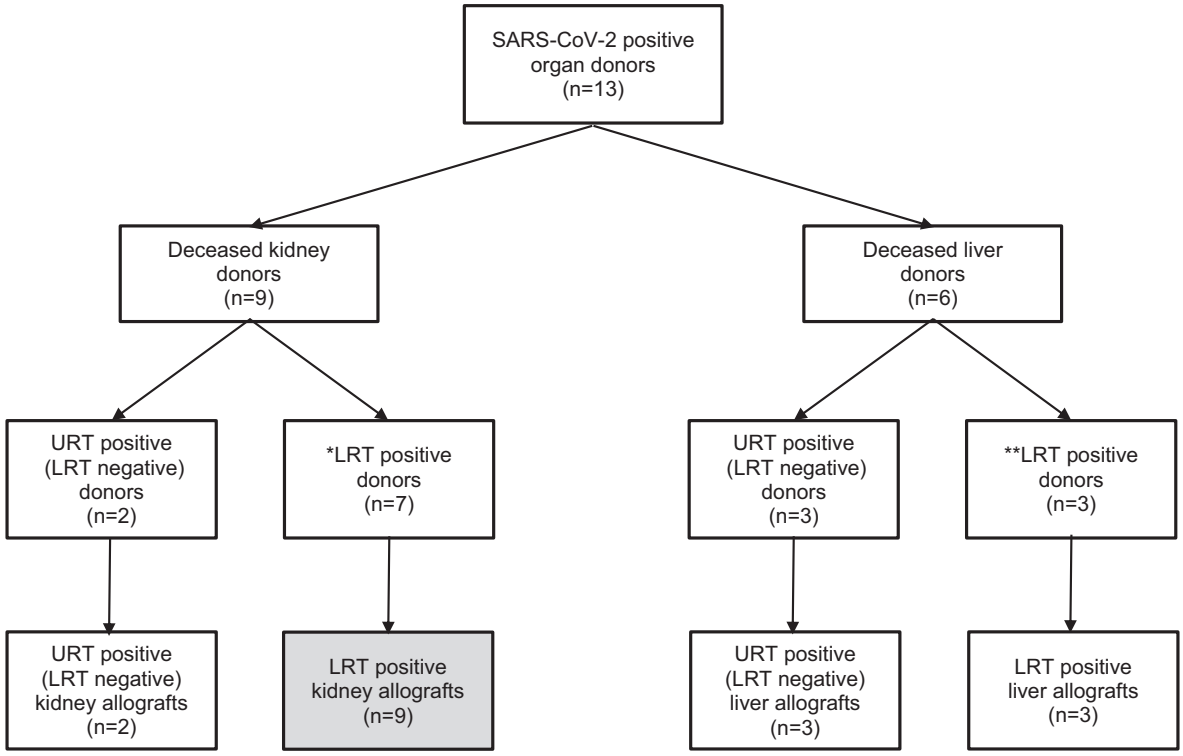

FIGURE 1 Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) NAT positive organ donors flow chart (NAT: nucleic acid testing; URT: upper respiratory tract; LRT: lower respiratory tract). *LRT-positive kidney donors include two cases of combined (URT + LRT) and five cases of isolated (LRT only) test results. **LRT-positive liver donors include: one case of combined (URT + LRT) and two cases of isolated (LRT only) test results

All nine kidney recipients underwent induction immunosuppression with thymoglobulin. Most recipients received standard 3-drug maintenance immunosuppression consisting of tacrolimus, mycophenolate, and steroids. One recipient was enrolled in a clinical trial examining dual co-stimulation blockade. Seven recipients (77.8%) had completed their COVID-19 vaccination series, of which two had received an additional booster, and two (22.2%) were unvaccinated (Table 1). None of the recipients received post-transplant prophylactic SARS-CoV-2 therapy and routine surveillance for SARS-CoV-2 was not performed. There were no major complications, graft loss, vessel thrombosis, or donor-derived COVID-19 infections. Two patients (22.2%) had DGF. The median hospital length of stay was four days. At 30-day follow-up, all recipients had satisfactory allograft function (median creatinine of 1.51 mg/dl) and were free from dialysis (Table 1).

4 | DISCUSSION

The "lower respiratory SARS-CoV-2 testing for lung donors" OPTN emergency policy introduced uncertainty in the abdominal transplant community, as to whether to use abdominal organs from donors that tested positive for SARS-CoV-2 in an LRT specimen. The initial hesitance to use organs from these donors was the risk of donor-derived COVID-19. We assessed the use of LRT NAT positive kidney allografts as this test became increasingly available at the time of organ offer and it was felt that evaluating recipient outcomes was important as results of this test may influence accept/turn-down decisions. Although the precise risk of disease transmission is unknown, it must be balanced with the risk of morbidity and mortality of remaining on the abdominal transplant waitlist. This is the first case series reporting outcomes from the use of SARS-CoV-2 LRT NAT positive deceased kidney donors for vaccinated and unvaccinated recipients, with 100% 1-month allograft survival. No prophylactic strategies were employed and there was no clinical evidence of donor-derived COVID-19 infection. Taken together, this experience, along with the known biology of COVID-19, recent case reports, and data reported by the Ad Hoc Disease Transmission Advisory Committee (DTAC), we believe that the benefits of using kidney allografts from LRT NAT positive donors may outweigh the morbidity and mortality of remaining on the kidney transplant waitlist.[1,4–6]

In September 2021, Kute et al. published a systematic review to evaluate the safety of transplants performed on donors with COVID-19.[2] Most of the reports described the use of organs from donors testing positive in a URT sample. The authors describe fifteen SARS-CoV-2 positive donors, for a total of 25 transplanted organs (16 kidneys, six livers, and three hearts). Among the sixteen transplanted kidneys, no donor-derived infection was identified, and no major complications were noted. The incidence of DGF was 18.8%.

The use of organs from SARS-CoV-2 LRT NAT positive donors was initially reported after the Italian Transplant Authority permitted to

TABLE 1 Lower respiratory tract nucleic acid testing (NAT) positive deceased kidney donors and recipients

Donor Data (*n* = 7)	
Age (years), median (IQR)	39.0 (23.0–46.0)
Gender, *n* (%)	
Female	2 (28.6%)
Male	5 (71.4%)
Race, *n* (%)	
White	4 (57.1%)
African American	2 (28.6%)
American Indian	1 (14.3%)
Sequence number, median (IQR)	15.0 (7.0–158.0)
Kidney Donor Profile Index, median (IQR)	35.0 (14.0–67.0)
Donor type, *n* (%)	
Brain death	2 (28.6%)
Cardiac death	5 (71.4%)
Cold ischemia time (h), median (IQR)	21.4 (7.9–27.4)
Positive upper respiratory tract infection, *n* (%)	2 (28.6%)
Positive lower respiratory tract infection, *n* (%)	7 (100.0%)
History of SARS-CoV-2 infection, *n* (%)	2 (28.6%)
SARS-CoV-2 cause of death, *n* (%)	1 (14.3%)
CT chest positive findings*, *n* (%)	3 (42.9%)
Terminal creatinine, median (IQR)	2.26 (0.59–4.84)
Recipient Data (*n* = 9)	
Age (y), median (IQR)	45.0 (32.0–54.0)
Gender, *n* (%)	
Female	5 (55.6%)
Male	4 (44.4%)
Race, *n* (%)	
White	4 (44.4%)
African American	3 (33.3%)
Hispanic/Latino	2 (22.2%)
Transplant indication, *n* (%)	
CKD	2 (22.2%)
ESRD	7 (77.8%)
Waitlist time (*d*), median (IQR)	75.0 (32.0–216.0)
Clinical history of SARS-CoV-2, *n* (%)	2 (22.2%)
SARS-CoV-2 vaccinations received, *n* (%)	
0	2 (22.2%)
2	5 (55.6%)
3	2 (22.2%)
Positive SARS-CoV-2 test on admission, n (%)	0 (0.0%)
Hospital length of stay (*d*), median (IQR)	4.0 (4.0–5.0)
Delayed graft function, *n* (%)	2 (22.2%)
Other major complication†, *n* (%)	0 (0.0%)
Post-transplant SARS-CoV-2 infection, *n* (%)	0 (0.0%)
14-day creatinine, median (IQR)	1.79 (1.37–2.19)
30-day creatinine, median (IQR)	1.51 (1.36–1.66)

*Defined as the presence of pulmonary ground-glass opacities, patchy opacities, or consolidations on radiologist read.
†Clavien Dindo ≥ Grade III requiring surgical, endoscopic, or radiologic intervention.

use of urgent liver transplantation in candidates who were SARS-CoV-2 positive or with past COVID-19 exposure. They have published the results of ten liver transplants within an Italian multicenter series, with all recipients having had evidence of prior infection with COVID-19. Five donors had a positive LRT SARS-CoV-2 NAT at the time of organ procurement.[5,6] After a median follow-up of 221 days, nine out of 10 recipients had satisfactory allograft function. On POD 75, one recipient died of sepsis secondary to Acinetobacter baumannii. We subsequently reported our experience with two SARS-CoV-2 LRT NAT positive liver donors with similar results.[4]

Other complimentary non-COVID data can also help assess the risks and benefits of utilization of this donor population. In a 10-year review of potential donor-derived events submitted to the DTAC community, respiratory viruses almost uniquely affected lung-transplant recipients.[7] Further, the OPTN DTAC has monitored the implications of its emergency policy and noted that from May to November 2021, 178 non-lung donor organs with a positive LRT SARS-CoV-2 NAT have been transplanted.[6]

The Center for Disease Control (CDC) has investigated three donor-derived COVID-19 infections which occurred in three lung recipients. The six non-lung organ recipients did not develop clinical evidence of SARS-CoV-2 infection. Additionally, the CDC has examined 40 potential COVID-19 donor-derived transmission events without identifying transmission to a non-lung recipient.[6] In sum, the available clinical data support that the risk of donor-derived COVID-19 from donors with a positive SARS-CoV-2 LRT NAT is likely very low, and consideration should be given to the utilization of extra-pulmonary organs in the appropriate clinical setting.

As a transplant community, we now move to the next phase of the evaluation of SARS-CoV-2 NAT positive donors, assessing short-term allograft outcomes. Renal involvement is common with SARS-CoV-2 infection, with one meta-analysis describing acute kidney injury (AKI) in about 17% of patients hospitalized due to COVID-19.[8] This complication was more common in older patients and those with comorbidities.[9] In autopsy studies, the most common abnormal finding in the kidneys was acute tubular necrosis.[10] A small proportion of patients with COVID-19 developed nephrotic range proteinuria and AKI with collapsing focal segmental glomerulosclerosis.[11] In addition to organ-specific findings, SARS-CoV-2 infection has also been associated with a hypercoagulable state characterized by microthrombi, venous thromboembolism, and arterial events that can affect the

allograft. These studies, raise the concern for sub-optimal post-transplant renal allograft function. However, it should be noted that the vast majority of donor allografts utilized in this study were from SARS-CoV-2 LRT NAT positive donors with a cause of death other than COVID-19. As mentioned, the one donor that died from COVID-19 had excellent renal function during admission and ultimately provided a zero-HLA-mismatch allograft. This study describes comparable short-term renal allograft function although it is acknowledged that the analysis is limited by the retrospective single-center study design, small sample size, lack of post-transplant SARS-CoV-2 PCR testing, and the inability to adequately control for all confounding variables. Multicenter studies that adequately control for confounding are required to further assess the longer-term allograft outcomes from SARS-CoV-2 LRT NAT positive donors.

In conclusion, we describe the first case series of SARS-CoV-2 LRT NAT positive deceased kidney donors for vaccinated and unvaccinated recipients with excellent short-term allograft outcomes and no clinical evidence of donor-derived COVID-19 post-transplantation. Indeed, although we do not yet have a 1-month follow-up since this report has been compiled, we have utilized an additional four livers and four kidneys from SARS-CoV-2 LRT NAT positive deceased donors- bringing our total to 20 abdominal organs transplanted from SARS-CoV-2 LRT NAT positive deceased donors. Given the increasing prevalence of SARS-CoV-2 in the population, utilization of SARS-CoV-2 LRT NAT positive deceased donors could be considered an acceptable source of organs for renal transplantation, especially as multi-center experiences and long-term follow-up emerge.

ACKNOWLEDGMENTS

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

FUNDING INFORMATION

No funding to disclose.

AUTHOR CONTRIBUTIONS

Study conception and design: Jorge A. Sanchez-Vivaldi, Madhukar S. Patel, Jigesh A. Shah La Hoz, Parsia A. Vagefi

Acquisition of data: Jorge A. Sanchez-Vivaldi, Madhukar S. Patel, Jigesh A. Shah, Benjamin K. Wang, Juan D. Salcedo-Betancourt, Christine S. Hwang, Ricardo M. La Hoz, Parsia A. Vagefi

Analysis and interpretation of data: Jorge A. Sanchez-Vivaldi, Madhukar S. Patel, Benjamin K. Wang, Juan D. Salcedo-Betancourt, Hwang, La Hoz, Christine S. Hwang, David Wojciechowski, Ricardo M. La Hoz, Parsia A. Vagefi

Drafting of the manuscript: Jorge A. Sanchez-Vivaldi, Madhukar S. Patel, Juan D. Salcedo-Betancourt, Ricardo M. La Hoz, Parsia A. Vagefi

Critical revision: Jorge A. Sanchez-Vivaldi, Madhukar S. Patel, Benjamin K. Wang, Jigesh A. Shah, Juan D. Salcedo-Betancourt, Christine S. Hwang, La Hoz, Hwang, David Wojciechowski, Ricardo M. La Hoz, Vagefi

ORCID

Madhukar S. Patel https://orcid.org/0000-0001-7508-899X
Ricardo M. La Hoz https://orcid.org/0000-0002-1560-3192

REFERENCES

1. Koval CE, Poggio ED, Lin YC, Kerr H, Eltemamy M, Wee A. Early success transplanting kidneys from donors with new SARS-CoV-2 RNA positivity: a report of 10 cases. *Am J Transplant*. 2021;21(11):3743-3749.
2. Kute VB, Fleetwood VA, Meshram HS, Guenette A, Lentine KL. Use of organs from SARS-CoV-2 infected donors: is it safe? *Contemp Rev Curr Transpl Rep*. 2021;8(4):1-12.
3. Organ Procurement and Transplantation Network. Lower respiratory testing of all potential lung donors for SARS-CoV-2 now required. 2021. https://unos.org/news/sars-cov-2-lower-respiratory-testing-potential-lung-donors-may-27/ Accessed September 30, 2021
4. 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*. 2022;24:e13757.
5. Romagnoli R, Gruttadauria S, Tisone G, et al. Liver transplantation from active COVID-19 donors: a lifesaving opportunity worth grasping? *Am J Transplant*. 2021;21(12):3919-3925.
6. Organ Procurement and Transplantation Network. Disease transmission advisory committee. 2022. https://optn.transplant.hrsa.gov/about/committees/disease-transmission-advisory-committee/
7. Kaul DR, Vece G, Blumberg E, et al. Ten years of donor-derived disease: a report of the disease transmission advisory committee. *Am J Transplant*. 2021;21:689-702.
8. Robbins-Juarez SY, Qian L, King KL, et al. Outcomes for patients with COVID-19 and acute kidney injury: a systematic review and meta-analysis. *Kidney Int Rep*. 2020;5:1149-1160.
9. Bowe B, Cai M, Xie Y, Gibson AK, Maddukuri G, Al-Aly Z. Acute kidney injury in a national cohort of hospitalized US veterans with COVID-19. *Clin J Am Soc Nephrol*. 2020;16:14-25.
10. Santoriello D, Khairallah P, Bomback AS, et al. Postmortem kidney pathology findings in patients with COVID-19. *J Am Soc Nephrol*. 2020;31:2158-2167.
11. Velez JCQ, Caza T, Larsen CP. COVAN is the new HIVAN: the re-emergence of collapsing glomerulopathy with COVID-19. *Nat Rev Nephrol*. 2020;16:565-567.

How to cite this article: Sanchez-Vivaldi JA, Patel MS, Shah JA, et al. Short-term kidney transplant outcomes from severe acute respiratory syndrome coronavirus 2 lower respiratory tract positive donors. *Transpl Infect Dis*. 2022;e13890. https://doi.org/10.1111/tid.13890