ORIGINAL ARTICLE



Solid organ transplantation from COVID positive donors in the United States: Analysis of United Network for Organ Sharing database

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Abstract

Background: Significant uncertainties remain regarding the utilization of organs for solid organ transplantation (SOT) from donors with coronavirus disease 2019 (COVID-19). The aim of this study was to assess the trends in utilization of organs from donors with COVID-19 and their short-term outcomes.

Methods: Deceased donors between March 2020 and December 2021 with a positive COVID nucleic acid test from respiratory tract within 14 days of transplantation were analyzed using the de-identified United Network for Organ Sharing (UNOS) database. Donor and recipient characteristics of COVID-19 positive (COVID+) organs were compared to COVID-19 negative (COVID-) organs during this period. We analyzed the trends in the utilization of SOT from COVID+ donors across the United States, donor characteristics, and the quality of donor organ and recipient outcomes (length of hospitalization, rates of organ rejection, delayed graft function, 30-day graft/patient survival).

Results: During the study period, 193 COVID+ donors led to the transplantation of 281-kidneys, 106-livers, and 36-hearts in 414 adult recipients. COVID+ patients donated a median of two organs. These donors were younger and had a lower median Kidney Donor Profile Index (0.37 vs. 0.50, p < .001), lower median serum creatinine (0.8 vs. 1.0 mg/dl, p = .003), similar median serum total bilirubin (0.6 mg/dl, p = .46), and similar left ventricular ejection fraction (60%, p = .84) when compared to COVID- donors. Short-term outcomes, including 30-day graft/patient survival, were similar in both groups.

Conclusions: Analysis of short-term outcomes from the UNOS database indicates that a positive COVID test in an otherwise medically suitable donor should not preclude consideration of non-lung solid organ transplantation.

KEYWORDS

COVID 19, solid organ transplant, United Network for Organ Sharing database

Abbreviations: ALD, alcohol-related liver disease; BMI, body mass index; CIT, cold ischemia time; COVID–1, COVID–19 negative; COVID+, COVID-19 positive; COVID-19, coronavirus disease 2019; DCD, donation after cardiac death; IQR, interquartile range; KDPI, kidney donor profile index; NAT, nucleic acid test; SARS-CoV-2, severe acute respiratory coronavirus-2; URT, upper respiratory tract.

1 | BACKGROUND

The Coronavirus disease 2019 (COVID-19) pandemic has had a significant impact on transplantation, including excess mortality in patients on waitlist, higher risk of hospitalization, and death in transplant recipients.^{1,2} Availability of vaccination and treatment options with antiviral agents and anti-spike monoclonal antibodies has led to improved morbidity and mortality among these patients.³⁻⁵ As transplant centers recovered from initial setbacks, important questions arose regarding the safety and timing of transplanting patients who had recovered from COVID-19 and the feasibility of accepting otherwise suitable organs from COVID-19 positive (COVID+) donors.^{6,7} Early experience showed the safety of performing solid organ transplantation (SOT) in patients who had recovered from COVID-19 as well as successful utilization of organs from donors with remote COVID-19.⁸ This was followed by reports where organs were successfully transplanted from patients with a positive COVID test.⁹⁻¹³ However, three reports of donor-derived infection in lung transplant recipients have been described.^{14,15} Despite encouraging early results, organ donation from a COVID+ donor remains a contraindication in many transplant centers. Here we describe the characteristics of COVID+ donors and recipients and clinical outcomes from the nationwide database between March 2020 and December 2021.

2 | METHODS

2.1 Study population

Data from deceased donors between March 2020 and December 2021 were analyzed using the de-identified United Network for Organ Sharing (UNOS) database. The variable "COVID19_NAT_TESTRESULT" was used to categorize the donors. Donors with a pending or indeterminate result were excluded. Transplant centers were categorized by the variable "CTR_CODE." Trends in the utilization of COVID+ donors were analyzed across the UNOS regions and the United States.

2.1.1 Definition of COVID positive donor

The deceased donor, who had a positive severe acute respiratory coronavirus-2 (SARS-CoV-2) nucleic acid test (NAT) result from either upper respiratory tract (URT) or lower respiratory tract (LRT) within 14 days from date of organ recovery, was defined as a COVID+ donor. Donors with a positive test result recorded more than 14 days from organ recovery were excluded. Three cases that included an error in the test year were corrected and included as the year of admission and date of organ recovery were concordant. A deceased donor with a negative COVID NAT result was defined as a COVID-19 negative (COVID–) donor.

2.1.2 | Recipients

The adult recipients (age \geq 18 years) who underwent a solid organ transplant (heart, lung, liver, pancreas, intestine, and kidney) from a COVID+ donor or a COVID- donor were analyzed.

2.2 | Outcome variables

Outcomes investigated were trends in utilizations of organs from COVID+ donors. Secondary outcomes were the quality of these donor organs, length of hospitalization, rates of organ rejection posttransplant, delayed graft function, 30-day graft survival, and 30-day patient survival.

2.3 | Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 26.0 (IBM Corp., Armonk, NY) and R-Studio using R Version 4.1.1 (R Studio, Boston, MA). Continuous variables were presented as the median (interquartile range: IQR). Between the groups, comparisons were made using chi-square or Fisher's exact tests for categorical and the Mann–Whitney *U* test for continuous. For all statistical analyses, *p* < .05 was considered significant.

3 | RESULTS

Between March 2020 and December 2021, 20 651 deceased donors were registered in the UNOS database. Donors with the test pending (370) and indeterminate (49) were excluded. There was a total of 333 donors with a positive NAT result. Of these, 238 (1.1%) donors had a positive NAT result within 14 days of transplant, with a simultaneous COVID antigen test positive in 8 (3.3%), negative in 5 (2.1%), and not available in 225 (94.5%). During the same period, 20 318 donors had a negative NAT result, with a simultaneous COVID antigen test positive in 559 (2.7%), and not available in 9 (0.04%), negative in 559 (2.7%), and not available in 97.1% of donors. Of positive NAT results, 206 (86.5%) were from URT, 31 (13%) were from LRT, and 1 (0.4%) were from a rectal swab.

3.1 | Transplantation and trends

During the study period, 193 COVID+ donors had the recovery of organs that led to transplantation. These included 281 kidneys, 106 livers, 36 hearts, 1 lung, 14 kidney-pancreas, 5 simultaneous liver-kidney, and 4 simultaneous heart-kidney transplants in 414 adult recipients (Figure 1). These events were first reported in July 2020 with the maximum number of organs from COVID+ donors being transplanted in October 2021 and the highest utilization of organs

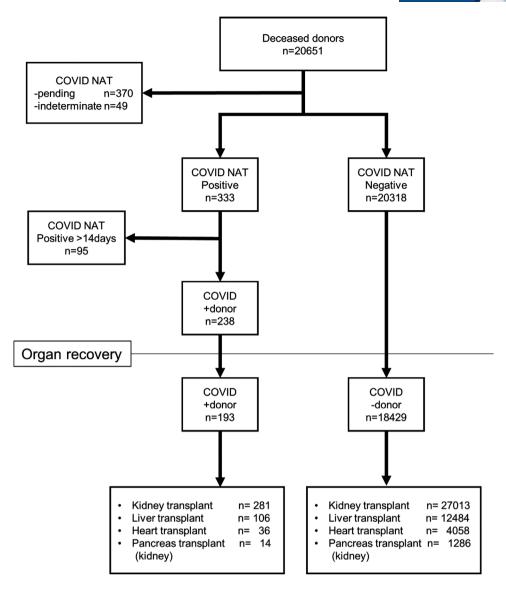


FIGURE 1 Donor and recipient selection criteria for solid organ transplants from COVID+ donors

from COVID+ donors in UNOS region 10. Chronological and regional distribution of these transplants is shown in Figure 2. As of December 2021, of all US transplant centers that performed more than five transplants per year, the center-wide acceptance rates of organs from COVID+ donors were 25% for heart, 41% for kidney, and 51% for liver transplants.

3.1.1 | Donor characteristics

Clinical characteristics of 193 COVID+ donors are summarized in Table 1.

The median time from a documented positive donor test to transplantation was 1 day (IQR: 0-4, range 0-14). When compared to COVID- donors, COVID+ donors were younger (median age: 37 vs. 41 years, p < .001) and had higher body mass index (BMI) (28.6 vs. 27.4, p = .020) with no difference in sex, race, ABO

blood type, and hepatitis C positivity. COVID+ donors had higher rates of donation after cardiac death (DCD) (34% vs. 25%, p =.015). The most common listed causes of death were anoxia (36%), head trauma (27%), cerebrovascular event/stroke (18%), and directly from COVID (9.8%). Six (3.1%) of the donors were on extracorporeal mechanical support at the time of transplantation. Prior to donation, the donors were hospitalized for a median of 5 days (IQR 3–7).

3.2 | Organs and quality

COVID+ patients donated a median of 2 organs (IQR 2-3), which was lower than COVID- donors (median three organs, IQR 2-4, p < .001). When compared to COVID- donors, COVID+ donors had a lower median Kidney Donor Profile Index (KDPI) score (0.37 vs. 0.50, p < .001), lower median serum creatinine (0.8 vs. 1.0 mg/dl, p = .003),

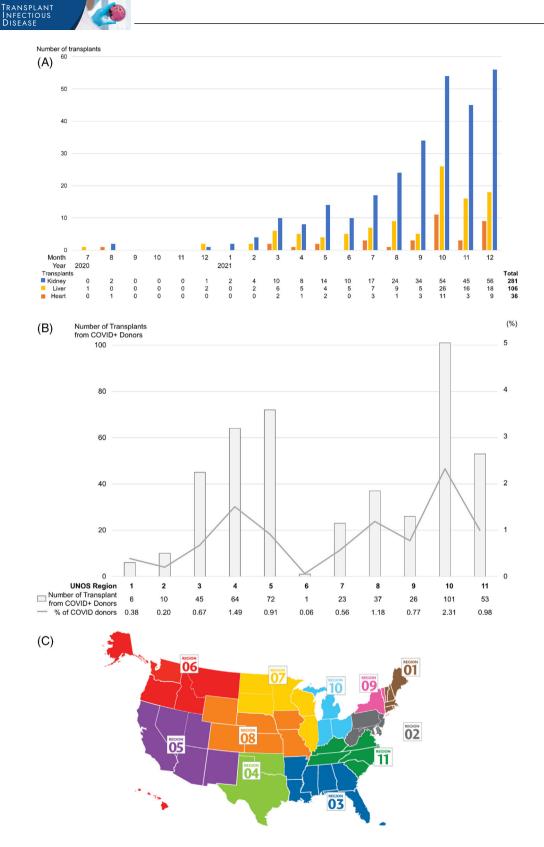


FIGURE 2 (A) Chronological trends in solid organ transplants from COVID+ donors, (B) regional trends in solid organ transplants from COVID+ donors, (C) Organ Procurement and Transplantation Network map

TABLE 1 Donor characteristics



	COVID positive donors, $n = 193$	COVID negative donors, <i>n</i> = 18 429	р
Age years, median (IQR)	37.0 (26.0-49.0)	41.0 (29.0-53.0)	<.001
Gender, <i>n</i> (%)			.25
Female	64 (33%)	6847 (37%)	
Male	129 (67%)	11 582 (63%)	
Race, n (%)			.26
White	131 (68%)	12 039 (65%)	
African American	28 (15%)	2938 (16%)	
Hispanic	28 (15%)	2717 (15%)	
Asian	1 (0.5%)	454 (2.5%)	
Others	5 (2.6%)	281 (1.5%)	
Blood type, n (%)			.20
A	81 (42%)	6741 (37%)	
AB	2 (1.0%)	575 (3.1%)	
В	22 (11%)	2127 (12%)	
0	88 (46%)	8986 (49%)	
Body mass index, kg/m ² , median (IQR)	28.6 (24.3-33.5)	27.4 (23.5-32.4)	.020
Donation type, n (%)			.015
Donation after brain death	127 (66%)	13 832 (75%)	
Donation after cardiac death	66 (34%)	4596 (25%)	
Serum total bilirubin, mg/dl, median (IQR)	0.6 (0.4–0.9)	0.6 (0.4-1.0)	.46
Serum creatinine, mg/dl, median (IQR)	0.8 (0.6-1.4)	1.0 (0.7-1.7)	0.003
Left ventricular ejection fraction, %, median (IQR)	60 (55–65)	60 (55–65)	0.84
Kidney Donor Profile Index, median (IQR)	0.37 (0.16-0.60)	0.50 (0.25-0.74)	<.001
Donor causes of death, n (%)			
Anoxia	69 (36%)	8714 (47%)	
Cardiovascular disease/stroke	35 (18%)	4373 (24%)	
Head trauma	52 (27%)	4823 (26%)	
Central nervous system tumor	0 (0%)	53 (0.3%)	
Others	37 (19%)	466 (2.5%)	
COVID	19 (9.8%)		
Extracorporeal support, n (%)	6 (3.1%)	115 (0.6%)	<.001
Number of organs transplanted, median (IQR)	2.0 (2.0-3.0)	3.0 (2.0-4.0)	<.001
Days from admission to donation, median (IQR)	6 (4-12.5)	5 (3-7)	<.001

Abbreviations: COVID, coronavirus disease; IQR, interquartile range.

similar median serum total bilirubin (0.6 mg/dl), and similar left ventricular ejection fraction (60%).

3.3 | Recipient characteristics

A total of 414 adult recipients received organs from COVID+ donors during the study period. In the final analysis, results from recipients of kidney, liver, heart, and kidney-pancreas were included. As the number of lung transplant recipients (N = 1) and intestine transplants (N = 0) were small during the study, they were excluded from the comparison. Characteristics of recipients of multi-organ transplants were included in each separate organ analysis. These results are further summarized in Tables S1–S6.

3.3.1 | Kidney transplantation

Adult recipients of 281 kidneys had a median age of 54 years (IQR 44-63) and a median wait time of 484 days (IQR 151-1017). When

compared to 27013 kidney recipients of COVID– donors during the study period, these recipients had a lower incidence of being on hemodialysis at time of transplant (79% vs. 86%, p = .005) but were similar for age, sex, race, ABO blood type, BMI, comorbidities, serum creatinine, and wait time. COVID+ donors of kidneys, when compared to COVID– donors, were younger (median age 36 vs. 40 years, p < .001), had lower serum creatinine (0.8 vs. 0.9 mg/dl, p < .001), lower KDPI (0.30 vs. 0.44, p < .001), a longer cold ischemia time (CIT) (19.6 vs. 18.2 h, p = .002), and longer distance from transplant center (114 vs.. 94 mi, p < .001). The median time from a documented test positive to transplant was 2.5 days (IQR 1–4, range 0–9 days).

3.3.2 | Liver transplantation

Adult recipients of 106 livers had a median age of 55 years (IQR 44-62) and a median wait time of 48 days (IQR 7.5-216). When compared to 12 484 liver recipients of COVID- donors during the study period, these recipients had a higher incidence of alcohol-related liver disease (ALD) as a primary diagnosis (47% vs. 39%), lower model for end-stage liver disease score (22 vs. 26, p = .14), a longer waiting time (48 vs. 26 days, p = .42), but were similar in age, sex, race, BMI, dialysis at the time of transplant, incidence of portal venous thrombosis, transjugular intrahepatic portosystemic shunt, previous abdominal surgery, and comorbidities. COVID+ donors of livers, when compared to COVID- donors, were younger (median age 33.5 vs. 40, p < .001), had lower donor risk index (1.58 vs. 1.67, p = .018), had longer distance from transplant center (204.5 vs.. 141 mi, p < .001), and were similar in serum bilirubin, sex, race, hepatitis C serology, and CIT. In a subgroup analysis of liver transplants performed for ALD, 50 recipients of COVID+ donor organs were similar in clinical characteristics when compared to 4861 recipients of COVID- donor organs. The median time from a documented test positive to transplant was 3 days (IQR 1-4, range 0-13 days).

3.3.3 | Heart transplantation

Adult recipients of 36 hearts had a median age of 58 years (IQR 49– 65) and a median wait time of 16 days (IQR 6–108). When compared to 4058 heart recipients of COVID– donors during the study period, these recipients had a shorter median waiting time (16 vs. 29 days, p= .49), higher incidence of hemodialysis at time of transplant (14% vs. 5.7%, p < .001), but were similar for age, sex, race, ABO blood type, BMI, listing status, occurrence of extracorporeal circulatory support, and prior cardiac surgery. COVID+ donors of hearts, when compared to COVID– donors, were younger (median age 28 vs. 32 days, p = .036), male predominant (89% vs. 73%, p = .034), but were similar in sex, race, serum creatinine, CIT, KDPI, and distance from transplant center. Time from a documented positive test to transplant was a median of 3 days (IQR 1–4, range 0–14 days).

3.3.4 | Kidney-pancreas transplantation

Adult recipients of 14 kidney–pancreas had a median age of 41 years (IQR 35–46) and median wait time of 167 days (IQR 60–266). When compared to 1286 kidney–pancreas recipients of COVID– donors during the study period, these recipients were similar in age, race, BMI, ABO blood type, comorbidities, waiting time, donor age, donor serum creatinine, donor KDPI, and CIT. The median time from a documented test positive to transplant was 3 days (IQR 1.8–4.3, range 0–6 days).

3.4 | Organ and patient outcomes

Organ and patient outcome data are summarized in Table 2.

3.4.1 | Kidney transplantation

Recipients of kidney transplants from a COVID+ donor compared to COVID- donors had a shorter length of stay (4 vs. 5 days, p < .001) and lower rate of delayed graft function (21.8% vs. 30.6%, p = .001). Outcomes were similar for rates of rejection before discharge, 30-day graft failure, and 30-day mortality. During a mean follow-up of 85 days in kidney recipients of COVID+ donors, overall mortality was 1.8%.

3.4.2 | Liver transplantation

Recipients of liver transplants from COVID+ donors compared to COVID- donors had shorter length of stay (9 vs. 10 days, p = .25), higher rate of rejection before discharge (9.4% vs. 4.5%, p = .016), and a higher rate of statistically nonsignificant 30-day graft failure (4.7% vs. 3.2%, p = .40). During a mean follow up of 93 days in liver recipients of COVID+ donors, overall mortality was 6.6%. Of seven patients who died, the causes of death were listed as hepatic artery thrombosis (1), sepsis (1), fungal infection (1), cardiac arrest (1), and unknown (3).

3.4.3 | Heart transplantation

Recipients of heart transplants from COVID+ donors, compared to COVID- donors, had a similar length of stay (16.5 vs. 17 days, p = .51) and a lower rate of rejection before discharge (8.8% vs. 18%, p = .26). There was no 30-day graft failure or 30-day mortality among heart recipients of COVID+ donors. During the mean follow-up of 89 days in heart recipients of COVID+ donors, overall mortality was 2.9%.

3.4.4 | Kidney-pancreas transplantation

Recipients of kidney-pancreas transplants from COVID+ donors, compared to COVID- donors, had a longer length of stay (10 vs. 8 days,

TABLE 2 Outcomes of solid organ transplants from COVID positive donors



Posttransplant LOS, days, median (IQR) 4 (3-5) 5 (4-7) < 0.001		COVID positive donors	COVID negative donors	р
Rejection before discharge, n(%)10.4%)233 (0.5%).74Delayed graft function, n(%)61(21.8%)233 (30.6%).00130-day graft failure, n(%)10.4%)174 (0.7%).7330-day mortality, n(%)10.4%)1512 (5.6%).74Mortality, n (%)511512 (5.6%).74Deaths from COVID0111.74Ivern = 106n = 12 484.74Posttransplant LOS, days, median (IQR)9(7-16)10(7-17).25Rejection before discharge, n(%)10(9.4%)564 (45%).01630-day graft failure, n(%)543.016.3030-day graft failure, n(%)10(9.4%).262 (6.9%).3030-day graft failure, n(%)76.6%).262 (6.9%).30Mortality, n(%)76.6%).262 (6.9%).51Causes of deathHAT (1)COVID = 94.51Posttransplant LOS, days, median (IQR).51 (1.3-3).51.51Indica crrest (1)Unknown (3)CoVID (0)Posttransplant LOS, days, median (IQR)0.60000	Kidney	n = 281	n = 27 013	
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Mortality, n (%) 0 43 (3%)	30-day graft failure, n (%)		59 (4.6%)	.49
Mortality, n (%) 0 43 (3%)	30-day mortality, n (%)	0	14 (1%)	
		0		
		0		

Abbreviations: COVID, coronavirus disease; HAT, hepatic artery thrombosis; IQR, interquartile range; LOS, length of stay.

p = .064) and a similar rate of delayed graft function. There was no 30-day graft failure, or 30-day mortality noted in kidney-pancreas recipients of COVID+ donors. During the mean follow-up of 53 days in heart recipients of COVID+ donors, overall mortality was 0%.

4 | DISCUSSION

In this study from a large national registry, the organs from COVID+ donors were medically acceptable, were from younger donors, and car-

ried a lower KDPI. Organs from COVID+ donors had an increased incidence of DCD, increased distance between donor and receiving transplant centers, and an increased CIT. Despite these factors, overall outcomes regarding the hospital length of stay, organ rejection before discharge, delayed graft function as well as graft, and patient survival were similar to the outcomes from COVID- donors. The acceptance of hearts from COVID+ donors also reduced the recipient's time on the waitlist. Although increased rejection prior to discharge was seen in liver recipients of COVID+ donors, it was not statistically significant. This maybe be due to the overall trend of using lower immunosuppression during the COVID pandemic¹⁶ and a possibly a higher risk of rejection in younger recipients with ALD.¹⁷

Although a donor with a remote history (>90 days) of a positive COVID test is unlikely to transmit SARS-CoV-2 infection to the recipient or health-care teams, data regarding risk of transmission from donors with a recent positive test are limited. So far, there is no reported transmission of SARS-CoV-2 from a COVID+ donor to the COVID- recipient with the use of a non-lung organ or with use of any blood products.^{9,12,18,19} In our study, the median time of test positive from transplantation was 1 day (IQR: 0-4, range 0-14), which likely denotes the last positive test prior to organ recovery. But with a short median hospitalization of 5 days prior to organ recovery while simultaneously excluding donors with a positive test >14 days, these data better reflect real-world decision-making dilemmas and outcomes of organ transplantation from a donor with recent COVID-19. A positive NAT result may represent various stages of clinical progression and infectivity associated with COVID, and its interpretation requires a careful review of donor and test characteristics.^{11,20} Although some of these tests may also be considered "false positives," the unknowns associated with this scenario may still preclude the use of organs from these donors in some transplant centers.

Our findings indicate an increasing acceptance of non-lung organs for transplantation from COVID+ donors in the Unites States. Our study also highlights the significant role played by UNOS and Organ Procurement and Transplantation Network Ad Hoc Disease Transmission Advisory Committee to collect medically useful data while providing surveillance for any possible adverse events during this unique pandemic.^{9,20} As the transplant community struggles with longer waitlist times and increased mortality among those awaiting transplant, efforts are needed to expand the donor pool. This includes a considering transplantation of organs from "marginal donors" and xenotransplantation.^{21,22} The uses of COVID+ donors offer another way to expand the availability of organs for transplantation. During the Omicron wave, these COVID+ donors included unvaccinated younger patients who had a significantly higher risk of hospitalization and death from COVID.^{23,24} Patients who were hospitalized and/or died of other causes, but were incidentally found to be positive for SARS-CoV-2, also become potential organ donors.²⁵ The only factor precluding donation of organs in this group was a positive COVID test.

Successful transplantation of organs from a COVID+ donor requires a collaboration between various team members who can carefully assess the quality of the donor organ, define the risk of transmission to recipient, and then match it with the right recipient. In an otherwise medically suitable COVID+ donor, these considerations may include donor clinical presentation, radiological findings, viral burden as measured by cycle threshold value from NAT, duration of test positivity, prior treatment of COVID, prior COVID-vaccination, current circulating viral strains as well as indirect complications of COVID-like thrombotic events that may involve various end-organs. Recipient considerations include the probability of death on the waitlist, poor quality of life with a long-anticipated wait time, highly immunologically sensitized candidate with limited donor pool, prior history of COVID, prior COVID-vaccination status, and the availability of adequate risk mitigation options. This personalized risk-benefit analysis is then discussed with the carefully selected recipient, and after appropriate consent and team agreement, the decision is made to proceed with the transplant.

Among the COVID+ donors, the long-term impact of increased CIT and increased rates of DCD need to be evaluated further. The only data presently bearing on this question come from a single center study, in which outcomes among recipients of COVID+ or COVID- donors were comparable at 6-month and 1-year follow-up.²⁶ Our results regarding the medical suitability of organs from COVID+ donors, in the absence of current evidence of transmission of infection to nonlung transplants recipients, and with encouraging short-term recipient outcomes suggest a path toward a larger organ donation pool.

5 | LIMITATIONS

Our study was retrospective in nature and did not include all information that could have potentially influenced transplant-related outcomes. The follow-up period was limited and variability in the quality of data was possible, as information was entered at a wide variety of centers. Data regarding onset and duration of symptoms in COVID+ donors as well as vaccination status of donors/recipients and possible COVID-related treatments and immunosuppression therapies (induction and maintenance) were not available. Nor were all possible data relating to clinical characteristic of organ recipients from COVID+ donors present in the database. We did not have access to information regarding SARS-CoV-2 test characteristics, including cycle threshold values and test platforms or the duration of test positivity prior to transplant. We therefore relied on a positive test within 14 days of transplant as a surrogate marker for recent COVID illness. We only included donors with an SARS-CoV-2 NAT positive result from respiratory tract while excluding donors with antigen alone positive test or an NAT positive result from non-respiratory sites. Our analysis also included multi-organ transplant recipients of COVID+ donors, as the study-focus was on utilization of every transplanted organ, its quality, utilization, and graft-related outcomes. We cannot fully exclude the possibility that such unaccounted factors in the UNOS database or sampling methods could have influenced outcomes. Missing data are explained further in Table S7. Finally, we acknowledge that the small number of kidney-pancreas and heart transplants or patients in other subgroups may have limited our ability to detect certain differences in outcomes. Due to the sample size, only univariate analyses of outcome measures were employed.

6 | CONCLUSIONS

Results from the UNOS database indicate that the center-wide acceptance rate of organs from COVID+ donors is increasing but is variable with current rates of 25% for heart, 41% for kidney, and 51% for liver transplants. As advances in prevention and treatment are achieved and long-term safety data become available, a positive COVID test in an otherwise medically suitable donor may not remain a contraindication for non-lung SOT.

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CONFLICT OF INTEREST

No author has any conflicts to declare.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article. How to cite this article: Dhand A, Okumura K, Nabors C, Nishida S. Solid organ transplantation from COVID positive donors in the United States: Analysis of United Network for Organ Sharing database. *Transpl Infect Dis.* 2022;e13925. https://doi.org/10.1111/tid.13925