BRIEF COMMUNICATION

Transplanting thoracic COVID-19 positive donors: An institutional protocol and report of the first 14 cases

Emily M. Eichenberger, MD,a Amanda C. Coniglio, MD,b Carmelo Milano, MD,c Jacob Schroder, MD,c Benjamin S. Bryner, MD, MS, c Philip J. Spencer, MD,c John C. Haney, MD,c Jacob Klapper, MD,c Carolyn Glass, MD, PhD, d Elizabeth Pavlisko, MD, d Louis Dibernardo, MD, d Chetan B. Patel, MD, b Adam D. DeVore, MD, MHS, b John Reynolds, MD, e and Cameron R. Wolfe, MBBS, MPHa

From the aDivision of Transplant Infectious Diseases, Department of Medicine, Duke University Medical Center, Durham, North Carolina, USA; bDivision of Transplant Cardiology, Department of Medicine, Duke University Medical Center, Durham, North Carolina, USA; cDivision of Cardiothoracic Surgery, Department of Surgery, Duke University Medical Center, Durham, North Carolina, USA; dDepartment of Pathology, Duke University Medical Center, Durham, North Carolina, USA; and the eDivision of Transplant Pulmonology, Department of Medicine, Duke University Medical Center, Durham, North Carolina, USA.

We present our institution’s protocol for evaluating and transplanting thoracic organs from COVID-19 positive donors and report the outcomes to date. Hearts from donors testing positive for COVID-19 on any test were eligible for transplantation at our institution provided the donor exhibited no evidence of hypercoagulability or COVID-19 induced hyperinflammatory state during terminal hospitalization. Lungs were eligible if the donor first tested PCR positive on nasopharyngeal swab (NPS) for COVID-19 > 20 days prior to procurement and had a negative lower respiratory tract specimen. We performed 14 thoracic transplants in 13 recipients using organs from COVID-19 positive donors. None of the recipients or healthcare members acquired COVID-19. No recipients suffered unexpected acute rejection. Patient survival is 92% to date, with graft survival 93%. The use of hearts from COVID-19 positive donors may be safe and effective. Transplantation of lungs is unresolved but may be cautiously pursued under the restricted circumstances.

J Heart Lung Transplant 2022;41:1376–1381

© 2022 International Society for Heart and Lung Transplantation. All rights reserved.

Keywords: COVID-19; heart transplant; lung transplant; organ donation; donor-derived infection

The COVID-19 pandemic has exacerbated the national shortage of thoracic organs. Understanding the safety of transplanting thoracic organs from COVID-19 positive donors is necessary to expand the donor pool for patients in critical need.1 We present our institution’s protocol for evaluating and transplanting thoracic organs from COVID-19 positive donors and report our outcomes.

Hearts and lungs from donors testing positive by PCR on nasopharyngeal swab (NPS) for COVID-19 were eligible
for transplantation provided the donor exhibited no evi-
dence of hypercoagulability or COVID-19 induced hyperin-
flammatory state during terminal hospitalization (Figure 1).
Lungs from donors whose first positive NPS COVID-19
test was <20 days prior to death were ineligible for trans-
plantation. All lung donors underwent lower respiratory
tract (LRT) testing for SARS-CoV-2. Lungs from any
donor with SARS-CoV-2 detected on bronchoalveolar
lavage (BAL) or tracheal aspirate were ineligible for trans-
plant. Thoracic donor organs meeting the eligibility criteria
were subsequently assessed for quality in accordance with
our standard institutional protocol prior to acceptance.
Repeat BAL with SARS-CoV-2 PCR was performed on
donor lungs at the time of transplant for added caution. See
Supplement for additional methods.

Under our institution’s protocol, 14 thoracic organs
including 12 hearts and 2 sets of lungs from COVID-19
positive donors were transplanted in 13 recipients between
January 1, 2021 and February 2, 2022 (Table 1). Dominant
strains were alpha and delta (subjects 1-10) and omicron
(subjects 11-13). No donors died from SARS-CoV-2 infec-
tion and no donors had moderate or severe COVID-19
symptoms. None of the recipients developed signs or symp-
toms of COVID-19 infection. Median duration of follow up
is 215 days. Patient survival is 92% to date, and graft is
survival 93%. No procurement or surgical team members
developed COVID-19 because of this protocol.

One heart-liver recipient (Subject #4) developed severe
intraoperative coagulopathy with massive hemorrhage and
thrombosis (Figure 2A, B). Right coronary artery thrombo-
sis and interventricular clot formed during implantation
resulting in irreversible right ventricular ischemia requiring
urgent re-do heart transplant utilizing a heart from another
COVID-19 positive donor. After re-do heart transplant, the
recipient did not develop recurrence of hypercoagulability.
See Supplement for pathological finding.

We present the largest cohort of cardiac transplant recip-
ients who received a heart from a COVID-19 positive donor
to date. Our cohort, along with prior reports1-3 provide evi-
dence that this practice may be safe and effective for
patients with end stage heart disease, as none of the recipi-
ents developed donor-derived SARS-COV-2 infection, and
to-date have expected graft function. While viral proteins
have been identified in cardiac tissue on autopsy,4 no data
indicates that viable, transmissible virus exists in organs
outside of the respiratory tract. Further, no unexpected
donor derived transmissions have occurred outside the
lung. Whether virus in cardiac tissue represents an innocu-
ous finding in the absence of moderate or severe symptoms,
normal echocardiogram, and otherwise normal gross organ

Figure 1  Protocol for Donors Testing Positive for COVID-19: LRT, lower respiratory tract, NPS, nasopharyngeal swab. Hypercoagula-
bility and hyperinflammatory syndrome as previously defined.6 For lung transplants, a period of <20 days was selected based on isolation
guidance for immunosuppressed patients from the Centers for Disease Control and Prevention.7 A lower respiratory tract specimen con-
sisted of either a bronchoalveolar lavage specimen or a tracheal aspirate.
Table 1  Donor and Recipient Characteristics

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Heart</td>
<td>No;</td>
<td>Not vaccinated</td>
<td>23 years male, no medical history</td>
<td>Motor vehicle accident</td>
<td>D-3: tracheal aspirate PCR +, CT = 38.1; D-2: tracheal aspirate PCR + D-1: tracheal aspirate −; NPS −</td>
<td>Yes</td>
<td>Unknown</td>
<td>53 years male, HCM</td>
<td>Status 2</td>
<td>No</td>
<td>1R, pAMR 0</td>
<td>EF &gt;55%</td>
<td>N/A</td>
</tr>
<tr>
<td>2</td>
<td>Heart</td>
<td>No; Unknown vaccination status</td>
<td>Unknown vaccination status</td>
<td>32 years male, history of substance abuse; Suspected epididymis</td>
<td>Drug overdose</td>
<td>D-2: NPS+, CT = 34</td>
<td>Yes</td>
<td>62 years male, NICM</td>
<td>NECM Status 2</td>
<td>No</td>
<td>2R, pAMR 0</td>
<td>EF &gt;55%</td>
<td>Negative</td>
<td>D+253, discharged home</td>
</tr>
<tr>
<td>3</td>
<td>Heart</td>
<td>No; asymptomatic; Unknown vaccination status</td>
<td>24 years male; no medical history</td>
<td>24 years male; no medical history</td>
<td>Drug overdose</td>
<td>D-5: NPS+, D-2: BAL +, CT = 13.26; NPS +, CT = 16.1</td>
<td>Yes</td>
<td>69 years male; NICM</td>
<td>Status 2</td>
<td>No; received monoclonal antibody post exposure prophylaxis</td>
<td>1R, pAMR 0</td>
<td>EF &gt;55%</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>4</td>
<td>Heart &amp; Liver</td>
<td>No; mild symptoms of headache; Not vaccinated</td>
<td>20 years male; history of depression; Cerebral abscess</td>
<td>20 years male; history of depression; Cerebral abscess</td>
<td></td>
<td>D-7: NPS +, CT = 41.9; NPS antigen −; BAL −</td>
<td>Yes</td>
<td>36 years male; congenital heart disease with double inlet left ventricle, AV atresia, VSD</td>
<td>Status 4</td>
<td>No; received monoclonal antibody post exposure prophylaxis</td>
<td>No</td>
<td>Severe biventricular graft dysfunction</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Heart</td>
<td>No; Unknown vaccination status</td>
<td>17 years male; no medical history; Suicide, gunshot wound</td>
<td>17 years male; no medical history; Suicide, gunshot wound</td>
<td></td>
<td>D-17: NPS +; D-5: NPS +, CT = 26 D-3 NPS +, CT = 20-21 and BAL +, CT for ORS gene = 32.7, CT for S gene = 39.0</td>
<td>Yes</td>
<td>Indication as above</td>
<td>Status 1</td>
<td>No</td>
<td>1R, pAMR 0</td>
<td>EF &gt;55%</td>
<td>N/A</td>
<td>D+68 deceased; primary cause of death: hemorraghic shock from aortic anastomosis breakdown and Rhizopus mediatinits</td>
</tr>
<tr>
<td>6</td>
<td>Heart</td>
<td>No; Unknown vaccination status</td>
<td>26 years male; no medical history; Gunshot wound to head</td>
<td>26 years male; no medical history; Gunshot wound to head</td>
<td></td>
<td>D-22: NPS + with CT= 31-34 D-1: NPS + with CT= 40; BAL −</td>
<td>Yes</td>
<td>48 years male with HCM</td>
<td>Status 3</td>
<td>No</td>
<td>2R, pAMR 1-I</td>
<td>EF &gt;55%</td>
<td>Negative</td>
<td>D+219, discharged home</td>
</tr>
<tr>
<td>7</td>
<td>Heart</td>
<td>No; Unknown vaccination status</td>
<td>24 years male; history of anxiety, depression and substance abuse; Drug overdose</td>
<td>24 years male; history of anxiety, depression and substance abuse; Drug overdose</td>
<td></td>
<td>D-2: NPS + with CT = 23</td>
<td>Yes</td>
<td>64 years male with ICM</td>
<td>Status 4</td>
<td>No</td>
<td>1R, pAMR 1-I</td>
<td>EF &gt;55%</td>
<td>N/A</td>
<td>D+216, discharged home</td>
</tr>
<tr>
<td>8*</td>
<td>Heart</td>
<td>No-mild symptoms; Unknown vaccination status</td>
<td>15 years female, no medical history; Pneumococcal meningitis</td>
<td>15 years female, no medical history; Pneumococcal meningitis</td>
<td></td>
<td>D-3: NPS+, CT=40.2, BAL −; D-2: NPS −</td>
<td>Yes</td>
<td>66 years male with cardiac sarcoidosis</td>
<td>Status 4</td>
<td>No</td>
<td>1R, pAMR 0</td>
<td>EF &gt;55%</td>
<td>N/A</td>
<td>D+215, discharged home</td>
</tr>
<tr>
<td>9</td>
<td>Lung</td>
<td>No-asymptomatic; Not vaccinated</td>
<td>18 years male with no medical history; Motor vehicle accident</td>
<td>18 years male with no medical history; Motor vehicle accident</td>
<td></td>
<td>D-38: NPS + D-3: NPS + with CT = 38.5; BAL −; D-2: NPS − D 0: BAL −</td>
<td>No</td>
<td>56 years male with pulmonary fibrosis due to inhalational lung injury and prior COVID-19 Lung Allocation Score: 63.1859</td>
<td>No</td>
<td>No rejection</td>
<td>N/A</td>
<td>No rejection</td>
<td>N/A</td>
<td>D+219, discharged home</td>
</tr>
<tr>
<td>10*</td>
<td>Heart</td>
<td>No-mild symptoms; Unknown vaccination status</td>
<td>15 years female, no medical history; Pneumococcal meningitis</td>
<td>15 years female, no medical history; Pneumococcal meningitis</td>
<td></td>
<td>D-3: NPS+ D-2: NPS+ D-1: NPS+</td>
<td>Yes</td>
<td>53 years female with NICM</td>
<td>Status 6</td>
<td>No</td>
<td>1R, pAMR 0</td>
<td>EF &gt;55%</td>
<td>N/A</td>
<td>D+205, discharged home</td>
</tr>
</tbody>
</table>

(continued on next page)
### Table 1 (Continued)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Lung</td>
<td>No- mild symptoms; Not vaccinated</td>
<td>25 years male, history of substance abuse, hepatitis C, history of Lyme disease; Cause of death unknown</td>
<td>N/A</td>
<td>D-30: NPS +, with CT = 34.4</td>
<td>N/A</td>
<td>1; Recipient also with history of COVID-19</td>
<td>69 years male with NECM Status 2</td>
<td>No</td>
<td>No</td>
<td>No rejection</td>
<td>N/A</td>
<td>D+92 index transplant hospitalization</td>
<td>N/A</td>
<td>3 days since transplantation and current recipient status</td>
</tr>
<tr>
<td>12</td>
<td>Heart</td>
<td>No- Unknown vaccination status</td>
<td>30y years male, no medical history; Drug overdose</td>
<td>Yes</td>
<td>D-3: NPS +, with CT = 28.1</td>
<td>D-2: BAL + with CT = 27.97</td>
<td>3; index transplantation</td>
<td>67 years male, history of ICM Status 2</td>
<td>No</td>
<td>No</td>
<td>No rejection</td>
<td>N/A</td>
<td>D+90 index transplantation</td>
<td>N/A</td>
<td>3 days since transplantation and current recipient status</td>
</tr>
<tr>
<td>13</td>
<td>Heart</td>
<td>No- Unknown vaccination status</td>
<td>23 years male, no medical history; Drug overdose</td>
<td>Yes</td>
<td>D-4: NPS + with CT = 34.6</td>
<td>D-2: BAL + with CT = 27.97</td>
<td>2; index transplantation</td>
<td>51 years male, ICM Status 4</td>
<td>No</td>
<td>No</td>
<td>No rejection</td>
<td>N/A</td>
<td>D+110 index transplantation</td>
<td>N/A</td>
<td>3 days since transplantation and current recipient status</td>
</tr>
</tbody>
</table>

\(a\)Dominant SARS-CoV-2 strains during this study period for subjects 1-10 were alpha and delta; for subjects 11-13 omicron.

\(b\)Genomic targets and sensitivity of SARS-CoV-2 testing platforms vary. Organ procurement centers did not provide information on assays used for each donor, or did the centers provide sequencing information.

\(c\)Heart function at procurement as assessed grossly and by echocardiogram was normal. All hearts had left ventricular EF \(\geq55\)%, normal right ventricular function and normal appearing valves.

\(d\)Graft function: Patients underwent routine scheduled allograft biopsies according to schedule discussed in Supplement. The biopsy with the greatest level of rejection is included in this table.

\(e\)Cycle threshold values not provided by Organ Procurement Centers.

---

**Notes:**
- NPS +, nasopharyngeal swab PCR positive for COVID-19; NPS -, nasopharyngeal swab PCR negative for COVID-19; CT, cycle threshold; D, number of days prior to organ procurement; BAL, bronchoalveolar lavage; EF, ejection; HCM, hypertrophic cardiomyopathy; fraction; NICM, nonischemic cardiomyopathy; ICM, ischemic cardiomyopathy; pAMR, pathologic antibody mediated rejection; AV, aortic valve; VSD, ventricular septal defect; N/A, not applicable.
- Median duration of follow up of recipients is 215 days (Q1: 110 days, Q3: 219 days).
assessment, or is a harbinger of longer-term organ dysfunction remains unknown. Because evidence suggests that transmissible virus does not exist outside the respiratory tree, our protocol is deliberately agnostic to the LRT results for heart donors.

Subject #4 experienced significant complications after heart/liver transplantation as previously described. The explanted heart was examined for signs of direct myocardial injury due to COVID-19. A single right ventricular biopsy on the explanted heart IHC stained positive for nucleocapsid protein, but no other pathologic findings indicated direct myocyte damage due to COVID-19. There was no evidence of myocarditis, the SARS CoV-2 PCR from the heart tissue was negative, and the left ventricle was without gross or histologic abnormality. Additionally, the liver was clinically and histologically unaffected. While the significance of the IHC result is unclear, the PCR results and remaining pathological findings were reassuring and supportive that no viable virus exists in these extra-pulmonary tissues. The cause of hypercoagulability and graft failure was ultimately attributed to liver cirrhosis and underlying congenital heart disease, not COVID-19 related organ failure.

COVID-19 is primarily transmitted via respiratory secretions, as evidenced by 3 cases wherein donor-derived COVID-19 transmitted unexpectedly to a recipient via lung transplantation. In each instance, the donor tested positive for SARS-CoV-2 on BAL. In April 2021, UNOS mandated all donors undergo LRT testing for SARS-CoV-2 prior to lung procurement. Donors with a negative LRT test, but positive NPS likely represent a different entity wherein cautious evaluation of donor history and lungs may be useful to determine usability for transplant. In such cases, if the donor initially tested positive for COVID-19 on NPS >20 days prior, the donor may have a resolved infection with persistent, dead viral shedding. While viral culture would offer definitive evidence for active infection vs dead viral shedding, this takes several days to complete, rendering it impractical in real-time donor evaluation. Despite donors having positive NP swabs, our lung transplant recipients did not develop COVID-19 and recovered from transplant uneventfully. These cases provide incremental evidence that transplanting lungs from COVID-19 positive donors meeting the protocol’s stringent criteria may provide a safe pathway to transplant for patients with end stage lung disease.

Seven donors had unknown vaccination status. A vaccinated donor may be less likely to develop hyperinflammatory/hypercoagulable complications, though unknown/negative donor vaccination did not preclude transplantation.

Our study has limitations. First, donor clinical information was limited to what OPOs collect and share, including COVID-19 assays used and donor vaccination. Second, sample size was small with only 14 recipients receiving thoracic organs from COVID-19 positive donors, including only 2 lung recipients. This reflects our abundant caution in evaluating lung donors with COVID-19, as prior
transmission has occurred in this setting.5,6 Our results should be interpreted with caution and with the understanding that additional information, including impact of new variants, is needed to fully comprehend the safety of thoracic organ transplantation using COVID-19 positive donors. As we begin to explore the utility of thoracic organ transplantation from COVID-19 positive donors, we encourage all transplant candidates to receive the COVID-19 vaccination series. Additionally, any transplant candidates in whom COVID-19 positive donors are being considered should undergo informed consent prior to transplantation.

Immunohistochemistry was performed using a Sars-Cov-2 Nucleocapsid Protein Polyclonal Antibody (Novus biologicals NB100-56576). The antibody was validated for research, and not clinical purposes. There was equivocal staining in the cardiomyocytes (granular brown pigmented areas) with unclear significance from the right ventricular biopsy of the donor heart in the patient who underwent retransplantation. However, the corresponding Sars-Cov-2 digital droplet PCR was negative for viral particles.

Author Contributions

All authors contributed to the conception, design, and drafting of the manuscript. All authors have approved of the final version to be published.

Disclosure statement

The authors of this manuscript have conflicts of interest to disclose. EP has participated in a physician advisory board for both Agilent and Dialecticals for which she was compensated for her time. CW serves on the Data Safety Monitoring Board for COVID Therapeutics at Biogen and Atea Pharmaceuticals and performs consultancy for Regeneron, Enzychem Biopharma, and Adagio Therapeuticsp

Work contained in this manuscript was made possible by the following grant from the National Institute of Allergy and Infectious Disease (T32 -AI100851 [EME]).

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.healun.2022.06.018.

References