Post–Lung Transplantation Outcomes and Ex Vivo Histopathological Findings in Severe Post-COVID-19 Pulmonary Disease—A Single-Center Experience

Hana Javaid,1 Masayuki Nigo,1 Bihong Zhao,2 Daniel Ocazionez Trujillo,3 Rodrigo Hasbun,1 Luis Ostrosky-Zeichner,1,4 Manish Patel,4 and Soma Jyothula5

1Division of Infectious Diseases, Department of Internal Medicine, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, Texas, USA, 2Division of Pathology and Laboratory Medicine, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, Texas, USA, 3Department of Diagnostic and Interventional Imaging, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, Texas, USA, 4Center for Advanced Cardiopulmonary Therapies and Transplantation, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, Texas, USA, and 5Division of Critical Care, Pulmonary, Sleep and Lung Transplant Medicine, Department of Internal Medicine, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, Texas, USA

Background. A significant proportion of patients with severe and persistent coronavirus disease 2019 (COVID-19) require continuous ventilatory support and occasional extracorporeal membrane oxygenation (ECMO) for acute respiratory distress syndrome (ARDS). Lung transplantation is a treatment option for patients who develop severe ARDS.

Methods. Our lung transplant database was retrospectively reviewed for patients who underwent lung transplantation for COVID-19 pulmonary disease at Memorial Hermann Hospital, Texas Medical Center, Houston, Texas, from January 2020 to March 2022. We evaluated outcomes of patients who were followed in our clinic at least 6 months post-transplant. Pretransplant patient characteristics, COVID-19-related treatment, histopathology results, and postdischarge course were evaluated.

Results. Among a total of 13 lung transplant recipients, 6 consecutive patients were identified who had a minimum of 6 months of follow-up post–lung transplantation. The average age of patients was 55 years, with a male predominance. The median time to transplantation was 111 days. All 6 patients had significant postinfectious complications due to COVID-19 before transplant. Histopathological findings from explanted lungs showed a predominance of fibrotic change. There were no reported cases of rejection or graft dysfunction. 5 patients had minimal to no post-transplant infectious complications. One patient died 218 days post-transplant from infectious complications.

Conclusions. Five out of six lung transplant recipients at our institution have demonstrated excellent long-term outcomes after index hospitalization, for a mean follow-up of 13 months post–lung transplantation. Lung transplantation for lung fibrosis due to COVID-19 is an acceptable salvage treatment option. Larger studies are warranted to confirm these findings.

Keywords. COVID-19; ARDS; hospitalization; lung transplantation; outcomes.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first observed in Wuhan, Hubei province, China, in December 2019 and has since become a global pandemic [1]. As of March 2022, >4 million cases worldwide and close to 6 million deaths internationally have been reported [2]. Acute respiratory distress syndrome (ARDS) due to coronavirus disease 2019 (COVID-19) is the major cause of prolonged hospitalization and mortality. A large case series from mainland China reported outcomes of 1099 patients with laboratory-confirmed COVID-19 infection; 61.6% of the patients achieved a composite end point of admission to the intensive care unit (ICU), requiring mechanical ventilation or resulting in death. Among those patients, 40.3% of patients developed ARDS [3]. Furthermore, case series from the Lombardy region in Italy reported high rates of mechanical ventilation (88%) and mortality (26%). Ninety-five percent of 1581 ICU patients hospitalized for COVID-19 in the study were still in the ICU five weeks after hospitalization [4]. This clinical finding is congruent with our institutional experience, with a significant proportion of patients requiring continuous ventilatory support and occasional ECMO support for severe and persistent COVID-19 ARDS. These clinical observations indicate a persistent COVID-19 ARDS phenotype, which includes significant respiratory impairment and a high risk of mortality.

Lung transplantation is considered a treatment option for patients who develop severe ARDS resulting in persistent severe lung damage without anticipated recovery of lung...
function. The first 3 lung transplants were performed at Shenzhen Third People’s and Wuxi People’s Hospital in June 2021 [5]. Since then, multiple groups from across the world have published their experience with lung transplantation in severe COVID-19 ARDS. Bharat et al. described early outcomes of lung transplantation in the first 12 consecutive severe COVID-19 patients from 6 centers across 4 countries [6]. The majority of reports have focused on immediate post-transplant outcomes. According to United Network for Organ Sharing (UNOS) registry data, 214 lung transplants were performed from August 1, 2020, to September 30, 2021, for COVID-19-related respiratory failure [7]. We describe our experience and the outcomes for the first 6 consecutive COVID-19 patients who had severe acute COVID-19 pneumonia complicated by ARDS who underwent bilateral lung transplant with at least 6 months of follow-up data at our institution starting from August 2020.

METHODS

The lung transplant database was retrospectively reviewed for patients who underwent lung transplantation for COVID-19-related pulmonary disease at Memorial Hermann Hospital, Texas Medical Center, Houston, Texas, since January 2020. To evaluate the long-term outcomes of these patients, we only included patients who were followed in our clinic for at least 6 months post-transplant. Lung transplantation was considered in patients who had a minimum of 4 weeks post-onset of COVID-19 ARDS and cleared the primary infection, confirmed by 2 negative nasopharyngeal polymerase chain reaction (PCR) assays. Patients with clinical evidence of severe respiratory impairment requiring high fraction of inspired oxygen (FiO2) supplementation, mechanical ventilation, or ECMO support were considered for lung transplant evaluation. Lung transplant candidates were evaluated by a multidisciplinary team for lung transplant candidacy. Patients were listed after approval by the institutional medical review board (MRB) per standard practice. The post–lung transplant recipients were followed per protocol with serial bronchoscopy, imaging, and pulmonary function tests. Maintenance immunosuppressive therapy was tacrolimus based, along with mycophenolic acid and prednisone. Standard post-transplant infection prophylaxis was like that of non-post-COVID-19 lung transplantation patients, including cytomegalovirus (CMV) prophylaxis for 12 months (based on serostatus), antifungal prophylaxis for 3 months, and Pneumocystis jirovecii pneumonia (PJP) prophylaxis (indefinitely). This study has been approved by the institutional review boards (IRBs) of the University of Texas Health Science Center and Memorial Hermann Hospital System.

RESULTS

Among a total of 13 patients who underwent lung transplantation after severe COVID-19 infection in our institution, 6 patients were identified who had a minimum of 6 months of follow-up post–lung transplantation. Pretransplant patient characteristics, COVID-19-related treatment, histopathology results, and postdischarge outcomes were evaluated. At the time of our analysis, the remaining 7 patients were <6 months out of transplant.

Pre– and Post–Lung Transplantation Recipient Patient Characteristics, Transplant Surgery, and Perioperative Outcomes

Table 1 summarizes patient characteristics. All patients other than patient 5 were initially managed for COVID-19 at other hospitals and transferred to our center for lung transplantation. All patients were unvaccinated for COVID-19 before transplant. COVID-19 variants were not reported at our institution; however, the dominant strain for patients 1–3 was Alpha, and for patients 4–6 it was Delta. All patients had 2 negative COVID-19 polymerase chain reaction (PCR) tests from nasopharyngeal swabs 24 hours apart. The first patient in the cohort was diagnosed with COVID-19 on July 1, 2020, in the seventh month of the pandemic. Medical management was evolving during that period. All patients received steroids as part of the management for COVID-19 and ARDS; dosing and duration varied markedly among the patients. Convalescent plasma was used in all patients. The median age of the cohort (range) was 60 (32–69) years. This was a male-predominant cohort of patients (67%). Three patients were obese at the time of diagnosis of COVID-19. All patients had a BMI <35 at the time of lung transplantation evaluation. Minorities are considered to have a higher risk of morbidity and mortality with COVID-19 [8], and this was reflected in our group of patients (Hispanic 67%). This may also reflect the demographic of the geographic region, as our transplant center is in the city of Houston in Southern Texas. Risk factors for chronic lung disease included smoking and occupational exposures. Patient 1 had an extensive history of exposure to dust as a lifelong construction worker. Patient 4 lived on a farm in close contact with various domestic animals and poultry. Patients 1, 2, 4, and 6 never received invasive ventilation and were on high-flow oxygen therapy with intermittent noninvasive ventilation (NIV). Patient 3 was intubated for 14 days early in her course and was referred from a long-term acute care facility due to profound hypoxic respiratory failure requiring high-flow/NIV. Patient 5 received ECMO along with invasive ventilation and was on high-flow oxygen therapy via tracheostomy tube at the time of transplant. All patients except patient 6 were COVID-19 immunoglobulin G (IgG) positive at the time of lung transplantation evaluation. The median duration from onset of diagnosis of infection to transplantation (range) was 111 (57–242) days. All patients were approved by the MRB for lung transplantation after completion of evaluation by a multidisciplinary team per institutional protocols. Details of the surgery and immediate perioperative outcomes are also listed. The median Lung Allocation Score (LAS) at the time of listing (range) was 75.9.
Table 1. Pre- and Post–Lung Transplantation Recipient Patients’ Characteristics

| Pretransplant Recipient Characteristics | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 | Patient 6 | Summary |
|----------------------------------------|-----------|-----------|-----------|-----------|-----------|-----------|---------|
| Age, y                                  | 69        | 63        | 47        | 58        | 32        | 62        | Mean 55 |
| Gender                                 | M         | M         | F         | M         | M         | F         | Male 4/6 |
| Ethnicity/race                          | Hispanic  | White     | Hispanic  | Hispanic  | White     | Hispanic  | 4/6     |
| BMI, kg/m²                              | 23.8      | 25.6      | 27.5      | 23.5      | 27.2      | 32.8      | Med. 26.4 |
| Comorbidities                          | HTN       | DM HLD    | HTN       | DM HLN    | Obesity   | Obesity   | Obesity 3/6 |
| Smoking status                         | Never     | Former    | Never     | Never     | Never     | Never     | Former 2/6 |
| Occupational history                   | Construction worker | None | None | Farmer | None | None | Exposures 2/6 |
| Day of ARDS diagnosis from admission   | 0         | 6         | 0         | 0         | 6         | 0         | ARDS 2/6 |
| First negative PCR after admission, d  | 41        | 34        | 89        | 33        | 45        | 156       | Med. 43 |
| COVID-19 IgG pretransplant             | Yes       | Yes       | Yes       | Yes       | Yes       | Neg       | Yes 5/6 |
| COVID-19 vaccine pretransplant         | No        | No        | No        | No        | No        | No        | No 6/6 |
| Ventilator support on day of lung transplant | iNIV/HFNC | iNIV/HFNC | iNIV/HFNC | HFOT      | HFNC      | 5/6 iNIV/HFNC |
| Prior mechanical ventilation           | No        | No        | Yes       | No        | Yes       | No        | Yes 3/6 |
| Prior ECMO use                         | No        | No        | No        | No        | Yes       | No        | Yes 1/6 |
| COVID-19-specific treatment            | CONV/DEX  | CONV/DEX  | CONV/DEX  | CONV/DEX  | CONV/DEX  | CONV/DEX  | CONV 6/6 |
| Thromboembolic complications           | No        | No        | No        | No        | No        | No        | 0/6     |
| Bacterial complications                | Yes⁴      | No        | Yes⁴      | Yes⁵      | No        | Yes       | Yes 3/6 |
| Fungal complications                   | No        | No        | No        | No        | No        | No        | 0/6     |
| Mycobacterium infection complications  | No        | No        | No        | No        | No        | No        | 0/6     |
| Post–lung transplant characteristics   | Hospital day of lung transplant | 57 | 68 | 137 | 85 | 167 | 242 | Med. 111 |
| Mean PA pressure                       | 22        | 19        | 26        | 16        | 25        | 17        | Med. 21 |
| CAD on LHC                             | Neg       | Non-ob    | Neg       | Non-ob    | No LHC    | Non-ob    | CAD 3/6 |
| LAS score                              | 78.4      | 67.2      | 88.2      | 60.2      | 73.4      | 87.3      | Med. 75.9 |
| CPB/ECMO intra-op                      | Yes       | Yes       | Yes       | Yes       | Yes       | Yes       | Yes | CPB 6/6 |
| Cold ischemic time, min                | R:232     | R:233 L:136 | R:221 L:291 | R:385 L:276 | R:309 L:227 | R:209 L:308 | Med. R:233 L:252 |
| PGD                                    | Grade 2   | Grade 3   | Grade 2   | Grade 3   | Grade 2   | Grade 3   | PGD 6/6 |
| Mechanical ventilation post-transplant | 1         | 1         | 2         | 3         | 4         | 1         | Yes 1/6 |
| Mechanical ventilation post-transplant | 1         | 1         | 2         | 3         | 4         | 1         | Med. 2 |
| ICU stay post-transplant               | 4         | 13        | 8         | 9         | 8         | 12        | Med. 9 |
| Tracheostomy post-transplant, d        | No        | Yes       | No        | No        | Preexisting | No | Tracheostomy 2/6 |
| Hospital stay post-transplant, d       | 11        | 28        | 24        | 18        | 28        | 18        | Med. 21 |

Abbreviations: ARDS, acute respiratory distress syndrome; BMI, body mass index; CAD, coronary artery disease; CMV, cytomegalovirus; CPB, cardiopulmonary bypass; CONV, COVID-19 convalescent plasma therapy; COVID-19, coronavirus disease 2019; DEX, dexamethasone; DM, diabetes mellitus; ECMO, extracorporeal membrane oxygenation; HLD, hyperlipidemia; HFNC, high-flow nasal cannula; HFOT, high-flow oxygen via tracheostomy; HTN, hypertension; ICU, intensive care unit; iNIV, intermittent noninvasive ventilation; intra-op, intra-operative; LAS, Lung Allocation Score; LHC, left heart catheterization; Med, median; MSSA, methicillin-susceptible Staphylococcus aureus; Non-ob, nonobstructive CAD; PCR, polymerase chain reaction; PGD, primary graft dysfunction; RMD, remdesivir; TOCI, tocilizumab; Tsp, transplants.

⁴Full record was not available as the patient was transferred from an outside hospital.
⁵This medication was given in clinical trials.
⁶Tocilizumab was given as it was available at the time.
⁷Catheter-related urinary tract infection due to Enterococcus spp.
⁸S. marcescens (cephalosporinase) and E. cloacae (wild-type) from sputum culture.
⁹MSSA bacteremia due to necrotizing pneumonia, requiring 6 weeks of intravenous cefazolin.

Deep venous thrombosis at suprarenal inferior vena cava.
Eighty-three percent of donors were CMV positive, and 33%

Table 2. Donor Characteristics of the 5 Lung Transplant Recipients

| Patient | Age, y | Gender | Ethnicity/race | Cause of death | Chest trauma | Smoking >20 PY | PaO2/FiO2 ratio at time of offer | Chest x-ray | CMV serostatus | COVID-19 PCR | Summary |
|---------|--------|--------|---------------|----------------|--------------|----------------|-------------------------------|-------------|----------------|-------------|---------|
| 1       | 39     | F      | African American | GSW           | No           | No             | 453                           | Normal      | Pos            | Neg         | Neg     |
| 2       | 40     | F      | White          | GSW           | No           | No             | 475                           | Abnormal    | Pos            | Neg         | Neg     |
| 3       | 49     | M      | African American | ICH           | No           | No             | 497                           | Abnormal    | Neg            | Pos         | Neg     |
| 4       | 28     | F      | White          | MVA           | No           | No             | 513                           | Abnormal    | Pos            | Pos         | 0/6     |
| 5       | 22     | M      | Hispanic       | Head trauma   | No           | No             | 581                           | Abnormal    | Neg            | Neg         | 0/6     |
| 6       | 37     | F      | White          | Drug overdose | No           | No             | 372                           | Abnormal    | Pos            | Pos         | 5/6     |

Abbreviations: CMV, cytomegalovirus; COVID-19, coronavirus disease 2019; FiO2, fraction of inspired oxygen; GSW, gunshot wound; ICH, intracerebral hemorrhage; Med, median; MVA, motor vehicle accident; Neg, negative; PaO2, partial pressure of oxygen in the arterial blood; PCR, polymerase chain reaction; Pos, positive; PY, pack-year.

All patients were participating in physical therapy and ambulatory at the time of transplant. The median PA pressure (range) was 21 (16–26) mm Hg. Nonobstructive CAD was noted in 3 out of 6 recipients on left heart catheterization (LHC). Patient 5 did not undergo LHC due to his age and lack of significant CAD risk factors. Basiliximab was used for induction per institutional protocol. A clamshell incision for bilateral lung transplant was performed on all patients. Significant pleural adhesions were noted in all recipients, with bleeding. Transplant surgery required cardiopulmonary bypass support with central cannulation. The median ischemic time (range) was 233 (209–232) R (right) and 252 (136–308) L (left) minutes. All patients were managed in the transplant ICU. Solumedrol, tacrolimus, and mycophenolate were used for immune suppression per protocol. Broad-spectrum antibiotics and fungal prophylaxis for Aspergillus using voriconazole were given. Primary graft dysfunction (PGD) incidence was 100%, with 50% of patients having grade 2 and 50% of patients having grade 3 dysfunction. PGD was managed with optimal fluid management and inhaled nitric oxide, with complete recovery of graft function by the time of discharge. Patient 2 required early tracheostomy due to PGD grade 3. The median number of days of mechanical ventilation (range) was 2 (1–4). The median ICU stay (range) was 9 (4–13) days. The median duration of hospitalization post-transplantation (range) was 21 (11–28) days.

Donor Characteristics of the 5 Lung Transplant Recipients

Table 2 provides details of donor characteristics. The median age of the donors (range) was 38 (22–49) years. No chest trauma or >20-pack smoking history was reported in donors. The median partial pressure of oxygen in the arterial blood (PaO2)/FiO2 ratio at the time of offer acceptance (range) was 486 (372–581). Eighty-three percent of donors were CMV positive, and 33% were male. Chest x-rays were reported abnormal in 67% of donors. Upon acceptance, all donors received broad-spectrum antibiotics and antifungal infusion per institutional protocol.

Radiological and Pathological Findings

Figures 1 and 2 demonstrate radiological and pathological findings in the recipients. CT of the chest without contrast was performed on all recipients as part of evaluation for lung transplantation. All patients showed ground-glass opacities with reticulations and bronchiectasis of varying degrees. Patient 3 showed changes mimicking a usual interstitial pneumonia (UIP) pattern on a preoperative CT scan. Patients 1 and 4 had consolidative and cavitary changes before transplant. Explant pathology showed diffuse alveolar damage (DAD) with organization and fibrosis in all patients. Patient 1 had significant vasculopathy with intimal thickening. Multiple foci of liquefied infarcts were noted. Patient 3 showed changes of microscopic honeycombing without temporal heterogeneity. Patient 6 showed areas of infarction.

Post-transplant Outcomes

Table 3 summarizes the postdischarge outcomes in the cohort. All patients received a tacrolimus-based immunosuppression regimen along with mycophenolate and prednisone. No CMV viremia was noted in patients to date. Patient 2 developed bacterial sinusitis during follow-up. Patient 6 developed recurrent Klebsiella pneumoniae pneumonia and methicillin-susceptible Staphylococcus aureus (MSSA) necrotizing pneumonia post-lung transplant. The patient received 1 dose of the COVID-19 Pfizer vaccine 3 months post-transplant. She subsequently contracted COVID-19 infection 5 months post-lung transplant in November 2021. Her COVID-19 IgG antibody was negative. Her course was complicated by MSSA and Escherichia Coli pneumonia. She recovered but presented again 6 months post-transplant in December of 2021 with persistent COVID-19 infection, at which time her COVID-19 IgG antibody was positive. Her hospital course was complicated by Fusarium species pneumonia and multidrug-resistant (MDR) Pseudomonas aeruginosa pneumonia with bacteremia. She died 7 months after lung transplantation. Patients 1 and 2
Figure 1. Histopathological findings of explanted recipient lungs. All stains H&E except Pt1-B with elastin stain. Pt1-A: extensive cystic degeneration of lung parenchyma, probably secondary to ischemic cause. Pt1-B: elastin stain that highlights thick intima of a middle-sized pulmonary artery. Pt1-C: fibrotic pleura with mild chronic inflammation. Pt2-A: relatively less affected area with well-preserved lung architecture but increased cellularity in alveolar wall, consistent with cellular NSIP pattern of injury. Pt2-B: interstitial emphysema with histiocytic infiltrate and numerous multinucleated giant cells. Pt2-C: more advanced fibrosis. Pt3-A: diffuse alveolar septal thickening with fibrosis, consistent with fibrotic NSIP pattern of injury. Pt3-B: early honeycombing and dilated pulmonary artery without thickening of the wall. Pt3-C: dilated vasculature without significant thickening of the wall. Pt4-A: diffuse alveolar septal thickening with both cellular and fibrosis, consistent with NSIP pattern of injury. Pt4-B: no significant vascular change. Pt4-C: no pathological change in pleura. Pt5-A: advanced fibrosis and altered architecture with cystic change. Pt5-B: intimal thickening of pulmonary artery. Pt5-C: focal acute pleuritis. Pt6-A: heterogeneous appearance of lung parenchyma with alternating dense fibrosis and relatively less affected area. Pt6-B: fibroblastic foci. Pt6-C: overlapping proliferative and fibrotic phases of DAD. Abbreviations: DAD, diffuse alveolar damage; H&E, hematoxylin & Eosin; NSIP, nonspecific interstitial pneumonia; Pt, patient.
received 3 doses of the COVID-19 vaccine post-transplant. Patients 3, 4, and 5 received 2 doses of the COVID-19 vaccine, and patient 6 received 1 dose. Patient 4 developed left anastomotic stricture and required balloon dilatation along with bronchial stent placement. No other airway complications were noted. Patients 2, 4, and 6 developed de novo donor-specific antibody (DSA) post-transplant. No definitive antibody-mediated rejection (AMR) was noted on transbronchial biopsies. No acute cellular rejection (ACR) was noted upon surveillance biopsies post-transplantation. No clinical evidence of chronic lung allograft dysfunction (CLAD) was found to date. The median Karnofsky performance score was 93 at the time of last follow-up. No oxygen supplementation at the time of discharge or subsequent postdischarge follow-up in the lung transplantation clinic were needed.

DISCUSSION

Our study describes the first 6 lung transplant recipients for severe COVID-19 ARDS who had at least 6 months of follow-up data at our institution. Sixty-seven percent of patients demonstrated minimal to no infectious complications during long-term follow-up, despite significant postinfectious complications due to COVID-19 before lung transplant. 5 patients survived with excellent functional scores. One patient died from COVID-19-related complications 218 days after lung transplantation. Having received high-dose steroids during the initial course of her second hospitalization for COVID-19 may have predisposed her to developing fungal pneumonia with *Fusarium* species as a complication before death. This was also the only patient to have received 1 dose of the COVID-19 vaccine post-transplant. Airway intervention to date has only been required in 1 out of the 5 surviving patients. There were no reported cases of rejection or graft dysfunction. To date, none of the survivors have required supplemental oxygen and have excellent functional status.

Outcomes of the remaining 7 patients who did not meet the criterion of at least 6 months of follow-up data at the time of our analysis include 1 recent death in a patient who received high-dose steroids and developed fungal pneumonia with *Zygomycetes* species. Interestingly, this patient also had *Pseudomonas aeruginosa* pneumonia and bacteremia. These features were similar to patient 6 in our study, who died. The symptoms of patient 1 in our study and the recently deceased patient are similar. One of the 7 patients has shown A1 rejection, and another A3 rejection. Two patients have had airway complications. No patients required supplemental oxygen post-transplant.

Multiple studies have shown the short outcome of lung transplantation after COVID-19. The most recent report showed that 7% of all lung transplants from August 1, 2020, to September 30, 2021, were due to COVID-19-related
Following this initial phase, cellular necrosis, inflammation, epithelium and capillary endothelium. Initially increased per mortality from COVID-19 was 95.6%. mortality from COVID-19, ranging from en alveolar injury and fibrosis ensue. The morphological picture is labeled diffuse alveolar damage and fibrosis that ultimately resulted in ARDS. A previous study showed a high incidence of ventilator support in ICU patients, which suggests persistent respiratory failure from ARDS. Case series from the Lombardy region of Italy and the New York City area showed a high incidence of persistent ICU stay and ventilator support. This clinical finding is congruent with our institutional experience, with a significant percentage of patients requiring continuous ventilator and occasional ECMO support for severe and persistent COVID-19 ARDS. These clinical observations indicate a persistent COVID-19 ARDS phenotype with significant respiratory impairment and high risk of mortality. Our transplant recipients stayed in the hospital for a median of 111 days before lung transplantation. Interestingly, only 2 patients (33%) required mechanical ventilation before lung transplantation. The remaining 4 patients required significant supplemental oxygen due to post-inflammatory pulmonary fibrosis despite never requiring intubation. This is also consistent with a recent study from the US UNOS data.

The limitations of our study include the small cohort of patients, follow-up limited to 6 months, and a single-center experience. Our study does not elaborate on data for non-COVID-19 lung transplant patients as a comparator. However, 16 patients underwent lung transplantation for non-COVID-19 chronic lung disease at the same time as the COVID-19 cohort. Three deaths were noted in the non-COVID-19 cohort within 6 months of transplantation. The cause of death was sepsis in 1 patient and airway complications in the other 2 patients. Considering an acceptable outcome as the pandemic is still ongoing since January 2020, this study provides details on postdischarge outcomes in patients who have undergone lung transplantation for severe COVID-19 ARDS.

### Table 3. Long-term Lung Transplant Characteristics

|                                | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 | Patient 6 | Summary |
|--------------------------------|-----------|-----------|-----------|-----------|-----------|-----------|---------|
| **Bacterial complications**    | No        | Sinusitis\* | No        | No        | No        | Pneumonia\* | Yes 2/6 |
| **Fungal complications**       | No        | No        | No        | No        | No        | Yes\*     | 0/6     |
| **Mycoplasma infection**       | No        | No        | No        | No        | No        | No        | 0/6     |
| **Airway issues requiring intervention** | No        | No        | Yes       | No        | No        | Airway 1/6 |         |
| **DSA**                        | No        | Yes       | No        | No        | Yes       | Yes       | DSA 3/6 |
| **Acute cellular rejection**   | No        | No        | No        | No        | No        | No        | 0/6     |
| **Definitive AMR**             | No        | No        | No        | No        | No        | No        | 0/6     |
| **CMV viremia**                | No        | No        | No        | No        | No        | No        | 0/6     |
| **CLAD**                       | No        | No        | No        | No        | No        | No        | 0/6     |
| **Oxygen supplementation post-transplant** | No        | No        | No        | No        | No        | No        | 0/6     |
| **Karnofsky functional status at last clinic visit** | 100      | 100       | 100       | 90        | 90        | 80        | Mean 93 |
| **No. of COVID-19 vaccines received** | 3         | 3         | 2         | 2         | 2         | 1         | Mean 2  |
| **Post-transplant, mo**        | 18        | 18        | 15        | 10        | 10        | 7         | Mean 13 |

Abbreviations: AMR, antibody-mediated rejection; CLAD, chronic lung allograft dysfunction; CMV, cytomegalovirus; COVID-19, coronavirus disease 2019; DSA, donor-specific antibodies; MDR, multidrug-resistant; MSSA, methicillin-susceptible Staphylococcus aureus.

\*Likely bacterial.

\*Pneumocystis jirovecii pneumonia, MSSA necrotizing pneumonia, MDR Pseudomonas aeruginosa pneumonia, and bacteremia in the setting of repeat COVID-19 infection.

\*Fusarium pneumonia in the setting of repeat COVID-19 infection.

\*Patient 4 had Moderna vaccine; the remaining patients had Pfizer vaccine.
CONCLUSIONS

Five out of six lung transplant recipients at our institution have demonstrated excellent long-term outcomes after index hospitalization, for a mean follow-up of 13 months post–lung transplantation. Lung transplantation for lung fibrosis due to COVID-19 is an acceptable salvage treatment option. Larger studies are warranted to confirm these findings.

Acknowledgments

Financial support. Research grant and personal fees received from Biofire and personal fees received from Melinta Pharmaceuticals.

Potential conflicts of interest. Rodrigo Hasbun, MD—BioFire Research. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Author contributions. S.J., H.J., and M.N. edited the manuscript. R.H., L.O., and M.P. critically reviewed and revised the manuscript. We acknowledge and thank Dr. Zhao and Dr. Ocazionez-Trujillo for providing the histopathologic and radiologic findings, respectively. Study conception and design: Jyothula and Javaid. Analysis and interpretation of data: Jyothula, Javaid, and Nigo. Drafting of manuscript: Jyothula, Javaid. Critical revision: Jyothula, Javaid, Nigo, Ostrosky, Hasbun, Zhao, Ocazionez, Patel.

Patient consent. This activity was reviewed and approved by The University of Texas Health Science Center Committee for the Protection of Human Subjects and was deemed to be exempt from individual informed consent.

References

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020; 382:727–33.
2. World Health Organization. Coronavirus (COVID-19) dashboard. Available at: https://covid19.who.int. Accessed February 15, 2022.
3. Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020; 382:1708–20.
4. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy. JAMA 2020; 323:1574–81.
5. Chen J-Y, Qiao K, Liu F, et al. Lung transplantation as therapeutic option in acute respiratory distress syndrome for coronavirus disease 2019-related pulmonary fibrosis. Chin Med J (Engl) 2020; 133:1390–6.
6. Bharat A, Machuca TN, Querrey M, et al. Early outcomes after lung transplantation for severe COVID-19: a series of the first consecutive cases from four countries. Lancet Respir Med 2021; 9:487–97.
7. Roach A, Chikwe J, Catarino P, et al. Lung transplantation for COVID-19-related respiratory failure in the United States. N Engl J Med 2022; 386:1187–8.
8. Escobar GJ, Adams AS, Liu VX, et al. Racial disparities in COVID-19 testing and outcomes: retrospective cohort study in an integrated health system. Ann Intern Med 2021; 174:786–93.
9. Kurihara C, Manerikar A, Querrey M, et al. Clinical characteristics and outcomes of patients with COVID-19-associated acute respiratory distress syndrome who underwent lung transplant. JAMA 2022; 327:652–61.
10. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA 2020; 323:2052–9.
11. Tomashefski JF. Pulmonary pathology of acute respiratory distress syndrome. Clin Chest Med 2000; 21:435–66.
12. Matthay MA, Zemans RL, Zimmerman GA, et al. Acute respiratory distress syndrome. Nat Rev Dis Primers 2019; 5:18.