Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of an ongoing global pandemic with Coronavirus Disease 2019 (COVID-19). Since its first confirmed case on January 20, 2020, the United States has developed the highest global incidence of COVID-19, with 1,920,904 confirmed cases and 109,901 deaths as of June 7, 2020. The surge of COVID-19 cases has necessitated critical evaluation of healthcare best practices to mitigate patient exposures and ensure judicious resource allocation.

In the United States, an overall national decline in organ transplants has accompanied the substantial burden of COVID-19. Amidst significant regional variations in COVID-19, lung transplantation (LTx) remains a critical life-saving operation. Our LTx practice during the early pandemic may provide a blueprint for managing LTx in an era of continued community prevalence. Patients who underwent LTx at our institution between March 1 and May 20, 2020 were included.Recipient, operative, and donor characteristics were compared to those from our program in 2019, and COVID-19 testing practices were evaluated for March, April, and May to understand how our practice adapted to the pandemic. Our program performed 36 LTx, 33% more than the same period in 2019. Recipient, operative, and donor characteristics during COVID-19 were similar to those in 2019. By April 1, all donors and recipients underwent pretransplant COVID-19 testing, all returning negative results. To date, no recipients have developed posttransplant COVID-19. At our institution, pretransplant COVID-19 testing, use of local donor lungs, and avoidance of donors from areas of increased community penetration supported a safe and effective LTx practice during the early COVID-19 pandemic. Continued follow-up is required to ensure the long-term safety of these newly transplanted patients.
waitlist. LTx candidates and recipients may be at particularly high risk for COVID-19 due to chronic lung disease and manifestation of COVID-19 as a predominantly respiratory illness. While understanding of COVID-19 in LTx recipients is limited, prior work indicates that waitlist mortality increases significantly when centers eschew acceptable donor offers. Thus, as we continue to elucidate the implications of COVID-19 in LTx recipients, the community requires new evidence to guide safe and effective LTx during this period.

At our institution, LTx continued as the COVID-19 pandemic evolved. We evaluated the safety and efficacy of our LTx practice during the first 12 weeks of the pandemic, and strategies to mitigate risks to recipients and providers moving forward.

2 | METHODS

2.1 | Study population

The first confirmed case of COVID-19 in North Carolina, USA was reported on March 3, 2020. Therefore, all patients who underwent isolated LTx at Duke University Hospital between March 1 and May 20, 2020 were included. For comparison, patients who underwent LTx between January 1 and October 31, 2019 (pre-COVID-19) were included to understand how our practice adapted to the pandemic. This study was approved by the Duke University Institutional Review Board (Pro00103325).

2.2 | Study design

Recipient and operative characteristics were obtained from institutional charts. Recipient variables included demographics, preoperative characteristics, and immunosuppression regimen. Perioperative outcomes included 30-day reintervention (surgical, bronchoscopic, radiologic), 30-day hospital or ICU readmission, posttransplant length of stay (LOS), primary graft dysfunction (PGD) grade 3 at 72 hours posttransplant, postoperative extracorporeal membrane oxygenation (ECMO), postoperative date of extubation, tracheostomy within 7 days, and reintubation or dialysis during the index hospitalization. At data collection, date of last follow-up, patient status (alive/deceased), and date of first biopsy-proven acute rejection episode were recorded.

Operative data included lung allograft ischemic time, use of cardiopulmonary bypass, donor type, use of ex-vivo lung perfusion (EVLP), donor/recipient weight ratio, donor and recipient serologies, and transplant type (single/bilateral).

Additional donor characteristics obtained from the United Network for Organ Sharing (UNOS) included age, US Public Health Service increased risk for disease transmission (IRD) classification, smoking history ≥20 pack-years, PaO2/FiO2 (P/F) ratio, cause and mechanism of death, clinical blood or pulmonary infection, final white blood cell count, distance between the donor hospital and the transplant center, state and geographic UNOS region in which lungs were recovered, match sequence at which donor lungs were placed, and whether lung procurement was performed by Duke or a local team.

2.3 | COVID-19 testing and incidence

The occurrence of donor and recipient COVID-19 testing was recorded for each transplant. For all cases in which testing was performed, test type, specimen type, test result, and reason for testing were noted. The burden of COVID-19 in donor and recipient states was assessed based on the cumulative incidence of COVID-19 on the date of transplant as reported by the Johns Hopkins COVID-19 incidence map. In all cases, the recipient state was considered to be North Carolina as all transplants occurred at Duke University Hospital.

2.4 | Statistical analysis

Recipient, operative, and donor characteristics were compared between COVID-19 and pre-COVID-19 LTx using Wilcoxon rank-sum tests for continuous variables and Chi-squared and Fisher’s exact tests for categorical variables. COVID-19 testing practices were explored for March, April, and May to elucidate trends in COVID-19 prevention strategies. A two-sided p-value less than 0.05 was considered statistically significant. All analyses were performed using R version 3.6.1 (Vienna, Austria).

3 | RESULTS

3.1 | Study population

Thirty-six LTx were performed at Duke University Hospital between March 1 and May 20, 2020, a 33% increase in transplant volume compared to the same period in 2019 and 71% more than 2018 (Figure 1). During this period, our kidney, liver, and heart transplant programs performed 27, 32, and 27 transplants, respectively (compared to 2019: kidney −46%, liver −22%, heart +4%) (Figure 2).

Among LTx performed during COVID-19, median recipient age was 64 years (interquartile range [IQR] 48-69), 15 (41.7%) were female, and 29 (80.6%) were white. Most patients (69.4%) had restrictive lung disease (group D). At transplantation, 4 (11.1%) patients were hospitalized, 1 (2.8%) was intubated, and 1 (2.8%) was on ECMO. Median lung allocation score (LAS) at transplantation was 44.5 (range 33.5-89.2) and median waitlist time was 13 days (IQR 6-24); pre-COVID-19, median LAS was 45.6 (range 32.6-91.5) and median waitlist time was 11 days (IQR 5-21) (both p > .05). No patients were hospitalized for presumed or confirmed COVID-19 prior to transplantation; in no case was listing delayed due to COVID-19 concerns (Table 1).

Recipient characteristics were similar between COVID-19 and pre-COVID-19 LTx. During both periods, basiliximab was the most
common induction agent and all patients received standard triple maintenance immunosuppression with a calcineurin inhibitor (tacrolimus or cyclosporine), an antimetabolite (mycophenolate mofetil or azathioprine), and corticosteroids (Table 1).

### 3.2 Operative characteristics

During COVID-19, median allograft ischemic time was 437 minutes (IQR 399-548), cardiopulmonary bypass was used in 6 (16.7%) cases, and bilateral lungs were transplanted in 34 (94.4%) cases. Nine (25.0%) patients received donation after circulatory death donor lungs and EVLP was used in 1 (2.8%) case. Operative characteristics were similar before and during COVID-19 (Table 2).

### 3.3 Donor characteristics

Among LTx performed during COVID-19, median donor age was 30 years (IQR 22-39), 12 (33.3%) were classified as IRD, 3 (8.3%) had smoking history ≥20 pack-years, and median P/F ratio was 446 (IQR 354-497) (all p > 0.05 vs. pre-COVID-19 donors). The most common cause and mechanism of death were anoxia (47.2% vs. 33.6% pre-COVID-19, p = 0.4) and drug intoxication (30.6% vs. 18.7% pre-COVID-19, p = 0.2), respectively. Median donor distance from the transplant center was 228 nautical miles (range 9-937) and most (61.1%) donor lungs were recovered from states in UNOS region 11, the same region as Duke University; pre-COVID-19, median donor distance from the transplant center was 225 nautical miles (range 0-4137) (p = 0.6). During COVID-19, 3 (8.3%) lung procurements were performed by local teams versus 7 (6.5%) pre-COVID-19 (p = 0.7). No donors were hospitalized for presumed or confirmed COVID-19 prior to donation (Table 3).

### 3.4 COVID-19 testing and incidence

#### 3.4.1 Recipient pretransplant testing

Pretransplant COVID-19 testing was performed for 22 (61.1%) patients; all returned negative results. In March, pretransplant testing was performed for 1 (6.7%) patient presenting with acute on chronic hypoxic respiratory failure from interstitial pulmonary fibrosis with a negative extended respiratory viral panel, but no other overt symptoms concerning for COVID-19. In April and May, all (100%) patients underwent asymptomatic pretransplant testing. Until April 14, all tests were performed on nasopharyngeal specimens using SARS-CoV-2 polymerase chain reaction (PCR); thereafter, the point-of-care SARS-CoV-2 rapid test was used, providing...
| Characteristic | LTx during COVID-19 | 2019 LTx (pre-COVID-19) | p-Value |
|---------------|---------------------|--------------------------|---------|
| **Age (years)** | 64 (48-69)          | 60 (47-67)               | .3      |
| **Sex**       |                     |                          | .9      |
| Female        | 15 (41.7%)          | 46 (43.0%)               |         |
| Male          | 21 (58.3%)          | 61 (57.0%)               |         |
| **Race**      |                     |                          | .7      |
| White         | 29 (80.6%)          | 92 (86.0%)               |         |
| Black         | 5 (13.9%)           | 12 (11.2%)               |         |
| Other         | 2 (5.6%)            | 3 (2.8%)                 |         |
| **Ethnicity (Hispanic)** | 1 (2.8%) | 2 (1.9%) | .7 |
| Class I       | 0 (0-0)             | 0 (0-0)                  | .4      |
| Class II      | 0 (0-0)             | 0 (0-0)                  | .5      |
| **Etiology of respiratory failure** | | | .9 |
| Alpha-1 antitrypsin deficiency | 1 (2.8%) | 3 (2.8%) | |
| Acute respiratory distress syndrome/pneumonia | 0 (0%) | 2 (1.9%) | |
| Autoimmune interstitial lung disease | 1 (2.8%) | 6 (5.6%) | |
| Bronchiectasis | 2 (5.6%) | 1 (0.9%) | |
| Chronic obstructive pulmonary disease/emphysema | 3 (8.3%) | 12 (11.2%) | |
| Cystic fibrosis | 2 (5.6%) | 10 (9.3%) | |
| Hypersensitivity pneumonitis | 1 (2.8%) | 2 (1.9%) | |
| Idiopathic pulmonary fibrosis | 22 (61.1%) | 49 (45.8%) | |
| Primary pulmonary hypertension | 1 (2.8%) | 3 (2.8%) | |
| Pulmonary veno-occlusive disease | 0 (0%) | 2 (1.9%) | |
| Re-transplant | 3 (8.3%)           | 10 (9.3%)                |         |
| Sarcoidosis   | 0 (0%)             | 3 (2.8%)                 |         |
| Other         | 0 (0%)             | 4 (3.7%)                 |         |
| **Disease group** | | | .8 |
| A             | 8 (22.2%)           | 17 (15.9%)               |         |
| B             | 1 (2.8%)            | 3 (2.8%)                 |         |
| C             | 2 (5.6%)            | 10 (9.3%)                |         |
| D             | 25 (69.4%)          | 77 (72.0%)               |         |
| **Status at time of transplant** | | | .2 |
| Inpatient/hospitalized | 4 (11.1%) | 22 (20.6%) | |
| Outpatient    | 32 (88.9%)         | 85 (79.4%)               |         |
| **Interventions at time of transplant** | | | |
| ECMO          | 1 (2.8%)           | 10 (9.3%)                | .3      |
| Intubated     | 1 (2.8%)           | 8 (7.5%)                 | .4      |
| History of prior lung transplant | 3 (8.3%) | 10 (9.3%) | .9 |
| Lung allocation score at time of transplant | 44.5 (38.9-50.7) | 45.6 (38.8-60.5) | .3 |
| Most recent 6-minute walk distance (feet) | 1449 (1256-1730) | 1364 (1098-1664) | .2 |
| Cardiac output (L/min) | 5.6 (5.1-6.3) | 5.4 (4.5-6.3) | .3 |
| Arterial pCO2 at transplant (mmHg) | 50 (42-56) | 46 (42-52) | .07 |
| Smoking history | 18 (50.0%) | 54 (50.5%) | .9 |
| Pack-years    | 23 (10-35)         | 20 (7-38)                | .9      |

(Continues)
results within 15 minutes versus approximately 6 hours with PCR (Table 4). Recipient teams wore standard surgical attire for all cases.

### 3.4.2 Recipient posttransplant testing

To date, 30 (83.3%) recipients have undergone posttransplant COVID-19 testing; all returned negative results. Posttransplant testing was most commonly performed as an asymptomatic screen prior to surveillance bronchoscopy (March: 85.7%; April: 100%; May: 83.3%). In March, 3 recipients underwent posttransplant testing due to symptoms including cough, shortness of breath, and dyspnea. Three recipients underwent testing due to otherwise unexplained radiographic findings or respiratory deterioration requiring reintubation during the transplant hospitalization (Table 5).

### 3.4.3 Donor testing

Twenty-six (72.2%) lung donors underwent predonation COVID-19 testing. The frequency of donor testing increased from 33.3% in March to 100% in April and May. All predonation COVID-19 tests were performed using SARS-CoV-2 PCR; all returned negative results. Among tested donors, 24 (92.3%) provided nasopharyngeal specimens and 4 (15.4%) provided bronchoalveolar lavage (BAL) specimens; one donor provided two nasopharyngeal specimens and two donors provided both nasopharyngeal and BAL specimens. Organ procurement organizations (OPOs) assessed COVID-19 risk factors including contacts, symptoms, and travel in 35 (97.2%) cases (Table 6). Duke procurement teams wore N95 masks with standard surgical attire for all donor operations.

### 3.4.4 COVID-19 incidence

The cumulative incidence of confirmed COVID-19 cases in donor and recipient states by date of transplant is shown in Figure 3. By May, the average number of confirmed COVID-19 cases in donor states was approximately 32,700 compared to 121 in March. Compared to the recipient state (North Carolina), on average, donor states had approximately 4,300 more confirmed cases of COVID-19 on the date of transplant (range of differences [donor-recipient state cases]: −5,100–62,200).

### 3.5 Posttransplant outcomes

Among LTx recipients transplanted during COVID-19, median posttransplant follow-up duration was 44 days (range 6-77). One (2.8%) patient had evidence of PGD grade 3 at 72 hours, six (16.7%)
required postoperative ECMO, eight (22.2%) remained intubated for >48 hours, six (16.7%) underwent tracheostomy placement within 7 days, and nine (25.0%) required reintervention (surgical: 9, radiologic: 1). No deaths have occurred (Table 7).

At data collection, 23 (63.9%) patients had been discharged from the hospital. Median posttransplant LOS was 20 days (IQR 16-30). Among recipients who had been discharged, two (8.7%) required hospital readmission and two (8.7%) required ICU readmission. Three (13.0%) patients were reintubated and one (4.3%) required dialysis during the transplant hospitalization. Six (26.1%) patients had evidence of acute rejection on a posttransplant biopsy; median time to first acute rejection episode was 51 days (range 33-63) (Table 8). Outcomes were similar between COVID-19 and pre-COVID-19 LTx recipients.

### DISCUSSION

In this single institution analysis of LTx during the COVID-19 pandemic, we found that transplant activity increased, although LTx recipients and lung donors were similar to their pre-COVID-19 counterparts. Donor and recipient pretransplant COVID-19 testing reached 100% by April 1, returning negative results in all cases. To date, no recipients have developed posttransplant COVID-19. Our findings suggest that LTx during the pandemic is safe and feasible with diligent donor and recipient testing and multi-institutional collaboration to minimize unnecessary travel and exposures for procurement teams.

Both the International Society for Heart and Lung Transplantation (ISHLT) and American Society of Transplant Surgeons (ASTS) have issued best practice guidelines for transplantation during the COVID-19 pandemic, citing expert opinion and available evidence regarding the risks of donor-derived infection and immunosuppression in newly transplanted recipients.22,23 Ongoing assessment of the risks and benefits of transplantation is recommended as the burden of COVID-19 and availability of hospital resources evolve.22–24 While the risks of donor-derived infection and induction immunosuppression remain uncertain, our findings are reassuring, with no evidence of COVID-19 among recipients up to 2 months posttransplant. Although negative SARS-CoV-2 PCR may

### TABLE 2 Operative characteristics

| Characteristica | LTx during COVID-19b N = 36 | 2019 LTx (pre-COVID-19)c N = 107 | p-Value |
|-----------------|-----------------------------|---------------------------------|---------|
| Ischemic time (minutes) | 437 (399-548) | 444 (377-536) | .6 |
| Cardiopulmonary bypass used | 6 (16.7%) | 23 (21.5%) | .5 |
| Bypass time (minutes) | 176 (151-189) | 263 (202-299) | .1 |
| Donor type | .1 |
| Donation after brain death donor | 27 (75.0%) | 92 (86.0%) | |
| Donation after circulatory death donor | 9 (25.0%) | 15 (14.0%) | |
| EVLP used | 1 (2.8%) | 3 (2.8%) | >.9 |
| Transfusion requirement (units) | | | |
| Red blood cells | 1 (0-2) | 1 (0-3) | .2 |
| Fresh frozen plasma | 0 (0-0) | 0 (0-1) | .049 |
| Cryoprecipitate | 0 (0-1) | 0 (0-1) | .7 |
| Platelets | 0 (0-0) | 0 (0-0) | .2 |
| Donor/recipient weight ratio | 1.03 (0.76-1.23) | 1.06 (0.92-1.24) | .4 |
| Serologies | | | |
| Donor Epstein-Barr virus positive | 29 (80.6%) | 95 (88.8%) | .4 |
| Donor cytomegalovirus positive | 26 (72.2%) | 67 (62.6%) | .3 |
| Recipient cytomegalovirus positive | 20 (55.6%) | 57 (53.3%) | .8 |
| Cytomegalovirus mismatch (D+/R-) | 11 (30.6%) | 31 (29.0%) | .9 |
| Transplant type | .8 |
| Bilateral | 34 (94.4%) | 102 (95.3%) | |
| Single, right | 1 (2.8%) | 4 (3.7%) | |
| Single, left | 1 (2.8%) | 1 (0.9%) | |

Abbreviations: COVID-19, Coronavirus Disease 2019; EVLP, ex-vivo lung perfusion; LTx, lung transplantation.
aPresented as median (interquartile range) for continuous variables and frequency (proportion) for categorical variables.
bMay 1 to May 20, 2020.
cJanuary 1 to October 31, 2019.
| Characteristic | LTx during COVID-19 | 2019 LTx (pre-COVID-19) | p-Value |
|---------------|--------------------|-------------------------|---------|
| **Age (years)** | 30 (22-39) | 32 (25-43) | .2 |
| **PHS increased risk** | 12 (33.3%) | 38 (35.5%) | .8 |
| **Smoking history ≥20 pack-years** | 3 (8.3%) | 10 (9.3%) | .8 |
| **PaO2/FiO2 ratio** | 446 (354-497) | 444 (366-494) | .8 |
| **Cause of death** | | | .4 |
| Anoxia | 17 (47.2%) | 36 (33.6%) | |
| Cerebrovascular accident/stroke | 8 (22.2%) | 27 (25.2%) | |
| Head trauma | 10 (27.8%) | 42 (39.3%) | |
| Other | 1 (2.8%) | 2 (1.9%) | |
| **Mechanism of death** | | | .2 |
| Asphyxiation | 0 (0%) | 3 (2.8%) | |
| Blunt injury | 6 (16.7%) | 26 (24.3%) | |
| Cardiovascular | 1 (2.8%) | 13 (12.1%) | |
| Drug intoxication | 11 (30.6%) | 20 (18.7%) | |
| Gunshot wound | 5 (13.9%) | 16 (15.0%) | |
| Intracranial hemorrhage/stroke | 8 (22.2%) | 25 (23.4%) | |
| Natural cause | 2 (5.6%) | 1 (0.9%) | |
| Seizure | 2 (5.6%) | 1 (0.9%) | |
| Other | 1 (2.8%) | 2 (1.9%) | |
| **Blood infection** | 1 (2.8%) | 9 (8.4%) | .5 |
| Pulmonary infection | 14 (38.9%) | 69 (64.5%) | .03 |
| **Final white blood cell count (10^3 cells/µL)** | 14.1 (9.5-18.2) | 13.2 (10.8-17.3) | .9 |
| Hospitalization for confirmed or presumed COVID−19 | 0 (0%) | | |
| **Distance from transplant center (nautical miles)** | 228 (116-380) | 225 (130-510) | .6 |
| **UNOS region** | | | .1 |
| 1 | 2 (5.6%) | 0 (0%) | |
| 2 | 4 (11.1%) | 4 (3.7%) | |
| 3 | 2 (5.6%) | 17 (15.9%) | |
| 4 | 1 (2.8%) | 7 (6.5%) | |
| 5 | 0 (0%) | 2 (1.9%) | |
| 6 | 0 (0%) | 4 (3.7%) | |
| 7 | 1 (2.8%) | 4 (3.7%) | |
| 8 | 1 (2.8%) | 4 (3.7%) | |
| 9 | 0 (0%) | 1 (0.9%) | |
| 10 | 3 (8.3%) | 3 (2.8%) | |
| 11 | 22 (61.1%) | 60 (56.1%) | |
| **Match sequence** | 29 (13-57) | 20 (8-54) | .2 |
| **Procurement team** | | | .7 |
| Duke | 33 (91.7%) | 100 (93.5%) | |
| Local | 3 (8.3%) | 7 (6.5%) | |

Abbreviations: COVID-19, Coronavirus Disease 2019; LTx, lung transplantation; PHS, US Public Health Service; UNOS, United Network for Organ Sharing.

*Presented as median (interquartile range) for continuous variables and frequency (proportion) for categorical variables.

*May 1 to May 20.

*January 1 to October 31, 2019.
be insufficient to definitively rule-out COVID-19, our findings align with the societal guidelines suggesting that negative donor and recipient pretransplant tests are the minimum necessary assurance that proceeding with transplantation is safe for both recipients and providers. While the sensitivity of SARS-CoV-2 PCR is significantly higher for BAL versus nasopharyngeal specimens (~90-95% versus ~60-80%), variable resource availability among donor hospitals may limit the safety and feasibility of performing BAL.

### TABLE 4  Recipient pretransplant COVID-19 testing

| Characteristic                  | March N = 15 | April N = 13 | May N = 8 | All LTx during COVID-19 N = 36 |
|--------------------------------|--------------|--------------|-----------|-------------------------------|
| **COVID-19 test performed**    |              |              |           |                               |
| Negative                       | 1 (100%)     | 13 (100%)    | 8 (100%)  | 22 (100%)                     |
| Positive                       | 0 (0%)       | 0 (0%)       | 0 (0%)    | 0 (0%)                        |
| **COVID-19 test type**         |              |              |           |                               |
| SARS-CoV-2 PCR, nasopharyngeal swab | 1 (100%)     | 5 (38.5%)    | 0 (0%)    | 6 (27.3%)                     |
| SARS-CoV-2 point-of-care rapid test, nasopharyngeal swab | 0 (0%)   | 8 (61.5%)    | 8 (100%)  | 16 (72.7%)                    |
| **COVID-19 test result**       |              |              |           |                               |
| Negative                       | 1 (100%)     | 13 (100%)    | 8 (100%)  | 22 (100%)                     |
| Positive                       | 0 (0%)       | 0 (0%)       | 0 (0%)    | 0 (0%)                        |
| **COVID-19 test reason**       |              |              |           |                               |
| Prebronchoscopy/preoperative screen | 12 (85.7%) | 10 (100%)    | 5 (83.3%) | 27 (90.0%)                    |
| Symptomatic COVID-19 rule out  | 3 (21.4%)    | 0 (0%)       | 0 (0%)    | 3 (10.0%)                     |
| Unexplained findings on posttransplant chest radiography | 1 (7.1%)  | 0 (0%)       | 0 (0%)    | 1 (3.3%)                      |
| Unexplained respiratory deterioration | 1 (7.1%)  | 0 (0%)       | 1 (16.7%) | 2 (6.7%)                      |

Abbreviations: COVID-19, Coronavirus Disease 2019; LTx, lung transplantation; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

*May 1 to May 20, 2020.

*At least one COVID-19 test performed.

*Among recipients who were tested.

### TABLE 5  Recipient posttransplant COVID-19 testing

| Characteristic                  | March N = 15 | April N = 13 | May N = 8 | All LTx during COVID-19 N = 36 |
|--------------------------------|--------------|--------------|-----------|-------------------------------|
| **COVID-19 test performed**    |              |              |           |                               |
| Negative                       | 14 (93.3%)   | 10 (76.9%)   | 6 (75.0%) | 30 (83.3%)                    |
| Positive                       | 0 (0%)       | 0 (0%)       | 0 (0%)    | 0 (0%)                        |
| **COVID-19 test type**         |              |              |           |                               |
| SARS-CoV-2 PCR, nasopharyngeal swab | 14 (100%)    | 10 (100%)    | 5 (83.3%) | 29 (96.7%)                    |
| SARS-CoV-2 PCR, bronchoalveolar lavage | 1 (7.1%)    | 0 (0%)       | 1 (16.7%) | 2 (6.7%)                      |
| **COVID-19 test result**       |              |              |           |                               |
| Negative                       | 14 (100%)    | 10 (100%)    | 6 (100%)  | 30 (100%)                     |
| Positive                       | 0 (0%)       | 0 (0%)       | 0 (0%)    | 0 (0%)                        |
| **COVID-19 test reason**       |              |              |           |                               |
| Prebronchoscopy/preoperative screen | 12 (85.7%) | 10 (100%)    | 5 (83.3%) | 27 (90.0%)                    |
| Symptomatic COVID-19 rule out  | 3 (21.4%)    | 0 (0%)       | 0 (0%)    | 3 (10.0%)                     |
| Unexplained findings on posttransplant chest radiography | 1 (7.1%)  | 0 (0%)       | 0 (0%)    | 1 (3.3%)                      |
| Unexplained respiratory deterioration | 1 (7.1%)  | 0 (0%)       | 1 (16.7%) | 2 (6.7%)                      |

Abbreviations: COVID-19, Coronavirus Disease 2019; LTx, lung transplantation; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

*May 1 to May 20, 2020.

*At least one COVID-19 test performed.

*Among recipients who were tested.
supporting the high prevalence of nasopharyngeal tests among donors in our study.\textsuperscript{22,25,26} While chest computed tomography (CT) is highly sensitive (~97%) for detecting COVID-19 and may help identify false-negative nasopharyngeal tests, the specificity of CT is poor (~25%),\textsuperscript{22,27} suggesting that routine use of CT in donor screening may result in considerable false positives, and avoidance of otherwise suitable donors. At our institution, ground glass opacities on CT were not considered sufficient to rule-out donors in the absence of positive SARS-CoV-2 PCR and risk factors concerning for recent COVID-19 exposure or infection. Alternatively, collection of multiple predonation nasopharyngeal specimens may be feasible to assure safe donation when BAL is unavailable.

Despite a national decline in LTx activity, the availability of deceased donor organs continues to increase.\textsuperscript{28} This discrepancy may be understood in the context of recent data suggesting that many LTx programs are operating with restrictions, and may have inactivated the majority of patients on the waitlist.\textsuperscript{29} Despite speculation that decreased travel due to social distancing and isolation may reduce donor availability,\textsuperscript{18} our findings suggest that continued growth of the potential donor pool may reflect an increasing proportion of deaths attributed to drug intoxication and fewer deaths attributed to blunt injury, gunshot wounds, and intracranial hemorrhage, that have previously been more prevalent.\textsuperscript{30} The increase in LTx activity at our institution may not be surprising in the context of these data.

### TABLE 6 Donor COVID-19 testing

| Characteristic                              | March N = 15 | April N = 13 | May$^a$ N = 8 | All LTx during COVID-19 N = 36 |
|--------------------------------------------|--------------|--------------|---------------|-------------------------------|
| COVID-19 test performed$^b$                | 5 (33.3%)    | 13 (100%)    | 8 (100%)      | 26 (72.2%)                    |
| COVID-19 test type$^c$                      |              |              |               |                               |
| SARS-CoV-2 PCR, nasopharyngeal swab        | 5 (100%)     | 13 (100%)    | 6 (75.0%)     | 24 (92.3%)                    |
| SARS-CoV-2 PCR, bronchoalveolar lavage     | 0 (0%)       | 1 (7.7%)     | 3 (37.5%)     | 4 (15.4%)                     |
| COVID-19 test result$^c$                    |              |              |               |                               |
| Negative                                   | 5 (100%)     | 13 (100%)    | 8 (100%)      | 26 (100%)                     |
| Positive                                   | 0 (0%)       | 0 (0%)       | 0 (0%)        | 0 (0%)                        |
| Risk assessment questionnaire administered | 14 (93.3%)   | 13 (100%)    | 8 (100%)      | 35 (97.2%)                    |

Abbreviations: COVID-19, Coronavirus Disease 2019; LTx, lung transplantation; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

$^a$May 1 to May 20, 2020.

$^b$At least one COVID-19 test performed.

$^c$Among donors who were tested.

### FIGURE 3 Cumulative incidence of confirmed COVID-19 cases in donor and recipient states by date of transplant. [Color figure can be viewed at wileyonlinelibrary.com]
which suggest that donor lungs are available in sufficient capacity to support ongoing transplantation at a high level for programs with adequate resources and an acceptable risk-benefit ratio to maintain LTx activity.

Already a program with extensive procurement resources, our institution appreciated the acuity of illness among our recipients and fortunate circumstances existed for our health system to support a safe and productive LTx practice as the pandemic evolved, while maintaining the ability to care for the local community. While many other programs paused or limited transplant activity, modest incidence of COVID-19 in our region and ongoing availability of hospital resources allowed for maximal use of available donor organs with the capacity to support newly transplanted recipients.5,29 As a temporary restriction on air travel for organ procurement constituted the primary alteration to our institution’s transplant policies, collaboration with local procurement teams, assessment of overall COVID-19 prevalence in donor regions, and evaluation of donor risk factors informed decisions, including avoiding donors from regions of increased geographic prevalence and those cared for in conjoined hospital units or by providers also caring for COVID-19 patients. Transplant recipients at our institution were concentrated in a single ICU to limit exposure to COVID-19 patients, and transplant infectious disease teams provided on-call consultative services for donors with indeterminate risk. While oversight of recipient and candidate safety is challenging in the outpatient setting, a modified pulmonary rehabilitation schedule has been implemented at our primary clinic to reduce patient exposures and contact as we continue to support this high-risk population while on the waitlist and beyond their transplant hospitalizations.

### TABLE 7
Posttransplant complications among all lung transplant recipients transplanted between March 1 and May 20, 2020 versus those transplanted in 2019

| Characteristic                                      | LTx during COVID-19b N = 36 | 2019 LTx (pre-COVID-19)c N = 107 | p-Value |
|----------------------------------------------------|-----------------------------|---------------------------------|---------|
| Clavien-Dindo grade III complication (reintervention) within 30 days | 9 (25.0%) | 33 (30.8%) | .5      |
| Surgical                                           | 9 (25.0%) | 30 (28.0%) | .7      |
| Radiologic                                         | 1 (2.8%)  | 3 (2.8%)   | >.9     |
| PGD grade 3 at 72 hours                            | 1 (2.8%)  | 10 (9.3%)  | .3      |
| Postoperative ECMO                                 | 6 (16.7%) | 11 (10.3%) | .4      |
| Extubated in >48 hours                             | 8 (22.2%) | 33 (30.8%) | .4      |
| Tracheostomy within 7 days                         | 6 (16.7%) | 16 (15.0%) | .8      |
| Death                                              | 0 (0%)    | 2 (1.9%)   | >.9     |

Abbreviations: ECMO, extracorporeal membrane oxygenation; LTx, lung transplantation; PGD, primary graft dysfunction.

*Presented as median (interquartile range) for continuous variables and frequency (proportion) for categorical variables.

bMay 1 to May 20.

cJanuary 1 to October 31, 2019.

### TABLE 8
Posttransplant complications among lung transplant recipients transplanted between March 1 and May 20, 2020 and discharged prior to data collection versus those transplanted in 2019

| Characteristic                  | LTx during COVID-19b N = 23 | 2019 LTx (pre-COVID-19)c N = 107 | p-Value |
|--------------------------------|-----------------------------|---------------------------------|---------|
| ICU readmission within 30 days  | 2 (8.7%)                    | 20 (18.7%)                      | .7      |
| Hospital readmission within 30 days | 2 (8.7%)       | 28 (26.2%)                      | .4      |
| Posttransplant length of stay (days) | 20 (16-30)    | 21 (16-39)                      | .4      |
| Reintubated                     | 3 (13.0%)                   | 25 (23.4%)                      | .4      |
| Dialysis                        | 1 (4.3%)                    | 15 (14.0%)                      | .3      |
| Acute rejection                  |                            |                                 |         |
| Within 30 days                  | 0 (0%)                      | 12 (11.2%)                      | .1      |
| After 30 days                   | 6 (26.1%)                   | 31 (29.0%)                      | >.9     |

Abbreviations: ICU, intensive care unit; LTx, lung transplantation.

*Presented as median (interquartile range) for continuous variables and frequency (proportion) for categorical variables.

bMay 1 to May 20.

cJanuary 1 to October 31, 2019.
Our early experience highlights several key strategies to support LTx amidst COVID-19. As COVID-19 prevalence rises and avoidance of donors from regions with high community penetration becomes unrealistic, donor risk factors must be scrutinized, considering the likelihood that each donor is a carrier of COVID-19 and undertaking more rigorous testing as pretest probability rises. Recognizing that BAL may be unavailable for even the highest risk donors, collection of at least one, and preferably multiple, nasopharyngeal specimens should be pursued, reserving CT for cases in which confidence remains low despite negative tests. Concurrently, ongoing multi-institutional collaboration is critical to limit procurement travel, maintain provider health and safety, and avoid exposures that could increase risk to recipients. While the paradigm of LTx must remain flexible, we must incorporate COVID-19 into routine risk-benefit determinations that predate the pandemic to ensure ongoing LTx despite these new challenges.

There are several limitations to our study. As we examined a series of LTx performed at a single, large academic institution in a region of the United States with modest incidence of COVID-19, our experience may not be generalizable to other programs. However, with a paucity of data regarding the safety of transplantation during the pandemic despite a continued need among waitlisted candidates, our experience may provide helpful insight to guide transplantation during this complex and evolving situation. Additionally, as we remain in the early stages of this pandemic, posttransplant follow-up in our study is short, which limits our ability to comment on the long-term implications of induction immunosuppression in recipients transplanted during this period. While our early findings among patients with up to 2 months of follow-up are reassuring, continued vigilance is critical to ensure that symptoms concerning for COVID-19 are identified and addressed promptly among these high-risk patients.

5  |  CONCLUSIONS

In this single institution analysis, we found that LTx activity was maintained safely and effectively during the early COVID-19 pandemic without significant changes in recipient and donor characteristics. While the long-term implications of transplantation amidst the pandemic remain unknown, our findings provide promising new evidence to support the feasibility of continuing to provide this lifesaving therapy to patients who otherwise may not survive to see the end of this unforeseen global challenge. Characterized by pretransplant testing, assessment of donor risk factors, and collaboration with OPOs and local procurement teams to minimize recipient and provider risks, our practice may provide a blueprint for transplantation during the chronic phase of the pandemic and support the expert societal recommendations.

ACKNOWLEDGMENTS

This work was supported by a Pfizer Foundation grant and the Duke Clinical Translational Science Institute (SEH). The content is solely the responsibility of the authors and does not necessarily represent the official views of the Pfizer Foundation or Duke Clinical Translational Science Institute.

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the American Journal of Transplantation.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

ORCID

Samantha E. Halpern https://orcid.org/0000-0001-7316-1989

REFERENCES

1. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet. 2020;395(10223):470–473.
2. Guan W-J, Ni Z-Y, Hu YU, et al. in China. N Engl J Med. 2019;2020;1–13.
3. Wu Z, McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(12):1239–1242.
4. Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. N Engl J Med. 2020;382(10):929–936.
5. Centers for Disease Control. COVID Data Tracker: United States COVID-19 Cases and Deaths by State. https://www.cdc.gov/covid-tracking/. Published 2020. Accessed June 7, 2020.
6. Holm AM, Mehra MR, Courtright A, et al. Ethical Considerations regarding Heart and Lung Transplantation and Mechanical Circulatory Support during the COVID-19 Pandemic: An ISHLT COVID-19 Task Force Statement. J Heart Lung Transplant. 2020;39(7):619–626.
7. Emanuel EJ, Persad G, Upshur R, et al. Fair allocation of scarce medical resources in the time of Covid-19. N Engl J Med. 2020;382(21):2049–2055.
8. Loupy A, Aubert O, Reese PP, Bastien O, Bayer F, Jacquelinet C. Organ procurement and transplantation during the COVID-19 pandemic. Lancet. 2020;395(10237):e95–e96.
9. Michaels MG, La Hoz RM, Danziger-Isakov L, et al. Coronavirus disease 2019: Implications of emerging infections for transplantation. Am J Transplant. 2020;20(7):1768–1772.
10. Moris D, Shaw BI, Dimitroklatis N, Barbas AS. Organ donation during the coronavirus pandemic: an evolving saga in uncharted waters. Transpl Int. 2020;33(7):826–827.
11. Aslam S, Mehra MR. COVID-19: Yet another coronavirus challenge in transplantation. J Heart Lung Transplant. 2020;39(5):408–409.
12. Vock DM, Durheim MT, Tsuang WM, et al. Survival Benefit of Lung Transplantation in the Modern Era of Lung Allocation. Ann Am Thorac Soc. 2017;14(2):172–181.
13. Kumar D, Manuel O, Natori Y, et al. COVID-19: A global transplant perspective on successfully navigating a pandemic. Am J Transplant. 2020;20(7):1773–1779.
14. Aigner C, Dittmer U, Kamler M, Collaud S, Taube C. COVID-19 in a lung transplant recipient. J Heart Lung Transplant. 2020;39(6):610–611.
15. Cozzi E, Faccioli E, Marinello S, et al. COVID-19 pneumonia in lung transplant recipients: report of two cases. Am J Transplant. 2020. https://doi.org/10.1111/ajt.15993
16. Koczulla RA, Szczepanski B, Koteczki A, et al. SARS-CoV-2 infection in two patients following recent lung transplantation. Am J Transplant. 2020. https://doi.org/10.1111/ajt.15998
17. Mulvihil MS, Lee HJ, Weber J, et al. Variability in donor organ offer acceptance and lung transplantation survival. J Heart Lung Transplant. 2020;39(4):353–362.
18. Woolley AE, Mehra MR. Dilemma of organ donation in transplantation and the COVID-19 pandemic. *J Hear Lung Transplant*. 2020;39(5):410–411.

19. North Carolina Department of Health and Human Services. North Carolina Identifies First Case of COVID-19. https://www.ncdhrs.gov/news/press-releases/north-carolina-identifies-first-case-covid-19. Published 2020. Accessed May 28, 2020.

20. Snell GI, Yusen RD, Weill D, et al. Report of the ISHLT Working Group on Primary Lung Graft Dysfunction, part I: Definition and grading—A 2016 Consensus Group statement of the International Society for Heart and Lung Transplantation. *J Hear Lung Transplant*. 2017;36(10):1097–1103.

21. Johns Hopkins University. COVID-19 United States Incidence Map. https://coronavirus.jhu.edu/us-map. Published 2020. Accessed May 28, 2020.

22. Guidance from the International Society of Heart and Lung Transplantation Regarding the SARS CoV-2 Pandemic. 2020. https://ishlt.org/ishlt/media/documents/SARS-CoV-2_Guidance-for-Cardiothoracic-Transplant-and-VAD-centers.pdf

23. ASTS COVID 19 Strike Force Guidance to Members on the Evolving Pandemic. March 24, 2020. https://asts.org/advocacy/covid-19-resources/asts-covid-19-strike-force/asts-covid-19-strike-force-initial-guidance#.XtLcHZ5KI3I. Published 2020. Accessed May 30, 2020.

24. ASTS Guidance on Transplant Capacity and Testing in the COVID-19 Era. April 28, 2020. https://asts.org/advocacy/covid-19-resources/asts-covid-19-strike-force/transplant-capacity-and-testing#.XtLcwZ5KI3I. Published 2020. Accessed May 30, 2020.

25. Sethuraman N, Jeremiah SS, Ryo A. Interpreting Diagnostic Tests for SARS-CoV-2. *JAMA*. 2020;2019:2019–2021.

26. Zitek T. The Appropriate Use of Testing for COVID-19. *West J Emerg Med*. 2020;21(May):470–472.

27. Xu B, Xing Y, Peng J, et al. Chest CT for detecting COVID-19: a systematic review and meta-analysis of diagnostic accuracy. *Eur Radiol*. 2020;(866). https://doi.org/10.1007/s00330-020-06934-2

28. United Network for Organ Sharing. COVID-19 and Solid Organ Transplant. https://unos.org/covid/. Published 2020. Accessed May 31, 2020.

29. Boyarsky BJ, Po-Yu Chiang T, Werbel WA, et al. Early Impact of COVID-19 on Transplant Center Practices and Policies in the United States. *Am J Transplant*. 2020. https://doi.org/10.1111/ajt.15915

30. Organ Procurement and Transplantation Network. National Data: Deceased Donors Recovered in the US by Mechanism of Death, Lung. https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/. Accessed May 31, 2020.

**How to cite this article:** Halpern SE, Olaso DG, Krischak MK, et al. Lung transplantation during the COVID-19 pandemic: SAFELY navigating the new "normal". *Am J Transplant*. 2020;20:3094–3105. https://doi.org/10.1111/ajt.16304