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.

0003-4975/$36.00
https://doi.org/10.1016/j.athoracsur.2022.09.039

A Matched Survival Analysis of Lung Transplant Recipients With Coronavirus Disease 2019–Related Respiratory Failure

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ABSTRACT

BACKGROUND Lung transplantation is an acceptable and potentially life-saving treatment option for coronavirus disease 2019 (COVID-19)–induced acute respiratory distress syndrome and pulmonary fibrosis. This study was conducted to determine whether recipients of lung transplantation (LT) for COVID-19–related lung disease have comparable outcomes to other recipients with a similar level of lung dysfunction.

METHODS The Organ Procurement and Transplant Network database was queried for adult LT candidates between 2006 and 2021. Recipients with COVID-19–related respiratory failure were matched 1:2 using a nearest-neighbor algorithm. Kaplan-Meier methods with log-rank tests were used to compare long-term survival. A proportional hazards model was used to calculate risk of death.

RESULTS A total of 37,333 LT candidates from all causes were compared with 334 candidates from COVID-19–related respiratory failure. COVID-19 recipients were more likely to be younger (50 vs 57 years, $P < .001$), male (79% vs 60%, $P < .001$), require extracorporeal membrane oxygenation (56.3% vs 4.0%, $P < .001$), and have worse lung function (lung allocation score, 82.4 vs 47.8; $P < .001$) at transplantation. Subsequently, 227 COVID-19 recipients were matched with 454 controls. Patients who received a transplant for COVID-19 had similar rates of mechanical ventilation, extracorporeal membrane oxygenation, postoperative complications, and functional status at discharge compared with controls. There was no difference in overall survival or risk of death from COVID-19 (hazard ratio, 0.82; 95% CI, 0.45-1.53; $P = .54$).

CONCLUSIONS Six-month survival for recipients of LT for COVID-19–related respiratory failure was comparable to that of other LT recipients.

(Ann Thorac Surg 2022;■:■-■)

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to a global pandemic that has caused acute lung injury in millions of people worldwide.[1] Respiratory failure in the form of acute respiratory distress syndrome (ARDS) or pulmonary fibrosis develops in a significant proportion of those who contract SARS-CoV-2.[2-6] Both can lead to prolonged mechanical ventilation, extracorporeal membrane oxygenation (ECMO), physical deconditioning, and the need for long-term supplemental oxygen.[7,8] Lung transplantation (LT) can be a life-saving procedure when used in patients with end-stage respiratory failure and has been proposed as a potential treatment option for coronavirus disease 2019 (COVID-19) when medical therapy fails.[9-11]

Previous studies have shown that patients with respiratory failure secondary to COVID-19 present novel challenges for LT centers. Notably, this cohort generally contains severely ill patients with acute lung injury due to a previously unknown infectious cause.[10,12,13] Studies indicate recovery from COVID-19-associated ARDS may

The Supplemental Tables can be viewed in the online version of this article [https://dx.doi.org/10.1016/j.athoracsur.2022.09.039] on https://www.annalsthoracicsurgery.org.

Accepted for publication Sep 26, 2022.

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Abbreviations and Acronyms

ARDS = acute respiratory distress syndrome
COVID-19 = coronavirus disease 2019
ECMO = extracorporeal membrane oxygenation
HR = hazard ratio
LAS = lung allocation score
LT = lung transplantation
OPTN = Organ Procurement and Transplant Network
SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2
UNOS = United Network for Organ Sharing

be slower and more prolonged, but how this affects LT recovery for COVID-19 is not understood.[8,14]

Several studies have aimed to examine this population and address concerns about the use LT for respiratory failure due to COVID-19.[10,15-17] These studies have shown that patients with COVID-19-related respiratory failure have higher acuity on presentation but similar survival after transplantation. How this patient population fares compared with recipients with equally poor lung function is unknown. The objective of this study was to determine whether recipients of LT for COVID-19-related lung disease have comparable outcomes to other recipients with a similar level of lung dysfunction. We hypothesized that LT recipients from COVID-19-related respiratory failure would have worse short-term outcomes but similar long-term survival compared with the matched controls.

PATIENTS AND METHODS

STUDY DESIGN. The University of Iowa Hospitals & Clinics Institutional Review Board exempted this retrospective analysis of the Organ Procurement and Transplant Network (OPTN) database (UIHC IRB 202206037). Eligible candidates and recipients were adults (aged >18 years) at the time of listing for LT or at the time of LT in the United States from January 1. 2006, to December 31. 2021.[18] Diagnostic codes 1616 “COVID-19: ARDS” or 1617 “COVID-19: Pulmonary Fibrosis” were used to denote COVID-19 diagnosis. All patients who received or were listed for other allografts were excluded (Figure 1).

STATISTICAL ANALYSIS. Before matching, waiting list death probability and transplant probability were calculated for all candidates listed for LT by using cumulative incidence functions. A proportional hazards model was generated to examine the risk of death on the waiting list, and an odds ratio was used to investigate transplant probability. Baseline characteristics of LT patients were compiled and analyzed using the Kruskal-Wallis test for continuous variables and the Pearson χ^2 test for categorical variables. The diagnostic groups used were described and defined using the United Network for Organ Sharing (UNOS; Policy 10.1.F.i).

Recipients resulting from COVID-19-related respiratory failure were matched with lung recipients based on demographic characteristics, diagnostic grouping, degree of medical acuity, and lung function at transplant (Figure 2). The match used a 1:2 nearest-neighbor matching algorithm with a width of 0.2 calipers to form matched pairs of recipients for COVID-19-related respiratory failure and recipients for other etiologies.[19,20] The effectiveness of bias reduction within the model after matching was assessed using standardized mean differences, with the Cohen suggested threshold of 0.2.[19]

After matching, baseline characteristics and unadjusted outcomes were treated as paired data, and the McNemar test for categorical variables and the Wilcoxon signed rank test for continuous variables were used.[21] The Kaplan-Meier method with log-rank test was used to compare survival between groups. A multivariate model was generated using backward selection from a list of recipient, candidate, and donor demographic and clinical variables (Supplemental Table 1). Proportional hazards regression was used to calculate risk-adjusted probability of death. Statistical significance was set at $P < .05$. Statistical analyses were performed using R 4.1.2 software (R Foundation for Statistical Computing).

RESULTS

UNMATCHED WAITING LIST CANDIDATE DEMOGRAPHICS, RISK OF DEATH, AND TRANSPLANT ODDS. There were 334 candidates listed for LT for COVID-19-related respiratory failure, and 37,333 candidates were listed for a single-organ LT for other etiologies (Figure 1). At listing, candidates with COVID-19 were more likely to have a higher LAS (78.3 vs 43.1, $P < .001$), be on ECMO (51.2% vs 1.8%, $P < .001$), have ventilator use (36.5% vs 3.0%, $P < .001$), and have worse functional status (Table 1). At 6 months, 87.9% of COVID-19 candidates received a transplant compared with 63.3% of all transplant candidates. During the same interval, COVID-19 candidates on the waiting list had lower mortality rates (4.1% vs 4.78%). On the waiting list, the risk of death for candidates with COVID-19-related respiratory failure was significantly lower (hazard ratio [HR], 0.169; 95% CI, 0.086-0.329; $P < .001$). At the same time, patients with COVID-19-related respiratory failure spent fewer days on the waiting list (26.4 days vs 191.3 for other candidates, $P < .001$), and the lifetime odds of receiving a transplant were not significantly different for COVID-19 candidates vs other candidates (odds ratio, 1.02; 95% CI, 0.79-1.32; $P = .90$) (Figure 3).

UNMATCHED RECIPIENT DEMOGRAPHICS. Baseline recipient characteristics have been previously described in detail.[16] The analysis included 270 recipients with COVID-19-related respiratory failure and 28,951

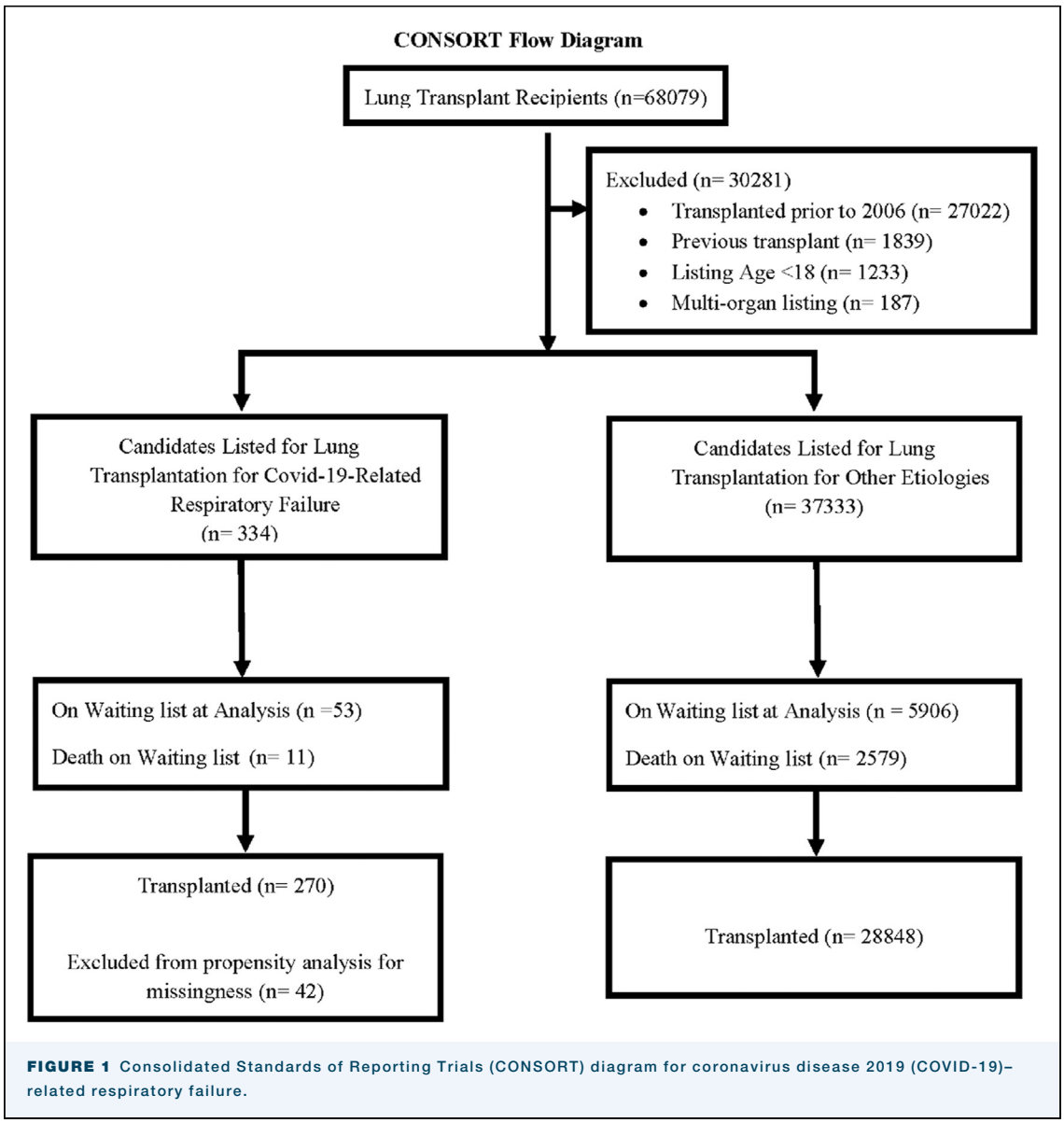

FIGURE 1 Consolidated Standards of Reporting Trials (CONSORT) diagram for coronavirus disease 2019 (COVID-19)–related respiratory failure.

recipients with other etiologies (Figure 1). LT recipients due to COVID-19-related respiratory failure had worse functional status, were more likely to be on ECMO (56.3% vs 4.0%), be on a ventilator (47.8% vs 5.4%, $P < .001$), and be in the intensive care unit (79.6% vs 7.7%, $P < .001$). Consequently, they had significantly higher LASs at transplant (82.4 vs 47.8, $P < .001$) and fewer days on the waiting list (17.7 days vs 141.6 days, $P < .001$) (Supplemental Table 2). Recipients with COVID-19-related respiratory failure were listed for transplant a median 14 days (95% CI, 11-17 days) after admission, whereas other LT recipients were listed for transplant a median 48 days before the index admission (95% CI, 47-49 days; $P < .001$). Recipients for COVID-19-related respiratory failure were more often hospitalized for at least 1 day before transplant (94.7% vs 58.6%, $P < .001$) and spent longer in the hospital before transplant (median 26.0 days vs 1 day, $P < .001$).

UNMATCHED PATIENT UNADJUSTED SHORT-TERM OUTCOMES. Length of stay was significantly longer for LT recipients for COVID-19-related respiratory failure (35.4 days vs 26.1 days, $P < .001$). LT recipients with COVID-19-related respiratory failure were more likely to remain intubated (58.5% vs 30.6%, $P < .001$) and on ECMO (26.1% vs 7.3%, $P < .001$) at 72 hours after transplant. They also had higher rates of posttransplant dialysis (12.8% vs 6.8%, $P < .001$). In-hospital mortality was not significantly different for COVID-19 recipients

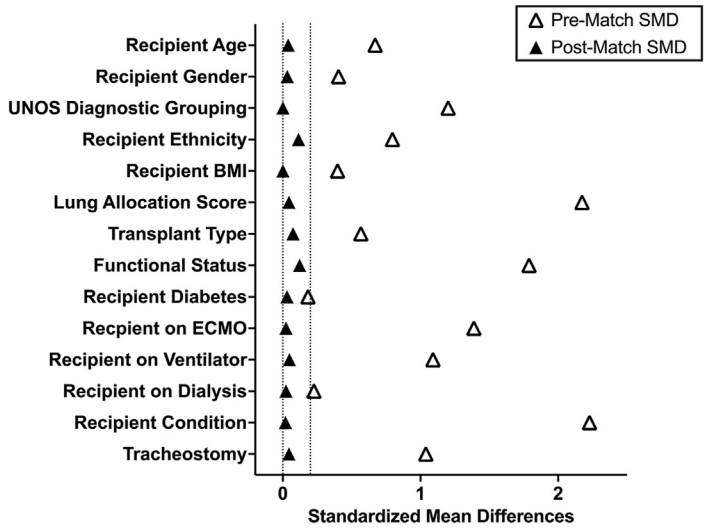

FIGURE 2 Standardized mean differences (SMDs) in baseline covariates before and after matching. (BMI, body mass index; ECMO, extracorporeal membrane oxygenation; UNOS, United Network of Organ Sharing.)

(respectively, 3.0% vs 4.4%; $P = .21$). Patients with COVID-19 had worse functional status at discharge; however, acute rejection and 30-day or 90-day mortality were similar (Supplemental Table 2).

UNMATCHED PATIENT SURVIVAL ANALYSIS AND ADJUSTED OUTCOMES. The overall survival probability was not significantly different between LT recipients with COVID-19 and the general recipient population (94.1% vs 92.1%, respectively, at 6 months; $P = .91$) (Figure 4). A COVID-19 diagnosis at transplant was not associated with a greater risk of death (HR, 1.06; 95% CI, 0.612-1.838; $P = .834$) (Table 2).

MATCHED PATIENT DEMOGRAPHICS. Given the considerable differences in baseline characteristics between recipients with COVID-19-related respiratory failure and the general population of LT recipients, a match was generated to compare cohorts with a similar acuity of illness. A total of 227 patients who received LT for COVID-19-related respiratory failure were matched to 454 lung recipients. No clinically significant differences in the baseline recipient characteristics, donor characteristics, or measures of lung function were observed between the matched cohorts (Figure 2, Supplemental Table 3).

MATCHED PATIENT UNADJUSTED SHORT-TERM OUTCOMES. Length of stay was not significantly different between the LT recipients with COVID-19-related respiratory failure and matched controls. Both groups had high but similar rates of ECMO and mechanical ventilation 72 hours after transplant, acute rejection, 30-day mortality, posttransplant stroke, and posttransplant dialysis. The matched controls had significantly higher 90-day mortality (9.1% vs 3.6%, $P = .016$) than COVID-19 LT recipients (Table 3).

MATCHED PATIENT SURVIVAL ANALYSIS AND ADJUSTED OUTCOMES. The probability of overall survival was not significantly different between the matched isolated LT recipients (94.4% for COVID-19 LT recipients vs 88.1% for matched controls at 6 months, $P = .26$) (Figure 5). After adjustment, patients receiving LT for COVID-19-related respiratory failure did not show an increased risk of death compared with matched recipients (HR, 0.824; 95% CI, 0.445-1.526; $P = .537$) (Table 2).

COMMENT

The emergence of SARS-CoV-2 led to a worldwide pandemic and resulted in ARDS and chronic pulmonary fibrosis in many. Despite early success, much is not yet understood about LT for COVID-19-related respiratory failure.[12,15,16,22] Among transplant candidates, patients with COVID-19-related respiratory failure rapidly become severely ill with acute lung injury due to an infectious cause.[5,10,12] We examined the United States' national experience with candidates and recipients of COVID-19-related respiratory failure. Our work showed that patients selected for transplant for COVID-19-related respiratory failure were a distinct, severely ill cohort at listing and received an allograft rapidly.

To further analyze this cohort, we used a matched analysis of the COVID-19 LT recipient population. Our data showed that the matched controls had a similar postoperative course, with no difference in 6-month survival. Likewise, in our adjusted analysis, a diagnosis of COVID-19 did not significantly increase the risk of death. Outcomes of patients with COVID-19-related respiratory failure were comparable overall to those of recipients with other etiologies with a similar disease burden before transplantation.

Our data showed that candidates listed for transplant with ARDS or pulmonary fibrosis from COVID-19 had a greater acuity of lung disease than the general LT candidate population. Most of these patients were on ECMO, mechanical ventilation, or in the intensive care unit at the time of listing. The high LAS at listing (78.30) likely resulted in the significantly shorter waiting list time and consequently minimized death on the waiting list. Although these patients had a shorter time on the waiting list than the general population of candidates (Figure 3), they did not have greater lifetime odds of receiving a transplant once listed.

Recent data analyzing 30 patients with COVID-19-associated ARDS by Bharat and colleagues[12,17] mirror

TABLE 1 Baseline Candidate Characteristics (N = 37,667)

Variables	All Candidates (n = 37,333)	COVID-19 (n = 334)	*P* Value
Age at listing, mean (SD), y	56.34 (12.60)	49.32 (10.73)	<.001
BMI at listing, mean (SD), kg/m^2 (n = 37,601)	26.86 (197.84)	28.72 (14.48)	.864
Male sex	21,093 (56.5)	250 (74.9)	<.001
Race/ethnicity			<.001
White	29,509 (79.0)	161 (48.2)	
Black	3660 (9.8)	27 (8.1)	
Asian	868 (2.3)	25 (7.5)	
Hispanic	3008 (8.1)	109 (32.6)	
American Indian/Alaska Native	137 (0.4)	6 (1.8)	
Multiracial	123 (0.3)	2 (0.6)	
Native Hawaiian/other Pacific Islander	28 (0.1)	4 (1.2)	
UNOS diagnostic group (%)			<.001
Cystic fibrosis or immunodeficiency disorder	3465 (9.3)	0 (0.0)	
Obstructive lung disease	10,637 (28.5)	0 (0.0)	
Pulmonary vascular disease	1965 (5.3)	0 (0.0)	
Restrictive lung disease	21,266 (57.0)	334 (100.0)	
Year of listing, mean (SD)	2014.20 (4.45)	2020.93 (0.26)	<.001
Creatinine at listing, mean (SD), mg/dL (n = 37,666)	0.84 (0.31)	0.64 (0.35)	<.001
Lung allocation score at listing, mean (SD)	43.08 (15.76)	78.30 (17.65)	<.001
Candidate diabetes (n= 37,482)	6921 (18.6)	87 (26.2)	.001
Candidate cigarette use	22,062 (59.1)	88 (26.3)	<.001
Candidate prior malignancy	2548 (6.8)	14 (4.2)	.246
Candidate prior cardiac surgery	1566 (4.2)	11 (3.3)	.001
Candidate prior lung surgery	1612 (4.3)	3 (0.9)	<.001
Candidate chronic steroid use	12,638 (33.9)	51 (15.3)	<.001
Life support at listing (n = 37,664)	2216 (5.9)	191 (57.2)	<.001
ECMO at listing (n = 37,667)	687 (1.8)	171 (51.2)	<.001
Mechanical ventilation at listing	1126 (3.0)	122 (36.5)	<.001
Functional status at listing (n = 37,283)			<.001
10%—moribund	568 (1.5)	43 (13.9)	
20%—very sick	2379 (6.4)	170 (54.8)	
30%—severely disabled	1380 (3.7)	37 (11.9)	
40%—disabled	6349 (17.2)	17 (5.5)	
50%—requires considerable assistance	5397 (14.6)	15 (4.8)	
60%—requires occasional assistance	9924 (26.8)	19 (6.1)	
70%—cares for self	8065 (21.8)	7 (2.3)	
80%—normal activity with effort	2583 (7.0)	1 (0.3)	
90%—able to carry on normal activity	294 (0.8)	0 (0.0)	
100%—normal	34 (0.1)	1 (0.3)	
Waiting list days, mean (SD)	191.28 (334.02)	26.39 (34.22)	<.001

Data are presented as n (%) unless indicated otherwise. BMI, body mass index; COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; UNOS, United Network of Organ Sharing.

our findings. Their recipients were also more likely to be on mechanical ventilation and ECMO before LT, albeit at lower rates than the national data. Similar to the OPTN data, patients with COVID-19-related respiratory failure had a higher LAS (85.8), shorter median waiting time after listing (11.5 days), and higher posttransplant survival (100%). Our study examined the national waiting list course of patients with COVID-19-related respiratory failure. Notably, Bharat and colleagues[17] showed a higher waiting list mortality (18.9%) among the cohort at their institution than our data on the general population of candidates (4.8%). This may be due to the smaller number of patients in their study or increased severity of illness in their cohort.

Currently, selection criteria for LT in patients with COVID-19-related respiratory failure are adopted by individual transplant centers. Several guidelines have been proposed for patient selection, but there are no current consensus guidelines.[3,12,22,23] The general criteria for transplantation for COVID-19-related respiratory failure proposed by Bharat and

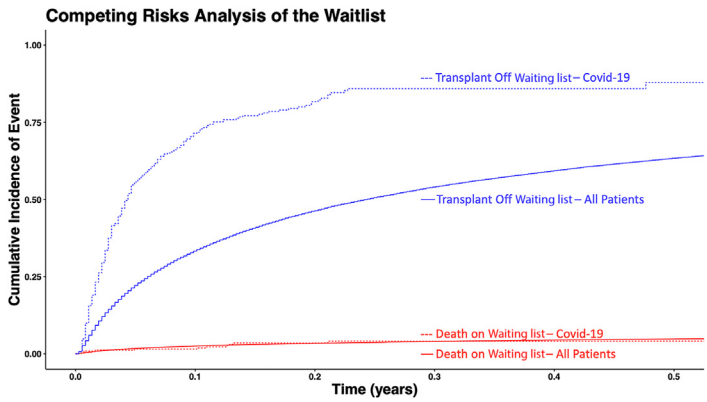

FIGURE 3 Cumulative incidence of death and transplant for transplant candidates. (COVID-19, coronavirus disease 2019).

colleagues[12] mirror the national experience in many respects. They suggested that the LT recipient cohort for COVID-19-related respiratory failure tended to be younger, have a lower body mass index, and have evidence of irreversible lung damage based on their high LAS scores and high use of ECMO. Conversely, the high rates of pretransplant dialysis and poor physical conditioning before transplantation are notable deviations from the proposed guidelines. Unfortunately, the national database did not capture other criteria such as social support, neurocognitive status, and COVID-19 status. The lack of current consensus guidelines leads to center variation in patient selection, which can bias the outcomes in smaller studies. Therefore, our data can help programs to understand national trends and early survival in this group of acutely ill patients.

This study's short-term outcomes after LT for COVID-19-related respiratory failure were similar to those reported in previous studies.[2,12,15,16] Recipients of COVID-19-related respiratory failure were more likely to stay on ECMO and be mechanically ventilated for 72 hours. In addition, they were more likely to receive posttransplant dialysis. Bharat and colleagues[12] also reported high rates of continued ECMO and mechanical ventilation after transplantation. Additionally, their recipients had a similar length of stay (37 days).[12]

LT recipients for COVID-19-related respiratory failure had notably worse functional outcomes than the general population of LT recipients at discharge. This likely represents significant physical deconditioning and acuity of disease before transplantation. Future longitudinal studies are needed to examine how often and how quickly recipients of LT for COVID-19-related respiratory failure return to their baseline functional status after transplant. Despite the higher burden of disease, this cohort did not have significantly worse overall survival at 6 months after transplant. The COVID-19 diagnosis was not associated with an increased risk of death.

Roach and colleagues[16] presented a preliminary analysis of the OPTN database and examined 214 recipients with COVID-19-related ARDS and pulmonary fibrosis. Most of their data corroborate our findings, including transplant recipient characteristics and short-term outcomes. Our analysis expands these initial data with our examination of United States waiting list data for LT due to COVID-19-related respiratory failure and with further analysis of mortality data. High early survival in the COVID-19 cohort at 30 days (97.7%), 90 days (95.9%), and 6 months (94.4%) suggests that COVID-19-realted respiratory failure was not an independent risk factor for death and is congruent with earlier reports. Bharat and colleagues[12] found 100% survival at 30 days and 92% survival at 80 days in their case series of 12 patients.

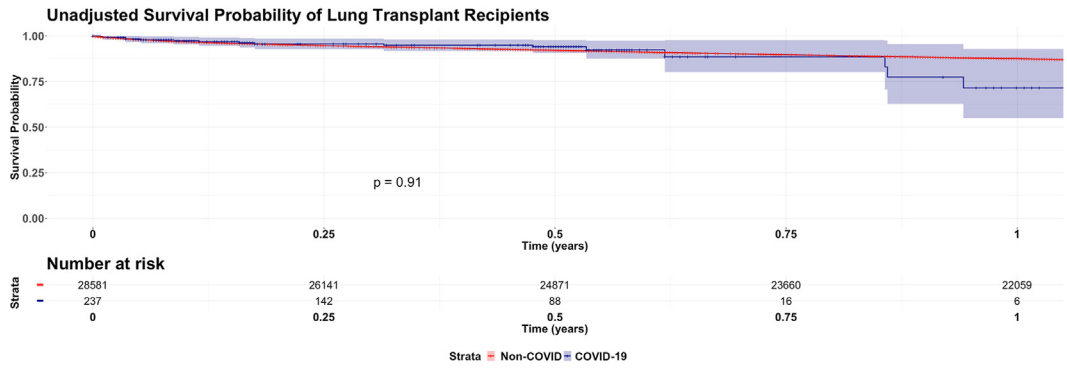

FIGURE 4 Kaplan-Meier survival analysis of recipients for coronavirus disease 2019 (COVID-19)–related respiratory failure compared with all recipients. The shaded areas indicate the 95% CI.

TABLE 2 Cox Proportional Hazards Model Characteristics

Variables	Hazard Ratio (95% CI)	*P* Value
Cox proportional hazards model of all candidates		
Age at listing	1.008 (1.005-1.012)	<.001
Candidate male sex	1.041 (0.958-1.132)	.342
UNOS race/ethnicity (ref = White)		
Black	0.979 (0.865-1.108)	.738
Asian	1.064 (0.85-1.333)	.588
Hispanic	1.041 (0.913-1.187)	.547
American Indian/Alaska Native	0.648 (0.308-1.361)	.252
Multiracial	0.995 (0.534-1.855)	.987
Native Hawaiian/Pacific Islander	0.967 (0.311-3.004)	.954
Candidate diabetes	0.963 (0.869-1.066)	.463
Candidate lung allocation score at listing	1.067 (1.064-1.069)	<.001
Candidate ECMO at listing	1.204 (1.005-1.364)	.045
Candidate mechanical ventilation at listing	1.691 (1.419-2.014)	<.001
Candidate creatine at listing	1.214 (1.12-1.315)	<.001
Candidate prior cardiac surgery	1.218 (1.014-1.465)	.035
Candidate COVID-19–related respiratory failure diagnosis	0.169 (0.086-0.329)	<.001
Cox proportional hazards model of all recipients		
Recipient male sex	1.049 (1.005-1.095)	.028
Recipient body mass index	1.001 (0.996-1.005)	.813
Recipient diabetes	1.069 (1.018-1.123)	.007
Recipient lung allocation score at transplant	1.00 (0.998-1.002)	.927
Obstructive lung disease (ref = restrictive)	1.008 (0.958-1.062)	.751
Pulmonary vascular disease (ref = restrictive)	0.968 (0.872-1.074)	.537
Cystic fibrosis or immunodeficiency disorder (ref = restrictive)	0.795 (0.729-0.866)	<.001
UNOS race/ethnicity (ref = White)		
Black	0.911 (0.854-0.972)	.005
Asian	0.813 (0.701-0.942)	.006
Hispanic	0.894 (0.827-0.967)	.005
American Indian/Alaska Native	0.909 (0.664-1.246)	.554
Multiracial	0.98 (0.723-1.329)	.899
Native Hawaiian/Pacific Islander	0.607 (0.273-1.353)	.222
Recipient functional status at transplant (vs 10%–moribund)		
20%—very sick	0.836 (0.737-0.948)	.005
30%—severely disabled	0.792 (0.685-0.917)	.002
40%—disabled	0.831 (0.719-0.961)	.013
50%—requires considerable assistance	0.769 (0.665-0.891)	<.001
60%—requires occasional assistance	0.752 (0.65-0.871)	<.001
70%—cares for self	0.756 (0.651-0.877)	<.001
80%—normal activity with effort	0.777 (0.661-0.913)	.002
90%—able to carry on normal activity	0.735 (0.595-0.908)	.004
100%—normal	0.61 (0.44-0.844)	.003
Prior cardiac surgery	1.262 (1.16-1.374)	<.001
Prior lung surgery	0.886 (0.821-0.957)	.002
Total bilirubin at transplant	1.04 (1.025-1.056)	<.001
Chronic steroid use	1.019 (0.982-1.058)	.319
Recipient cigarette use	1.104 (1.056-1.153)	<.001
Creatine at listing	1.142 (1.083-1.203)	<.001
Pretransplant dialysis	1.122 (0.833-1.513)	.449
Recipient ECMO at transplant	0.815 (0.717-0.926)	.002
Recipient mechanical ventilation at transplant	1.073 (0.972-1.185)	.16
Intensive care unit at transplant (ref = hospitalized)	0.954 (0.865-1.053)	.355
Not hospitalized at transplant (ref = hospitalized)	0.881 (0.811-0.956)	.002
Transplant type (ref = single lobe)	1.533 (1.472-1.596)	<.001

(*Continued*)

TABLE 2 Continued

Variables	Hazard Ratio (95% CI)	*P* Value
No acute rejection (ref = yes)	0.935 (0.789-1.107)	.434
Posttransplant dialysis	3.162 (2.96-3.378)	<.001
Posttransplant stroke	1.819 (1.643-2.015)	<.001
Reintubated after transplant	1.418 (1.355-1.485)	<.001
Donor cigarette use	1.087 (1.022-1.155)	.008
Donor hypertension	1.096 (1.049-1.144)	<.001
Donor creatine	1.019 (1.007-1.031)	.002
Donor male sex	0.977 (0.937-1.018)	.263
Recipient COVID-19–realted respiratory failure diagnosis	1.06 (0.612-1.838)	.834
Cox proportional hazards model of matched recipients		
Transplant type (ref = single lobe)	1.511 (0.959-2.379)	.075
No acute rejection (ref = yes)	1.531 (0.372-6.309)	.555
Posttransplant dialysis	3.27 (2.299-4.652)	<.001
Posttransplant stroke	2.605 (1.256-5.402)	.01
Donor cigarette use	1.094 (0.619-1.932)	.758
Prior lung surgery	1.566 (0.945-2.594)	.082
Intensive care unit at transplant (ref = hospitalized)	0.745 (0.488-1.137)	.173
Not hospitalized at transplant (ref = hospitalized)	0.471 (0.228-0.974)	.042
Recipient COVID-19–related respiratory failure diagnosis	0.824 (0.445-1.526)	.537

COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; UNOS, United Network of Organ Sharing.

Roach and colleagues[16] reported 95.6% survival at 3 months in 183 patients. This excellent survival is notable given the high acuity of illness at listing and transplantation in this population. The cause is likely multifactorial and may include careful patient selection, younger age of COVID-19 patients, the nature of the disease, and/or recent improvements in critical care and ECMO. Overall, the data are encouraging for all LT recipients and show that even the sickest recipients can have favorable outcomes.

TABLE 3 Matched and Unadjusted Baseline Recipient Short-term Outcomes

Short-term outcomes	Total (N = 681)	Matched Recipients (n = 454)	COVID-19 Recipients (n = 227)	*P* Value
Length of stay, mean (SD), d	639	37.99 (43.20)	35.74 (29.99)	.506
Acute rejection episode	670	42 (9.3)	13 (6.0)	.152
Recipient on ECMO at 72	542	77 (23.8)	58 (26.5)	.55
Recipient on mechanical ventilation at 72 h	540	195 (60.7)	131 (59.8)	.899
Posttransplant stroke	665	9 (2.0)	7 (3.2)	.507
Posttransplant dialysis	670	90 (20.0)	30 (13.7)	.061
Reintubation	666	69 (15.4)	25 (11.4)	.2
Functional status at discharge	430	(n = 51)	(n = 101)	.554
10%—moribund		8 (15.7)	19 (18.8)	
20%—very sick		35 (68.6)	58 (57.4)	
30%—severely disabled		3 (5.9)	12 (11.9)	
40%—disabled		2 (3.9)	8 (7.9)	
50%—requires considerable assistance		0 (0.0)	1 (1.0)	
60%—requires occasional assistance		2 (3.9)	1 (1.0)	
70%—cares for self		1 (2.0)	2 (2.0)	
30-day mortality	673	21 (4.7)	5 (2.3)	.191
90-day mortality	673	41 (9.1)	8 (3.6)	.016

Data are presented as n (%) unless indicated otherwise.

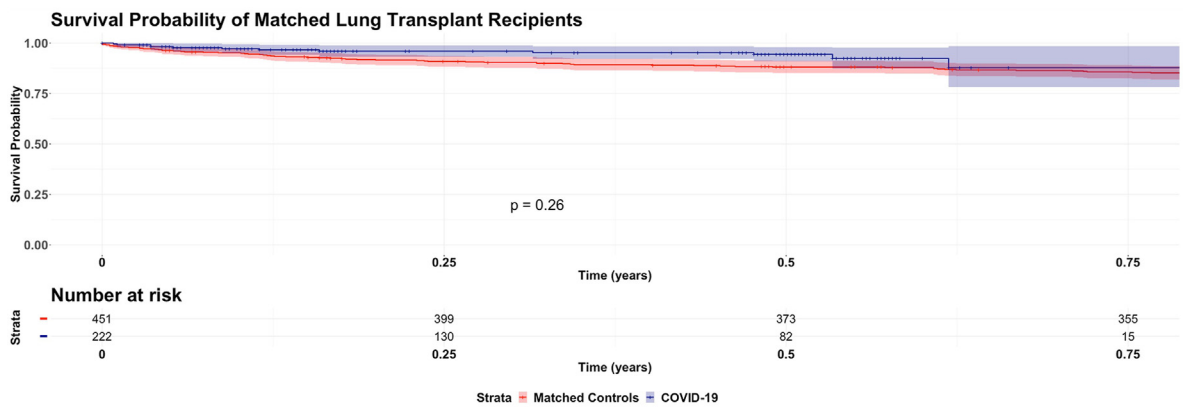

FIGURE 5 Kaplan-Meier survival analysis of recipients for coronavirus disease 2019 (COVID-19)–related respiratory failure compared with matched recipients. Shaded areas indicate the 95% CI.

Additionally, the population of recipients for COVID-19 had considerable baseline differences assessed against the general population of LT recipients, and our data used a matching algorithm to compare this unique cohort to patients with an equal acuity of illness. The matched controls and COVID-19 recipients underwent LT with a high LAS while on EMCO or intubated and in the intensive care unit. They were equally likely to remain on ECMO, remain intubated, and have prolonged stays in the hospital, regardless of etiology. In our study, matched controls had significantly higher 90-day mortality rates; however, 30-day mortality and 6-month survival were not significantly different. As a whole, our comparison demonstrates that LT candidates with high acuity of disease at transplant are likely to have a longer postoperative course and require more support, regardless of etiology.

LIMITATIONS. Our study has several limitations. This study was a retrospective review of the OPTN database, and there may be selection bias for LT or coding errors inherent in the database. Additionally, the criteria for listing COVID-19 patients and subsequent transplantation are still evolving and vary from center to center. Short of a randomized controlled trial, a national analysis remains the best option to attempt to answer this question of LT outcomes for COVID-19-related respiratory failure.

Our study did not capture differences in immunosuppressive regimens, type of ECMO support, pretransplant selection, or posttransplant care with granularity due to the nature of the national database. There may be unmeasured confounders that may have clarified the selection for LT over further medical care.

By limiting our analysis to adult patients after 2006, we attempted to limit the dramatic differences in transplant care or lung allocation.[18] Additionally, we could not analyze patients with COVID-19 who were not listed for transplantation.

CONCLUSIONS. Early survival for recipients of LT for COVID-19-related respiratory failure was comparable to that of other LT recipients. Candidates listed for LT for COVID-19-related respiratory failure had higher acuity of illness at listing and had notably shorter waiting list times. When matched with patients with similar characteristics and level of lung dysfunction, there were comparable similar short- and long-term outcomes. Carefully selected patients with end-stage respiratory disease due to COVID-19 may benefit from transplantation.

FUNDING SOURCES

The authors have no funding sources to disclose.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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