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Lung Transplantation for COVID-19 Related Lung Disease: A Follow-Up Study of Outcomes from a Medium-Size Lung Transplant Programd

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Abstract

In the United States of America, COVID-19 acute respiratory distress syndrome (ARDS) and post-COVID pulmonary fibrosis (PCPF) are raising indications for lung transplant (LT). Another indication for LT is underlying fibrosis with SARS-CoV-2 induced interstitial lung disease exacerbation or rapid progressing fibrosis. Only a few centers have reported on their long-term outcomes after LT for COVID-19. Single center retrospective chart review of patients transplanted for COVID-19 related lung disease. The Henry Ford Health System Institutional Board Review Board approved this study as minimal-risk research using data collected for routine clinical practice (#14953). During the study period from January 2021 to June 2023, 12 patients underwent bilateral LT for COVID-19 related lung disease: 6 for COVID-19 ARDS, 4 with worsening of idiopathic pulmonary fibrosis (IPF) and 2 for PCPF. Median survival after LT in months are 18.5 (IQR 12.9, 26) for ARDS; 20.5 (IQR 13.1, 26) for IPF; and 12.6 months for PCPF. Hospital discharge survival was 83% for ARDS and 100% for the fibrotic types of lung

disease. The 30-day and 3-month survival was 100% and 91%, respectively, for all COVID-19 related lung diseases. At the time of data collection, 3 patients in this cohort died (2 in the ARDS group). Eight patients were alive over 1-year post-transplant (4 ARDS, 3 patients with IPF prior to COVID-19 and 1 patient with PCPF). LT for COVID-19 related lung disease is associated with several challenges from patient selection to perioperative management. Short- and long-term survival is promising but associated with significant morbidity.

Keywords
COVID-19 related lung disease; ARDS; ECMO; post-COVID fibrosis; lung transplantation

1. Introduction

COVID-19 can cause irreversible lung damage from acute respiratory distress syndrome (ARDS), or chronic respiratory failure associated with post-COVID-19 de novo fibrosis, sometimes referred to as post-COVID pulmonary fibrosis (PCPF) [1]. Worsening of an underlying fibrotic lung disease with acute exacerbation or rapid progressing fibrosis after SARS-CoV-2 have also been described [2]. There has been a rapid increase in the number of lung transplantations (LT) performed for COVID-19 in the United States of America and some estimations put COVID-19 as the indication for LT in 7% of the total number of LT [3]. Based on data from the Organ Procurement and Transplant Network in the United States, from the beginning of the pandemic to February 2023, over 450 LT have listed COVID-19 as the diagnosis indication. COVID-19 ARDS was the indication for LT in 254 patients (254/450, 57%). Limited data exists on long-term outcomes after LT for COVID-19 related lung disease.

Hospitals in Michigan and neighboring states without a LT program have contacted our hospital to discuss transfer for LT evaluation of patients with severe refractory hypoxic respiratory failure secondary to COVID-19 ARDS on extracorporeal membrane oxygenation (ECMO) but unable to wean.

This ARDS patient population in general compromised a very sick group of otherwise healthy and younger individuals with a critical but acute illness that despite maximal life support (ventilator and/or ECMO), the likelihood of recovery was deemed dismal with a very high risk of death and more complications while supported with machines in the intensive care unit (ICU). Rehabilitation potential prior to acute illness must has been present. Other absolute contraindications for LT in the general population of end-stage lung diseases must has not been present. This group of patients were more frequently supported with ECMO. Many of them were deeply sedated and have developed critical illness associated weakness.

For the sickest group with COVID-19 ARDS as the indication for LT evaluation, LT was considered only for individuals <65 years-old, with single organ failure (lungs), body mass index less than 35 kg/m^2, 2 consecutive lower respiratory fluid polymerase chain reaction tests negative for SARS-CoV-2 on specimens obtained by endotracheal aspirate or bronchoscopy 24 hours apart, and enough clinical data to support an end-stage condition with inability to wean off life support with the ventilator and/or ECMO. Only patients deemed to have rehabilitation potential were considered

and when unable to participate in treatment discussion, a family member or legally appointed surrogate advocated and consented for transplant.

Patients with persistent hypoxic respiratory failure post-acute COVID-19 were evaluated in our clinic if they were discharged with oxygen therapy, had fibrotic-like lesions on computed tomography (CT) and a restrictive pattern in lung function. They were followed on a periodic basis to assess for disease progression.

For pulmonary fibrosis with exacerbation or rapid progression after COVID-19, our approach was in line with those under lung transplant evaluation for idiopathic pulmonary fibrosis (IPF), following the International Society for Heart and Lung Transplantation (ISHLT) guidelines.

2. Materials and Methods

The Henry Ford Health System Institutional Board Review Board approved this case series as minimal-risk research using data collected for routine clinical practice (#14953). Informed consent was waived. SARS-CoV-2 infection was confirmed by nasopharyngeal swab with real-time polymerase chain reaction and computed tomography scan of the chest showed changes typical of COVID-19 pneumonia in all cases. During the study period from January 2021 to June 2023, we conducted a retrospective review of electronic medical records with analysis of demographics, baseline comorbidities, COVID-19 related data, lung allocation score (LAS), waitlist time, ECMO support, pre- and post-transplant related characteristics, and outcomes (primary graft dysfunction [PGD]), postoperative invasive mechanical ventilation days, ICU utilization, hospital length of stay, discharge disposition, survival, Karnofsky score and last office obtained spirometry with report of forced expiratory volume in 1-second or FEV1.

2.1 Statistical Analysis

The sample size was equal to the number of patients treated during the study period and no statistical sample size was calculated. Continuous variables were presented as medians and IQRs. Categorical variables were expressed as frequency rates and percentages.

3. Results

During the third and fourth waves of the COVID-19 pandemic (between December 2020 and December 2021 with community circulation of the SARS-CoV-2 delta variant) many requests for transfers to our hospital did not occur due to several reasons: patients not meeting the minimal criteria to be considered for evaluation, or clinical improvement, or lack of bed availability at the receiving hospital, or full ECMO capacity in our hospital at the time of request, or death, or decompensation prior to transfer. Between December 2020 and July 2022, approximately 78 unique external referrals for LT evaluation for COVID-19 related lung disease were reviewed by our LT team. Amongst them, 38 patients completed evaluation: 16 ARDS on ECMO, 12 post-COVID fibrosis or PCPF, and 10 underlying fibrosis worse after COVID-19 (Figure 1). Twelve of these patients underwent bilateral LT during the study period.

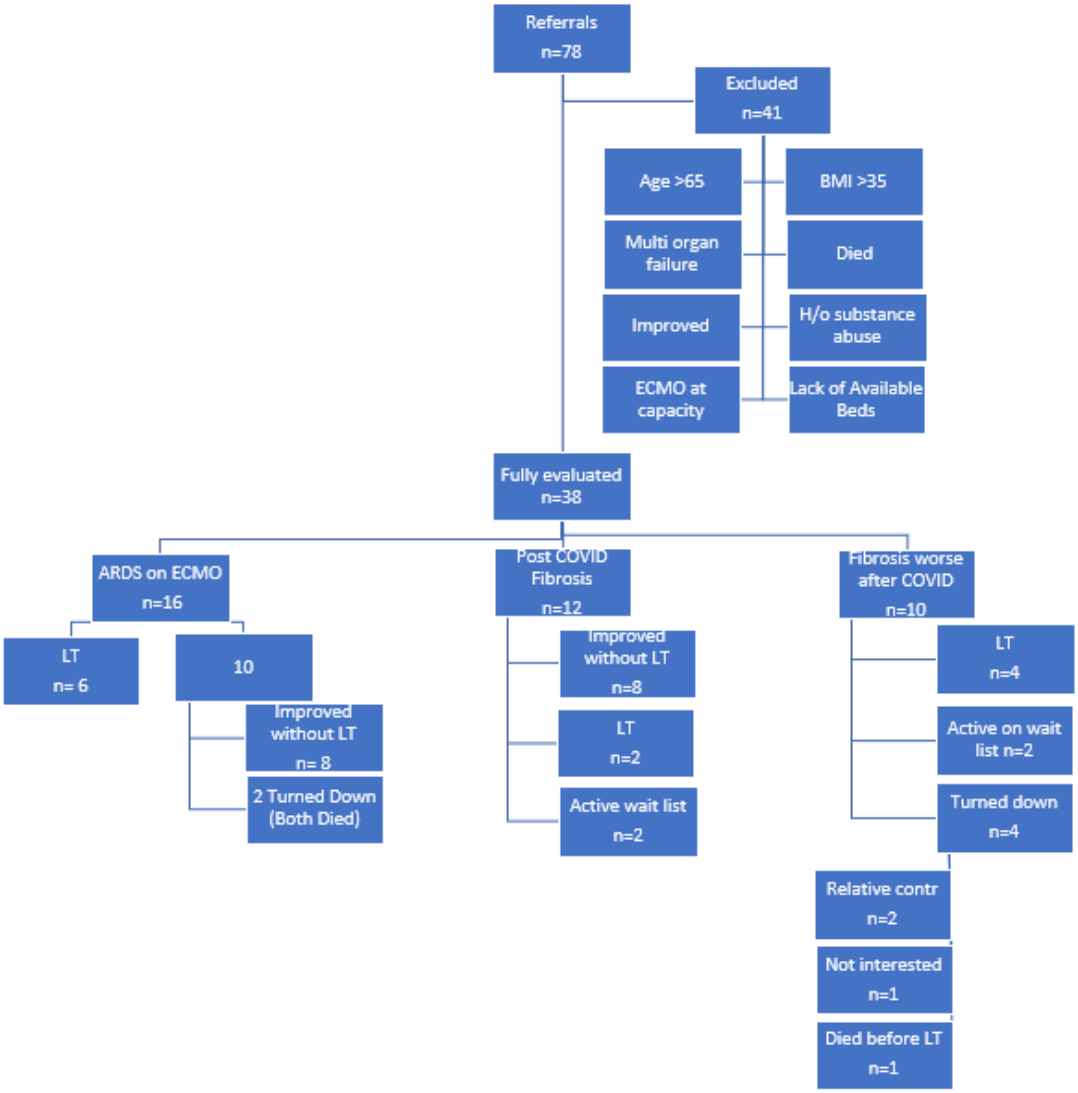

Figure 1 Flowchart. Abbreviations: ARDS, acute respiratory distress syndrome; contr, contraindication; ECMO, extracorporeal membrane oxygenation; H/o, history of; LT, lung transplant.

Patients with COVID-19 ARDS and PCPF patients were transplanted while being hospitalized, most from the ICU. Patients' characteristics and explant pathology with histologic findings are described in Table 1 and Table 2.

Table 1 Baseline characteristics and post-LT follow-up.

	COVID-19 ARDS	**AE-IPF or Rapid IPF Progression since SARS-CoV-2**	**Post-COVID Fibrosis**
	6 patients received BLT	4 patients received BLT	2 patients received BLT
Sex	4 males, 2 females	4 males	2 males
Median age (years)	43	69	54 and 55
COVID-19 diagnosis to LT (days)	60.5 (IQR 57, 96)	62	150 and 480 days
Median LAS	87.7	65.1	81.3 and 89.47
Waitlist time median (days)	5	158 • AE-IPF (N = 2): 31 days • IPF rapid progression (N = 2): 299 days	22 and 47 days
MCS before LT	100% • VV ECMO in 5 patients; 2 with single double lumen and 3 femoral-femoral (1 converted to venopulmoarterial oxyRVAD) • 1 VV converted to VAV ECMO Femoral-femoral to femoral artery	25% • VV ECMO in 1 patient with single double lumen cannula	Heated high-flow nasal cannula and heated high-flow alternating with BPAP

	• 1 transplanted from mechanical ventilator		
Median operation time (hours)	7.1	8.3	9.3 and 9.5
Total ischemia time (hours)	5.5 (IQR 4.7, 6.2)	5.4 (4.5, 398)	5 and 3.5
ICU LOS post-BLT median (days)	28	6	10 and 13 days
Post-BLT median duration of hospitalization (days)	54	30	15 and 16 days
Post-BLT median survival (months)	18.5 (IQR 12.9, 26)	20.5 (13.1, 26)	11.6 and 14

AE-IPF, acute exacerbation of idiopathic pulmonary fibrosis; ARDS, acute respiratory distress syndrome; BLT, bilateral lung transplant; BPAP bilevel positive airway pressure; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range; IPF, idiopathic pulmonary fibrosis; LAS, lung allocation score; LOS, length of stay; LT, lung transplant; MCS, mechanical support; oxyRVAD, venopulmoarterial ECMO; VAV, venous-arterial-venous; VV, venous-venous. Numbers represent median and interquartile 25%-75%. Operation time is from anesthesia start to chest closure.

Table 2 Histopathology of explanted lungs.

	Indication for LT	**UIP**	**DAD**	**DAH**	**OP**	**NSIP**	**Other interstitial fibrosis**	**PAH**	**Bronchopneumonia**	**Granuloma**
1	COVID-19 ARDS		x	x			x			
2	COVID-19 ARDS			x	x	x	x			x
3	COVID-19 ARDS		x	x			x	x	x	
4	COVID-19 ARDS		x	x			x			
5	COVID-19 ARDS		x	x			x			x
6	COVID-19 ARDS					x				x
7	AE-IPF	x	x							
8	AE-IPF	x	x							
9	IPF worsen	x	x							

10	IPF worsen	x									
11	Post-COVID fibrosis		x		x		x		x		x
12	Post-COVID fibrosis				x			x	x		

AE, acute exacerbation; ARDS, acute respiratory distress syndrome; DAD, diffuse alveolar damage; DAH, diffuse alveolar hemorrhage; IPF, idiopathic pulmonary fibrosis; LT, lung transplant; NSIP, non-specific interstitial pneumonia; OP, organizing pneumonia; PAH, pulmonary arterial hypertension; UIP, usual interstitial pneumonia.

Out of 16 patients with COVID-19 ARDS on ECMO, 6 patients underwent bilateral LT. In the case of transplanted patients with COVID-19 ARDS, venous-venous ECMO was instituted in 5 patients: 3 with the goal of bridging to transplant; and in 2 patients ECMO was used as bridge to recovery, but due to dependence on mechanical support without evidence of lung recovery ECMO ultimately allowed for evaluation and transplantation. All patients bridged with ECMO received a tracheostomy to allow for lowering sedation. Attempts to wean sedation were frequently associated with worsening respiratory status and ventilator dyssynchrony, worsening hypoxia and hemodynamic instability.

The median time from onset of COVID-19–ARDS to LT in this study was 60.5 days. All patients were supported with invasive mechanical ventilation and/or ECMO with a median time to LT of 48.5 days (IQR 40, 70). For those on ECMO (5/6, 83.3%), the median time from ECMO to LT was 32 days (IQR 4, 23.5).

Twelve patients with PCPF were fully evaluated in the LT clinic. Only 2 patients were transplanted to date (5 and 16 months after acute COVID-19 diagnosis), whereas 2 patients are active in the LT wait list by the time of data census. The two transplanted patients were hospitalized with severe refractory hypoxemia requiring heated high-flow oxygen in one patient and heated high-flow alternating with BPAP in the other. They both had radiographic evidence of fibrotic-like changes on CT scan with lack of clinic radiologic improvement with prolonged systemic corticosteroids treatment in case of organizing pneumonia. In one patient the radiographic findings were more consistent with irreversible fibrosis with presence of bilateral macrocystic lesions of the apices with diffuse traction bronchiectasis. The other patient had less extensive traction bronchiectasis and diffuse interstitial thickening. Interestingly, this patient with less fibrotic-like changes developed severe pulmonary hypertension not explained by presence of chronic thromboembolism.

Out of 10 patients with underlying pulmonary fibrosis (idiopathic or connective tissue disease related), 4 received LT for either rapid progressive fibrotic interstitial lung disease (ILD) post-COVID or for acute ILD exacerbation due to COVID-19. Two patients with idiopathic pulmonary fibrosis or IPF had an acute exacerbation as demonstrated by presence of ground-glass opacities on CT chests and significant worsening hypoxemia that required hospitalization. Another 2 patients with worsening IPF without acute exacerbation had rapid disease progression: increase in their outpatient oxygen flow and decline in lung function. Their chest high-resolution CT scans revealed evidence of a definite usual interstitial pneumonia (UIP) pattern with progression.

Only bilateral LT were performed in the total cohort of 12 recipients, regardless of underlying lung disease or acuity. Veno-arterial ECMO was the preferred method for cardiopulmonary support in the operative room in 83% of patients (n = 10). One patient's transplant was completed off cardiopulmonary bypass and another individual required conversion to cardiopulmonary bypass from VA ECMO due to bleeding from the pulmonary artery. Although all patients were successfully decannulated from ECMO in the operative room, PGD grades 2 and 3 were common in 2 out of 6 patients in the ARDS group (33%) versus 1 patient (17%) in the non-ARDS group.

Except for 1 patient with COVID-19 ARDS and history of recurrent infections with multidrug resistant respiratory organisms and bacteremia, standard induction immunosuppression with basiliximab, mycophenolate and corticosteroids were used. Standard prophylaxis and maintenance anti-rejection drugs using a combination of a calcineurin inhibitor, cell-cycle inhibitor and corticosteroids were used following our institution protocol for the care of LT recipients.

Median follow-up in months based on LT indication are 18.5 (IQR 12.9, 26) for ARDS; 20.5 (13.1, 26) for fibrotic lung disease worse after COVID-19; and 12.6 months for PCPF. Hospital discharge survival was 83% for ARDS (1 patient died in the hospital 6 weeks after LT), and 100% for the fibrotic type of lung disease. The 30-day and 3-month survival was 100% and 91%, respectively, for all COVID-19 related lung diseases. By June 2023, 2 of the ARDS transplanted patients died (2/6, 33%), 1 patient with IPF prior to COVID-19 died (1/4, 25%) whereas the 2 patients transplanted for PCPF are alive. Eight patients were alive over 1-year post-transplant (5 patients with ARDS, 3 patients with history of IPF prior to COVID-19 and 1 patient with PCPF). Lung function test and functional capacity were very reassuring in these patients based on FEV1 and Karnofsky score one-year post-LT as seen in Table 3.

Table 3 One-year post-LT outcomes.

	LT indication	Post-LT follow-up (days)	Last FEV1 (L); %best predictive	Karnofsky score	ACR, AMR	Vital Status
1	COVID-19 ARDS	785	3.38; 99	80	A1	Alive
2	COVID-19 ARDS	63	NA	NA		Died
3	COVID-19 ARDS	641	2.99; 99	80		Alive
4	COVID-19 ARDS	856	2.46; 92	90	A1, A1, A1	Alive
5	COVID-19 ARDS	389	0.56; 25	NA		Died
6	COVID-19 ARDS	471	2.6; 78	90	A1, A1, A2	Alive
7	AE-IPF	761	3.14; 99	90	A1	Alive
8	AE-IPF	814	2.55; 96	80		Alive
9	IPF worsen	493	3.14; 100	80	A1	Alive
10	IPF worsen	314	NA	NA		Died
11	PCPF*	335	NA	50	A3, AMR	Alive
12	PCPF	425	1.83; 97	80		Alive

AE, acute exacerbation; ARDS, acute respiratory distress syndrome; IPF, idiopathic pulmonary fibrosis; LT, lung transplant; AE-IPF, acute exacerbation of IPF; PCPF, post-COVID pulmonary fibrosis; FEV1, forced expiratory volume in 1 second; ACR, acute cellular rejection; AMR, antibody mediated rejection; *alive patient with tracheostomy in place; NA, data not available.

The median length of stay post-LT for ARDS was 54 days. The median post-LT length of stay was 22.5 days (IQR 14, 115) for the group with underlying IPF before COVID-19, and 15 and 60 days in the two patients with PCPF, respectively. Two transplanted patients were discharged to an inpatient rehabilitation unit (both with underlying COVID-19 ARDS as the indication for LT), while 10 patients returned home from the hospital after transplantation.

The cause of death in the 3 patients are described. A 37-year-old man transplanted for COVID-19 ARDS died 6 weeks after LT due to septic shock from several infectious complications and necrotizing pancreatitis. A 36-year-old post-partum woman transplanted for COVID-19 ARDS died 13 months after LT with chronic hypoxic/hypercarbic respiratory failure secondary to end-stage bronchiolitis obliterans. A 71-year-old man transplanted for IPF with rapid progression after COVID-

19 died 11 months post-LT under hospice care. He developed recurrent pneumonias, critical illness myopathy and persistent respiratory failure since the time of transplant and was ventilator dependent via tracheostomy.

4. Discussion

Although experts have issued guidelines on transplant candidacy for the uncommon indication of ARDS, the lack of good understanding on long-term outcomes and the optimal transplant candidate remains elusive. LT for ARDS poses several challenges and is reserved for the minority of carefully selected patients dependent on extracorporeal life support as in most cases have been performed off ECMO [4, 5]. Studies prior to the COVID-19 pandemic showed promising survival of high-risk transplanted patients from the ICU including those bridged to transplantation on ECMO [6, 7]. Compared to the population of patients that did not require ECMO bridge, LT for COVID-19 was associated to very good short- and long-term outcomes when the transplant occurred in a large program size and with use of ambulatory ECMO [8-11]. Most of these studies have used venous-venous ECMO as a bridge to LT. Familiarity and increased availability of ECMO, better understanding of patient-machine interactions, care standardization, as well as technological advances have been proposed as the reasons for improved outcomes post-LT with ECMO as a bridge to LT [12, 13]. The 2021 ISHLT Consensus document for the selection of LT candidates lists ARDS as an indication for lung transplant in carefully selected patients [14]. Based on the experience with LT for COVID-19, experts recommend careful selection of patients for LT in cases of irreversible, end-stage COVID-19 lung disease based on clinical grounds and evidence of extensive fibrotic lung disease as demonstrated on computed tomography [4].

Our experience with high-risk transplantation for non-COVID-19 patients shows similar outcomes to larger volume centers. From 2015 to date, we have transplanted 23 patients off ECMO. The 30-day survival rate was 100%, 3-month survival was 100%, and 1-year survival was 87%, outcomes very comparable to the general LT population at large. This includes 13 patients (13/23; 56%) placed on ECMO as a bridge to decision that eventually received bilateral LT.

Long-term outcomes after LT for COVID-19 related lung disease remains unknown with only a few centers across the United of States of America reporting on their outcomes [15, 16]. When compared to hospitalized patients transplanted for restrictive lung disease, Razia et al described 11 patients with COVID-19 ARDS with comparable 1-year survival rate post-LT of approximately 90% [15]. Another study queried the Organ Procurement and Transplant Network database and described similar outcomes and 6-month survival in 227 patients transplanted for COVID-19 related lung disease when compared to 454 matched controls. Eighty-seven percent (293/334, 87%) of these patients were either on mechanical ventilation and/or ECMO [17].

Most LTs for COVID-19 ARDS have been bilateral LT due to the frequent presence of pulmonary hypertension and superimposed bacterial pneumonias. In the largest single center series of COVID-19 ARDS, Kurihara et al described the outcomes of 30 patients transplanted for this indication in Chicago, 57% of them were supported on ECMO [16]. Patients were not ambulatory although able to participate to some degree with physical therapy. We have previously published a detailed report of the first 5 patients transplanted for COVID-19 ARDS at our institution with their short-term outcome [18]. Compared to the COVID-19 ARDS cohort from Chicago, only 1 patient did not require ECMO and was transplanted off the ventilator, whereas the other 5 patients with COVID-19 ARDS

required ECMO and the ventilator as a bridge to transplant (BTT). Only 2 COVID-19 ARDS patients in our cohort were able to consent for transplantation and participated in pulmonary rehabilitation, which was limited to exercises in bed.

None of our COVID-19 ARDS patients were ambulatory, similar to previous case series of lung transplanted patients with COVID-19 ARDS [17-19]. Although common complications of critical illness acquired weakness (both myopathy and neuropathy) were common, most of our patients improved over time with rehabilitation treatment after lung transplant.

Our COVID-19 ARDS survival post-LT is consistent with other reports. The increased hospital length of stay after transplant is also consistent with other centers' reports of higher morbidity in patient transplanted for this indication [15, 16].

Most patients with PCPF showed improvement in lung function over a variable period that extended from 3 to 17 months post-acute COVID-19. Lung improvements were demonstrated both radiographically and with lung function test as it has been previously described [19-22] after severe COVID-19 pneumonia. Older males, long hospital stay, use of positive mechanical ventilation and higher burden of reticulations and consolidation on CT scan at the time of admission were found to be the main risk factors associated to pulmonary sequelae in survivors of severe COVID-19 [22, 23].

In the particularly vulnerable population of patients with underlying ILD, COVID-19 has been reported to be associated to severe illness and death [24, 25] likely related to the variable lung reserve and sometimes immunosuppressed state depending on its association with autoimmunity or not. UIP, lower FVC and DLco at baseline were also associated with worse outcomes in COVID-19 infection [25]. Acute exacerbation of ILD is not uncommon with an acute viral infection. In a multicenter study, COVID-19 in IPF patients was associated with disease severity and high hospitalization and mortality rate [26].

Another important aspect that negatively impacted this population during the COVID-19 pandemic has to do with interruptions or limited access to in-person evaluations and testing's affecting the ability to timely diagnose and treat, detect disease progression, or diagnose acute complications. Like with immunosuppression, those on antifibrotics are also in need of frequent blood tests to monitor for drug related toxicity. Furthermore, for those on immunosuppressants (especially cell cycle inhibitors) there is a blunted immune response to immunization negating the benefits of vaccines to prevent COVID-19.

Ethical principles must be carefully considered in the selection of these unique patients. Many are sedated and unable to participate in decision making, including understanding the complexity of transplant and associated lifestyle changes. In some situations, the decision to proceed is made by the patient's surrogate, which can lead to a myriad of psychological sequelae. In addition, the benefit of working with patients and their support system in an ambulatory setting is lacking in these acutely ill individuals and therefore the ability to adapt to many lifestyle modifications following transplant is difficult to predict.

The use of surrogates to make decisions to proceed with evaluation and transplantation, and the ethical principles of beneficence were invoked by the lung transplant teams when deciding candidacy. The question of ECMO bridging in non-awake, non-ambulatory patients for evaluation and listing continues to spark controversy, and consensus is lacking. Most experts would discourage this practice, reserving ECMO BTT for patients with chronic lung diseases fully or nearly fully evaluated, deemed candidates for transplant and allowing awake and ambulatory ECMO to continue with physical therapy to reduce physical deconditioning. Older patients compared to the

younger patients with ARDS that underwent LT, normally present with several other comorbid conditions that increase the risk of several other complications, and in which body deconditioning should be avoided.

Other ethical principles, such as utility, justice, and efficiency need to be addressed [27]. Acute illness in these younger patients who were healthy at baseline may possess a different rehabilitation potential. With the new composite allocation score or CAS and the continuous distribution that in the United States replaced the LAS, understanding long term outcomes in patients with the highest acuity supported with ECMO is of paramount importance to allocate resources to those in greatest need and with the highest chances of survival and associated good quality of life post-LT.

During this study, we did not observe an increase in waitlist mortality in the non– COVID-19 cohort at our center; however, this needs to be studied in other centers with a different supply of donor lungs. All the patients transplanted for COVID-19 related lung disease had high LAS and many were on mechanical support including ECMO, representing a medical urgency. The younger age of the sickest patients in this group is another example of justice as an ethical principle being applied.

5. Limitations

This is a single center retrospective chart review study describing our experience with a small number of patients and a limited follow-up. Other important variables were not explored in this study including quality-of-life post-LT and re-hospitalizations. These are important clinical outcomes especially considering the high prevalence of PGD, weakness associated with severe illness and prolonged post-LT hospitalization.

6. Conclusions

LT for COVID-19 related lung disease have their own inherent challenges in each stage from candidate selection and perioperative management. Their long-term outcome is unknown due to limited available data. Prior to COVID-19, LT for an acute illness, like ARDS, was uncommon. The decision to proceed with LT evaluation should be made by a multidisciplinary care team that specializes in ARDS management and LT. LT for ARDS, is recommended to be performed in centers with experience in high-risk transplantation (including experience on ECMO) due to the challenging perioperative and postoperative care with expected prolonged ICU stay.

LT reports for post-COVID fibrosis or PCPF are scarce, as we have seen very few cases of post-COVID fibrosis in need of LT. When given enough time, most of these patients will recover lung function without the necessity of oxygen therapy for the rest of their lives.

Although we are unable to draw major conclusions with a small number of patients, short and long-term survival is promising but associated with significant morbidity. There are significant differences between these group of patients with COVID-19 related lung disease, and we recommend reporting them separately as opposed to grouping them as one single entity.

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Author Contributions

D.J.F.-P. designed the study. D.J.F.-P. and J.S. collected the data. D.J.F.-P. wrote the manuscript draft. D.J.F.-P., L.A., L.S. K.B, J.S. and H.N. critically revised the manuscript for important intellectual content. All authors have read and agreed to the published version of the manuscript.

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Competing Interests

The authors declare no conflict of interest.

References

1. Hage R, Schuurmans MM. COVID-19-associated lung fibrosis: Two pathways and two phenotypes, lung transplantation, and antifibrotics. Transplantology. 2022; 3: 230-240.
2. King CS, Mannem H, Kukreja J, Aryal S, Tang D, Singer JP, et al. Lung transplantation for patients with COVID-19. Chest. 2022; 161: 169-178.
3. Roach A, Chikwe J, Catarino P, Rampolla R, Noble PW, Megna D, et al. Lung transplantation for COVID-19–related respiratory failure in the United States. N Engl J Med. 2022; 386: 1187-1188.
4. Cypel M, Keshavjee S. When to consider lung transplantation for COVID-19. Lancet Respir Med. 2020; 8: 944-946.
5. International Society of Heart and Lung Transplantation. Deceased donor and recipient selection for cardiothoracic transplantation during the COVID-19 pandemic: Recommendations from the ISHLT COVID-19 Task Force. Texas: ISHLT; 2021 [cited date 2023 March 29]. Available from: https://ishlt.org/ishlt/media/documents/COVID-19_GuidanceDocument_Deceased-donor-and-recipient-selection-for-cardiothoracic-transplantation.pdf.
6. George TJ, Beaty CA, Kilic A, Shah PD, Merlo CA, Shah AS. Outcomes and temporal trends among high-risk patients after lung transplantation in the United States. J Heart Lung Transplant. 2012; 31: 1182-1191.
7. Hayanga JA, Hayanga HK, Holmes SD, Ren Y, Shigemura N, Badhwar V, et al. Mechanical ventilation and extracorporeal membrane oxygenation as a bridge to lung transplantation: Closing the gap. J Heart Lung Transplant. 2019; 38: 1104-1111.
8. Halpern AL, Kohtz PD, Helmkamp L, Eldeiry M, Hodges MM, Scott CD, et al. Improved mortality associated with the use of extracorporeal membrane oxygenation. Ann Thorac Surg. 2019; 108: 350-357.

9. Hoetzenecker K, Donahoe L, Yeung JC, Azad S, Fan E, Ferguson ND, et al. Extracorporeal life support as a bridge to lung transplantation-experience of a high-volume transplant center. J Thorac Cardiovasc Surg. 2018; 155: 1316-1328.e1.
10. Tipograf Y, Salna M, Minko E, Grogan EL, Agerstrand C, Sonett J, et al. Outcomes of extracorporeal membrane oxygenation as a bridge to lung transplantation. Ann Thorac Surg. 2019; 107: 1456-1463.
11. Xia Y, Ragalie W, Yang EH, Lluri G, Biniwale R, Benharash P, et al. Venoarterial versus venovenous extracorporeal membrane oxygenation as bridge to lung transplantation. Ann Thorac Surg. 2022; 114: 2080-2086.
12. Tsiouris A, Budev MM, Yun JJ. Extracorporeal membrane oxygenation as a bridge to lung transplantation in the United States: A multicenter survey. ASAIO J. 2018; 64: 689-693.
13. Patterson CM, Shah A, Rabin J, DiChiacchio L, Cypel M, Hoetzenecker K, et al. Extracorporeal life support as a bridge to lung transplantation: Where are we now? J Heart Lung Transplant. 2022; 41: 1547-1555.
14. Leard LE, Holm AM, Valapour M, Glanville AR, Attawar S, Aversa M, et al. Consensus document for the selection of lung transplant candidates: An update from the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. 2021; 40: 1349-1379.
15. Razia D, Olson MT, Grief K, Walia R, Bremner RM, Smith MA, et al. Hospitalized patients with irreversible lung injury from COVID-19 have higher morbidity but similar 1-year survival after lung transplant compared to hospitalized patients transplanted for restrictive lung disease. J Heart Lung Transplant. 2023; 42: 255-263.
16. Kurihara C, Manerikar A, Querrey M, Felicelli C, Yeldandi A, Garza-Castillon R, et al. Clinical characteristics and outcomes of patients with COVID-19–associated acute respiratory distress syndrome who underwent lung transplant. JAMA. 2022; 327: 652-661.
17. Freischlag K, Lynch TJ, Ievlev V, Gries C, Keech JC, Arshava EV, et al. A matched survival analysis of lung transplant recipients with coronavirus disease 2019–related respiratory failure. Ann Thorac Surg. 2022. doi: 10.1016/j.athoracsur.2022.09.039.
18. Franco-Palacios DJ, Allenspach L, Stagner L, Pinto J, Olexsey K, Sherbin E, et al. A center experience with lung transplantation for COVID-19 ARDS. Respir Med Case Rep. 2022; 36: 101597.
19. Steinbeis F, Thibeault C, Doellinger F, Ring RM, Mittermaier M, Ruwwe-Glösenkamp C, et al. Severity of respiratory failure and computed chest tomography in acute COVID-19 correlates with pulmonary function and respiratory symptoms after infection with SARS-CoV-2: An observational longitudinal study over 12 months. Respir Med. 2022; 191: 106709.
20. Amin BJ, Kakamad FH, Ahmed GS, Ahmed SF, Abdulla BA, Mikael TM, et al. Post COVID-19 pulmonary fibrosis; a meta-analysis study. Ann Med Surg. 2022; 77: 103590.
21. Ambardar SR, Hightower SL, Huprikar NA, Chung KK, Singhal A, Collen JF. Post-COVID-19 pulmonary fibrosis: Novel sequelae of the current pandemic. J Clin Med. 2021; 10: 2452.
22. Cocconcelli E, Bernardinello N, Giraudo C, Castelli G, Giorgino A, Leoni D, et al. Characteristics and prognostic factors of pulmonary fibrosis after COVID-19 pneumonia. Front Med. 2022; 8: 823600.
23. Han X, Fan Y, Alwalid O, Li N, Jia X, Yuan M, et al. Six-month follow-up chest CT findings after severe COVID-19 pneumonia. Radiology. 2021; 299: E177-E186.

24. Lee H, Choi H, Yang B, Lee SK, Park TS, Park DW, et al. Interstitial lung disease increases susceptibility to and severity of COVID-19. Eur Respir J. 2021; 58: 2004125.
25. Esposito AJ, Menon AA, Ghosh AJ, Putman RK, Fredenburgh LE, El-Chemaly SY, et al. Increased odds of death for patients with interstitial lung disease and COVID-19: A case-control study. Am J Respir Crit Care Med. 2020; 202: 1710-1713.
26. Cilli A, Hanta I, Uzer F, Coskun F, Sevinc C, Deniz PP, et al. Characteristics and outcomes of COVID-19 patients with IPF: A multi-center retrospective study. Respir Med Res. 2022; 81: 100900.
27. Holm AM, Mehra MR, Courtwright A, Teuteberg J, Sweet S, Potena L, 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: 619-626.