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Lung Transplantation in Patients With COVID-19-The Early National Experience

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Lung transplant (LT) has become a viable option for COVID-19 patients suffering from end-stage Acute Respiratory Distress Syndrome (ARDS). This analysis sought to describe the early national experience of COVID-19 patients who received LT and compare transplant characteristics and short-term outcomes of COVID-19 and non-COVID-19 ARDS LT recipients. We queried the Organ Procurement and Transplantation database for adults (≥ 18 years old) receiving LT from January 2009 to March 31, 2022 with diagnoses of COVID-19 or ARDS. We identified 353 COVID-19 and 64 non-COVID-19 ARDS LT recipients. COVID-19 recipients were older (median age: 51, interquartile range [40-57] years vs 41 [26-52]; $P < 0.001$), more predominantly male (78% ($n = 274$) vs 55% ($n = 35$), $P < 0.001$), and had higher body mass indices (median 27.2 interquartile range [24.5-30.9] vs 25.4 [22.1-28.6]; $P < 0.01$) than non-COVID-19 ARDS recipients. COVID-19 LT recipients were less frequently reliant on extra-corporeal membrane oxygenation at 72 hours after transplant (26% ($n = 80$) vs 31% ($n = 15$), $P < 0.001$), and were less frequently dependent on dialysis post-transplant than non-COVID-19 ARDS LT recipients (14% ($n = 43$) vs 23% ($n = 14$); $P = 0.01$). Survival at 90 days post-transplant was comparable for the non-COVID ARDS (90%, $n = 54$) and COVID-19 (94%, $n = 202$) LT recipients with available follow-up ($P = 0.17$). LT appears to be a viable therapy for COVID-19 patients with end-stage lung disease. COVID-19 LT and non-COVID-19 ARDS LT recipients have comparable 90 days post-transplant survival.

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Keywords: COVID-19, Acute Respiratory Distress Syndrome (ARDS), Lung transplantation, Post-transplant survival

Abbreviations: LT, lung transplant; ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane oxygenation

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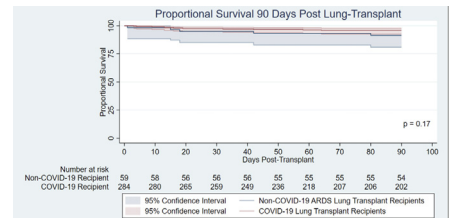
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Proportional Survival Post Lung Transplant for non-COVID-19 ARDS and COVID-19 Recipients.

Central Message

Limited short-term data suggests that lung transplantation is a viable therapy for COVID-19 patients with end stage lung disease.

Perspective Statement

Limited short-term data from April 2020 to March 31, 2022 for 353 patients who received lung transplants due to disease processes stemming from COVID-19 indicate that LT is a viable therapy for COVID-19 refractory to conventional care. COVID-19 LT and non-COVID-19 ARDS LT recipients have comparable 90 days post-transplant survival.

INTRODUCTION

As of June 2022, there have been 534 million reported cases of Coronavirus Disease 2019 (COVID-19) worldwide, with over 6.2 million reported deaths.¹ In the United States, over 85 million cases and one million deaths have been reported.¹ The clinical course of COVID-19, caused by the coronavirus SARS-CoV-2, is highly variable. Severe cases (6-10%) can result in acute respiratory distress syndrome (ARDS), a condition marked by hyper-inflammation resulting in potentially irreversible parenchymal lung damage, thus severely impairing oxygenation and ventilation.^{2,3} Known therapies for ARDS include supportive care, lung-protective mechanical ventilation, and veno-venous extra-corporeal membrane oxygenation in severe cases.^{4,5} Since 2005, lung transplantation (LT) for ARDS has been accepted as a therapy for the most extreme or refractory cases of organ damage, with post-transplant outcomes that are comparable to other restrictive lung diseases.⁶

ARDS due to COVID-19 is a highly lethal disease, with mortality of patients receiving mechanical ventilation for COVID-19 ARDS as high as 40%.^{7,8} Additionally, one third of patients hospitalized with COVID-19 develop pulmonary fibrosis, or scarring of lung tissue.^{9–12} LT has also been shown to be a promising therapy in select patients with severe irreversible lung compromise due to COVID-19.^{13–18} Initial reports described LT as therapy for COVID-19 patients with no evident lung recovery as soon as 4 weeks after the onset of COVID-19 ARDS.^{13,14} Currently, there are more COVID-19 LT candidates on the waitlist than all non-COVID ARDS patients on the waitlist since LT started.¹⁹ Despite the use of vaccinations for COVID-19, new strains of the virus have led to a surge in COVID-19 cases and hospitalizations.¹

Current literature regarding LT in the setting of COVID-19 is limited. To date studies have reported on the preliminary experience of LT in the setting of COVID-19 in the United States,²⁰ have evaluated racial disparities in LT recipients with disease processes associated with COVID-19,²¹ and have concluded that patients with irreversible lung damage to COVID-19 suffer high mortality if they do not receive LT.²² Though LT has long been therapeutic for patients with ARDS, clinical presentations of COVID-19 and non-COVID-19 ARDS patients differ.²³ Moreover, while LT is established as a viable treatment for refractory non-COVID-19 ARDS, the differences in clinical presentation and outcomes of COVID-19 and non-COVID-19 ARDS LT recipients have not been well described but can guide future practice. The primary aim of this analysis is to describe the early national experience of COVID-19 patients who received LT. The secondary aim of this paper is to compare pre-transplant disease characteristics, clinical variables, and perioperative and short-term outcomes of patients receiving LT as therapy for COVID-19 vs non-COVID-19 ARDS. We hypothesize that LT is a viable therapy for individuals suffering from COVID-19 refractory to conventional medical treatment, and that despite differing pre-transplant presentations, post-operative outcomes of LT for COVID-19 and non-COVID-19 ARDS are similar.

MATERIALS AND METHODS

We retrospectively queried the Organ Procurement and Transplantation Network (OPTN) database, which is a national transplant database administered by the United Network of Organ Sharing. With the onset of the COVID-19 pandemic, 2 new options were added to the category of Group D restrictive lung disease: COVID-19 ARDS and COVID-19 fibrosis.²⁴ We included for analysis adults (≥ 18 years of age) who received LT from January 2009 to March 31, 2022 with primary diagnoses of ARDS (non-COVID-19; diagnosis code 402). We also queried the OPTN database for adults (≥ 18 years of age) who received LT from March 13, 2020 (the announcement of the COVID-19 national emergency)²⁵ and March 31, 2022 with primary diagnoses of COVID-19 (diagnosis codes 1616 [COVID-19 ARDS] or 1617 [COVID-19 pulmonary fibrosis]), or presence of “COVID” in the open text of the diagnosis

variable DIAG_OSTXT). This study was approved by the local institutional review board (IRB00254563) and conducted in compliance with the International Society for Heart and Lung Transplantation Ethics Statement.

Recipient descriptive variables included in this analysis were age at listing, gender, race, body mass index, history of previous malignancy, diabetes, cigarette use, prior cardiac surgery, Lung Allocation Score at listing, Lung Allocation Score at transplant, use of ventilatory support at transplant, use of extra-corporeal membrane oxygenation (ECMO) at listing and transplant, receipt of pre-transplant tracheostomy, and type of transplant (single or double). Pre-transplant clinical variables included donor age, recipient mean arterial pressure at transplant, ischemic time, recipient functional status at listing, recipient functional status at transplant, total days on the waiting list, receipt of pre-transplant dialysis since listing, and receipt of transfusions since listing. Perioperative outcomes data included recipient use of ECMO at 72 hours after transplant, length of stay from transplant to discharge, recipient stroke post-transplant, and recipient dialysis post-transplant.

Our primary outcome was 90-day survival. Post-transplant survival was displayed as Kaplan-Meier survival curves. Log rank-testing stratified by diagnosis (non-COVID-19 ARDS vs COVID-19) was used to assess post-transplant mortality. Individuals with either no follow-up, or follow-up less than 90 days following transplant were excluded from the survival analysis. Patients who received LT through December 31, 2021 were considered in the 90-day follow-up analysis, and patients who received LT through February 28, 2022 were included in the 30-day follow-up analysis.

Statistical Analysis

Descriptive characteristics, pre-transplant clinical variables, and perioperative outcomes data were compared for the COVID-19 and non COVID-19 ARDS patient groups using chi-squared analyses for categorical variables and Wilcoxon signed-rank tests for continuous variables. Statistical significance was set at $P < 0.05$ (2-tailed). All analyses were performed using STATA software (Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC).

RESULTS

Study Population

We identified 67 LT recipients with a primary diagnosis of ARDS from 2009 to March 2022 and 356 LT recipients with a primary diagnosis of COVID-19 in the first 2 years of the pandemic. Three ARDS and 3 COVID-19 patients received simultaneous heart and lung transplants and were excluded from the analysis, leaving a sample population of 64 ARDS and 353 COVID-19 LT recipients. Of the COVID-19 patients, 61% ($n = 215$) had a diagnosis of COVID-19 ARDS, 37% ($n = 131$) had a diagnosis of COVID-19 fibrosis, and 2% ($n = 7$) had a non-specific diagnosis of COVID-19 (Fig. 1). The incidence of LT for ARDS was highest in 2020 (Fig. 2), while the incidence

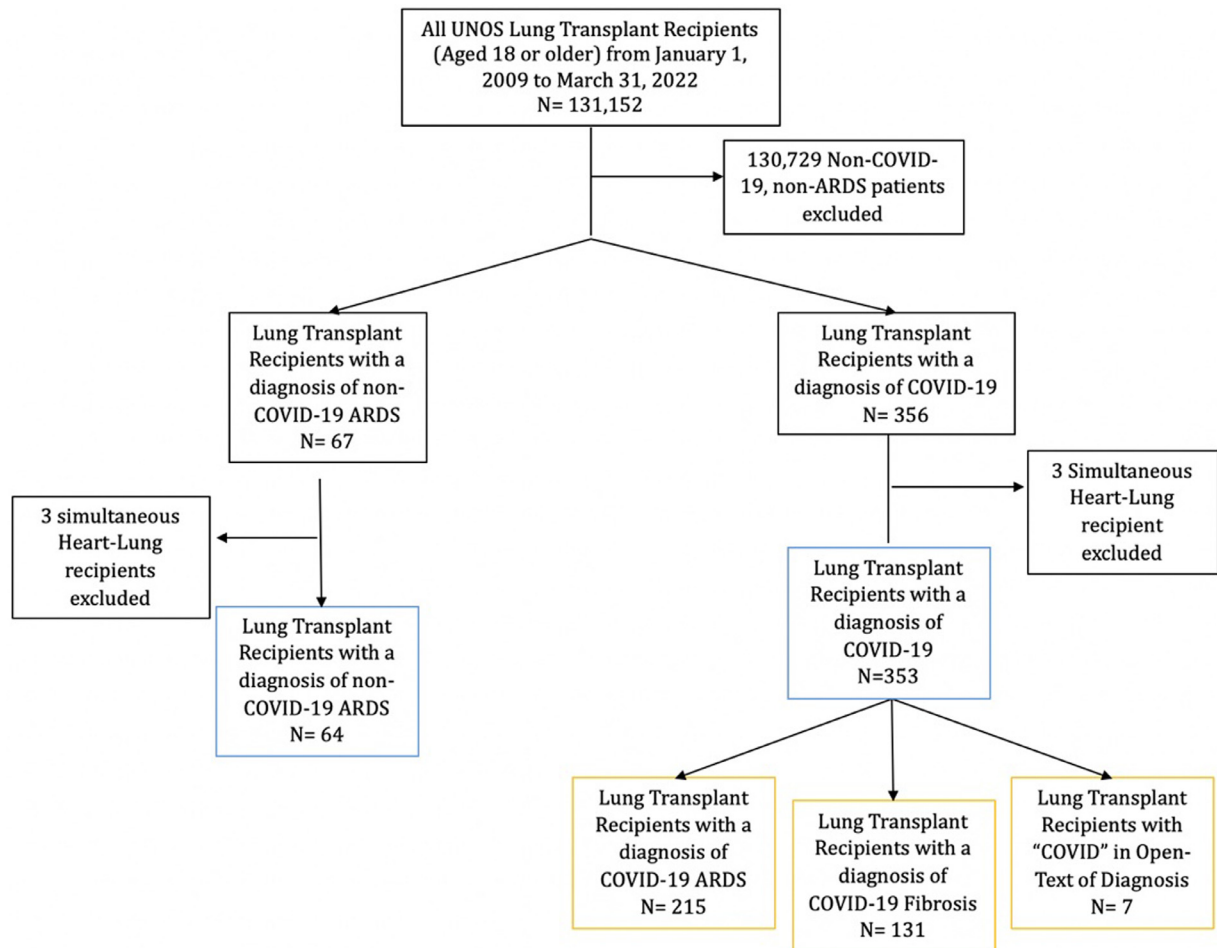


Figure 1. Patient inclusion criteria. The blue boxes identify our final study population, comprised of lung transplant recipients with a diagnosis of non-COVID-19 Acute Respiratory Distress Syndrome (ARDS) and of lung transplant recipients with a diagnosis of COVID-19. The yellow boxes identify the sub-diagnoses of the COVID-19 Lung Transplant recipients, which includes COVID-19 ARDS and COVID-19 Fibrosis.

of LT for COVID-19 was highest in March and April of 2021 (Fig. 3).

NON-COVID ARDS VS COVID ANALYSIS

Patient Descriptive Characteristics

LT recipients with a primary diagnosis of COVID-19 were older (median age: 51, interquartile range, IQR [40-57] years vs 41 [26-52]; $P < 0.001$) and more predominantly male (78% ($n = 274$) vs 55% ($n = 35$), $P < 0.001$) than LT recipients with a primary diagnosis of non-COVID ARDS (Table 1). COVID-19 LT recipients had higher body mass indices at time of listing than did non-COVID 19 ARDS LT recipients (median 27.1 IQR [24.4-30.6] vs 25.4 [20.9-28.6]; $P < 0.01$) (Table 1). LT recipients with a diagnosis of COVID-19 ARDS were less frequently dependent on ECMO at listing (51% ($n = 171$) vs 83% ($n = 53$); $P < 0.001$) and at transplant (56% ($n = 196$) vs 80% ($n = 51$); $P < 0.001$) than were non-COVID-19 ARDS LT recipients (Table 1).

Pre-Transplant Clinical Variables

LT recipients with a primary diagnosis of COVID-19 had a slightly improved functional status at listing ($P < 0.001$) and time of transplant ($P < 0.001$), and experienced slightly lower arterial pressures at transplant (median 25 mm Hg IQR [20-30] vs 36 [23-47]; $P < 0.001$) than did non-COVID-19 ARDS LT recipients (Table 2).

Perioperative Outcomes Data and Short-Term Survival

COVID-19 LT recipients were less frequently reliant on ECMO at 72 hours after transplant (26% ($n = 80$) vs 31% ($n = 15$), $P < 0.001$) and were less frequently dependent on dialysis post-transplant than non-COVID-19 ARDS LT recipients (14% ($n = 43$) vs 23% ($n = 14$); $P = 0.01$) (Table 3).

Of the ARDS LT recipients, 63 patients were eligible for the 30-day survival analysis, and 60 patients were eligible for the 90-day survival analysis. Rates of follow-up for the ARDS LT recipients at 30 days and 90 days post-transplant were 95% ($n = 60$) and 100% ($n = 60$); survival at 30 days was 93% ($n = 56$), and survival at 90 days was 90% ($n = 54$) (Table 3, Fig. 4).

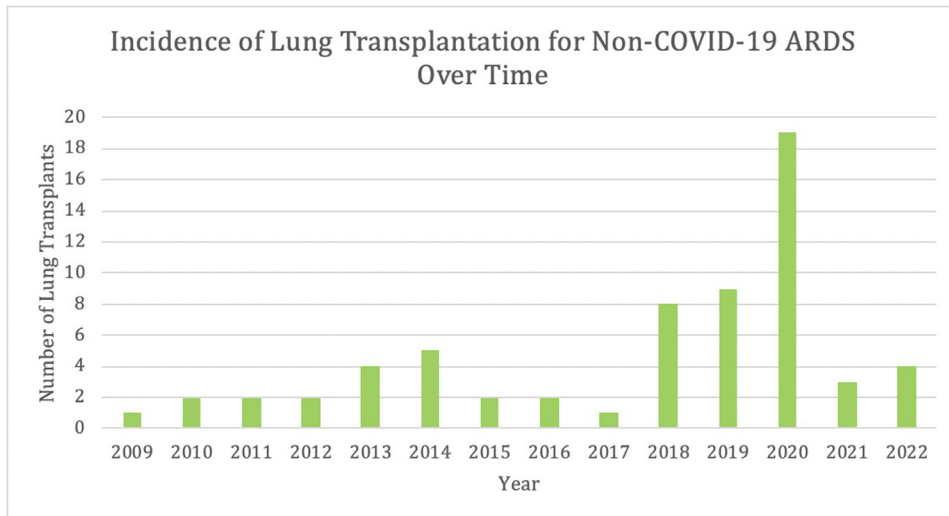


Figure 2. Incidence of lung transplantation for non-COVID-19 acute respiratory distress syndrome (ARDS) over time. The incidence of lung transplantation for non-COVID-19 ARDS increased substantially in 2018 and 2019, and peaked in 2020.

Of the COVID-19 LT recipients, 339 patients were eligible for the 30-day survival analysis, and 288 patients were eligible for the 90-day survival analysis. Rates of follow-up for the COVID-19 LT recipients at 30 days and 90 days post-transplant were 83% ($n = 281$) and 74% ($n = 214$); survival at 30 days was 97% ($n = 273$), and survival at 90 days was 94% ($n = 202$) (Table 3, Fig. 4, Fig. 5, Video Abstract).

Survival at 90 days post-transplant was not statistically significantly different between the non-COVID-19 ARDS and COVID-19 LT recipients ($P = 0.17$) (Fig. 4).

DISCUSSION

Using a national transplant database we identified 353 patients with COVID-19 who received lung transplants from August 16, 2020 to March 31, 2022. Of these patients, 61% presented with a primary diagnosis of COVID-19 ARDS, 37%

with a primary diagnosis of COVID-19 fibrosis, and 2% with nondescript COVID-19 indications. This analysis sought to compare descriptive characteristics, pre-operative clinical variables, and perioperative and short-term outcomes of non-COVID-19 ARDS and COVID-19 LT recipients.

We found that COVID-19 LT recipients were older, more predominantly male, had a better functional status, and were less frequently dependent on ECMO at the time of listing and transplant than their ARDS counterparts. The discrepancy in age and gender in the ARDS and COVID-19 LT recipients is likely a consequence of the differential baseline characteristics of critically-ill ARDS and COVID-19 patients, and is in agreement with prior literature. A previous study comparing COVID-19 ARDS and non-COVID-19 ARDS patients receiving mechanical ventilation similarly found that COVID-19 ARDS patients were slightly older and more predominantly male than

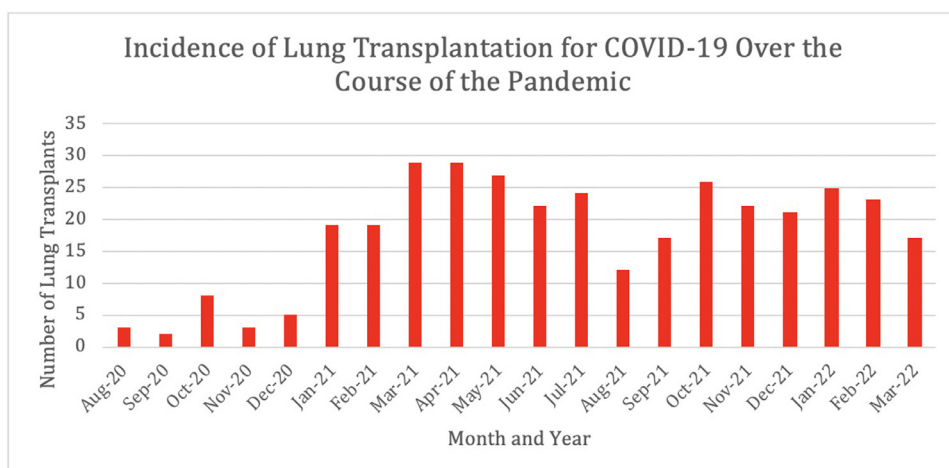


Figure 3. Incidence of lung transplantation for COVID-19 over the course of the pandemic. The incidence of lung transplantation for COVID-19 was highest in March and April of 2021.

Table 1. Descriptive Characteristics and Dependence on Ventilation/ECMO, Non-COVID-19 ARDS vs All COVID-19 Patients

Characteristic, n (%)	Non-COVID-19 ARDS Patients (N = 64)	COVID-19 Patients (N = 353)	P-value
Recipient age at listing in y, median (IQR)	41 (26-52)	51 (40-57)	<0.001*
Recipient female gender	29 (45)	79 (22)	<0.001*
Race			
White	33 (52)	183 (52)	0.97
Black	9 (14)	29 (8)	0.13
Hispanic	16 (25)	110 (31)	0.32
Other	22 (34)	141 (40)	0.40
Recipient BMI, median (IQR)	25.4 (20.9-28.6)	27.1 (24.4-30.6)	<0.01*
Previous malignancy	3 (5)	20 (6)	0.75
Diabetic	11 (17)	81 (23)	0.31
Recipient history of cigarette use	13 (20)	84 (24)	0.54
Recipient prior cardiac surgery (non-transplant)	3 (5)	8 (2)	0.49
Initial calculated lung allocation score, median (IQR)	87.6 (79.3-89.4)	87.0 (64.9-89.6)	0.95
Lung allocation score at transplant, median (IQR)	88.6 (86.5-90.0)	88.0 (79.1-90.3)	0.30
Patient on ventilator support at transplant	33 (52)	164 (46)	0.45
Recipient ECMO at listing	53 (83)	179 (51)	<0.001*
Recipient on life support ECMO at transplant	51 (80)	196 (56)	<0.001*
Pre-transplant tracheostomy	28 (46)	135 (42)	0.58
Type of transplant			0.36
Double	61 (95)	325 (92)	
Single	3 (5)	28 (8)	

BMI, body mass index; ECMO, extracorporeal membrane oxygenation.

*Significant at $P < 0.05$.

non-COVID-19 ARDS counterparts.²⁶ Another study identified older age as a risk factor for the development of COVID-19 ARDS,²⁷ possibly contributing to this difference in age between the LT patient cohorts. The worsened functional status of non-COVID-19 ARDS patients at the time of listing and transplant is likely a consequence of the chronicity of COVID-19 ARDS, with non-COVID-19 ARDS patients having a longer disease

course and COVID-19 patients having more acute to sub-acute symptoms.

We report slight differences in the post-operative course of COVID-19 and non-COVID19 ARDS LT recipients within the context of overall similar post-operative length of hospitalization. COVID-19 patients were less frequently dependent on ECMO 72 hours post-transplant, and on dialysis post-

Table 2. Pre-Transplant Clinical Variables, Non-COVID-19 ARDS vs All COVID-19 Cohorts

Characteristic, n (%)	Non-COVID-19 ARDS Patients (N = 64)	COVID-19 Patients (N = 353)	P-value
Recipient functional status at time of listing (Karnofsky Scale)			
10% - Moribund, fatal processes progressing rapidly	20 (31)	41 (12)	<0.001*
20% - Very sick, hospitalization necessary: active treatment necessary	28 (44)	189 (54)	
Other	16 (25)	122 (35)	
Recipient functional status at transplant (Karnofsky Scale)			<0.001*
10% - Moribund, fatal processes progressing rapidly	30 (49)	41 (13)	
20% - Very sick, hospitalization necessary: active treatment necessary	22 (36)	176 (55)	
Other	9 (14)	104 (30)	
Total d on waiting list (including inactive time), median (IQR)	7.0 (4.0-29.5)	11.0 (6.0-26.0)	0.05
Recipient pre-transplant dialysis - since listing	4 (7)	15 (5)	0.06
Number of recipients receiving transfusions - since listing	28 (46)	123 (38)	0.02*
Donor age in y, median (IQR)	32 (24-49)	33 (24-43)	0.53
Recipient pulmonary arterial pressure mm Hg at transplant, median (IQR)	36 (23-47)	25 (20-30)	<0.001*
Ischemic time in h, median (IQR)	5.3 (5.0- 6.7)	5.8 (5.0-6.9)	0.33

*Significant at $P < 0.05$.

Table 3. Perioperative Outcomes Data, Non-COVID-19 ARDS vs All COVID-19 Cohorts

Characteristic, n (%)	Non-COVID-19 ARDS Patients (N = 64)	COVID-19 Patients (N = 353)	P-value
Recipient ECMO at 72 h After Transplant	15 (31)	80 (26)	<0.001*
Length of stay Tx to discharge in d, median (IQR)	32.0 (22.0-53.0)	26.0 (18.0-45.0)	0.08
Recipient stroke post-transplant	1 (2)	7 (2)	0.71
Recipient dialysis post-transplant	14 (23)	43 (14)	0.01*
Patients eligible for 30 d survival analysis	63	339	
Patients with available 30 d survival data	60 (95)	281 (83)	
Patients alive at 30 d post-transplant	56 (93)	273 (97)	0.30
Patients eligible for 90 d survival analysis	60	288	
Patients with available 90 d survival data	60 (100)	214 (74)	
Patients alive at 90 d post-transplant	54 (90)	202 (94)	0.17

ECMO, extracorporeal membrane oxygenation.

*Significant at $P < 0.05$.

operatively. Though COVID-19 impacts multiple organ systems,^{28,29} the more rapid onset and progression of COVID-19 is likely responsible for the increased post-operative stability of COVID-19 LT recipients, relative to non-COVID-19 ARDS counterparts. Similar post-operative hospital stays to non-COVID-19 ARDS LT recipients suggest that the mild differences in post-operative courses in the 2 patient cohorts did not significantly impact post-transplant recovery. Though limited follow-up data exists for the COVID-19 LT recipients, the available data revealed a high 90-day survival of 94% for this patient cohort, indicating stable post-transplant recovery of COVID-19 LT recipients. Moreover, post-transplant survival among COVID-19 LT recipients was comparable to that of non-COVID-19 ARDS LT recipients.

This analysis has several limitations. Firstly, the retrospective nature of this database is susceptible to selection bias and does not allow for causal inference. In this study, ARDS lung transplant cases were collected from 2009 to 2022. It is likely that changes in technique/care made over this time period could have biased our findings. Additionally, while the patients in the non-COVID ARDS cohort experienced the same disease pathology, subclassifications between COVID-19 ARDS and COVID-19 fibrosis were up to the discretion of the individual centers, and could have added heterogeneity to our COVID-19 cohort and confounded our findings. Further, COVID-19 diagnosis codes were only activated in October 2020 in the transplant database.²⁴ It is possible that some initial COVID-19 transplants were captured as ARDS cases, as emphasized by the

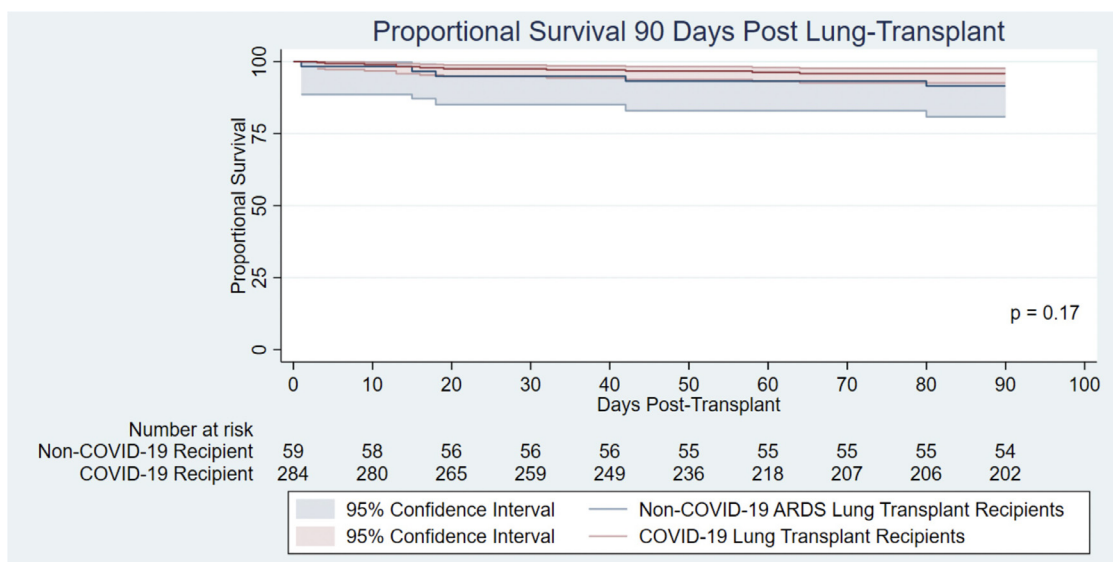


Figure 4. Proportional survival post lung-transplant. Proportional survival following lung transplant is graphed in blue for lung transplant recipients with a diagnosis of non-COVID-19 Acute Respiratory Distress Syndrome. The shaded blue region represents the 95% Confidence Interval. Proportional survival following lung transplant is graphed in red for lung transplant recipients with a diagnosis of COVID-19. The shaded red region represents the 95% Confidence Interval. Survival 90-days post-transplant is not statistically significantly different for the 2 patient cohorts ($P = 0.17$). (Color version of figure is available online.)

Lung Transplantation in Patients with COVID-19: The Early National Experience

Florissi et al.

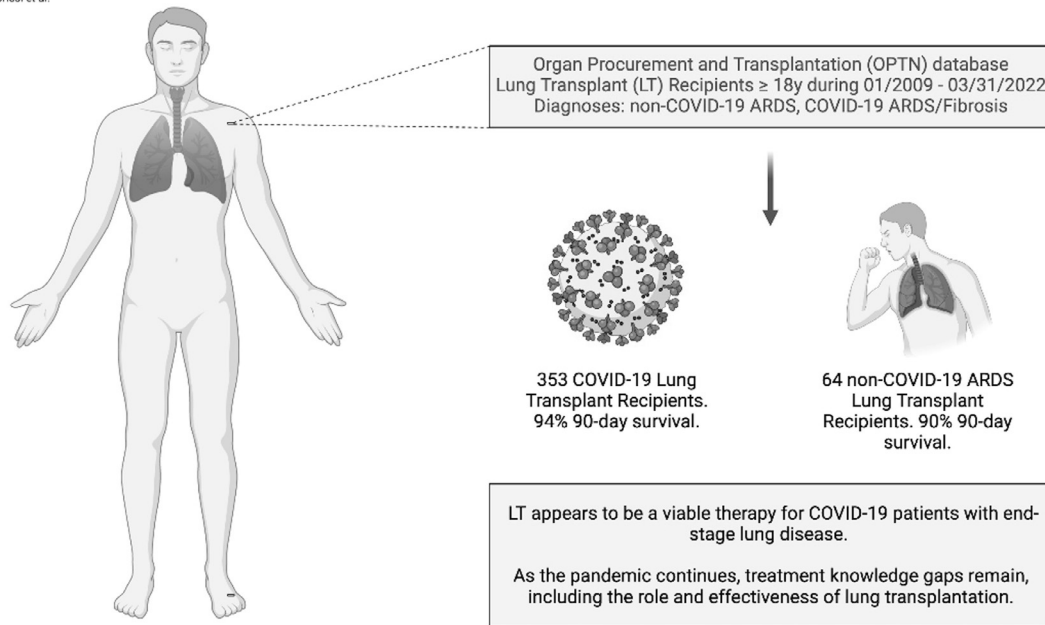


Figure 5. Graphical abstract- lung transplantation in patients with COVID-19, the early national experience.

sudden surge in waitlist candidates with a diagnosis of ARDS in 2020¹⁹ and by the uptick in incidence of LT for ARDS in 2020, as compared to previous years. In fact, while the first recorded LT for COVID-19 ARDS was performed on June 5, 2020,¹³ the first LT for COVID-19 in our cohort was performed on August 16, 2020. Additionally, the small cohort size and incompleteness of some variables might also bias our analyses. Similarly, the follow-up data for this study was limited.

Despite these limitations, our study comes at an important time. Recent reports have found that approximately 10% of current lung transplants have been administered as therapy for COVID-19, thus highlighting the importance of studies such as this project that elucidate the outcomes of LT in a high-risk population that may be preventable by vaccination.³⁰ Though the increased demand for double lung transplants in the setting of COVID-19 has raised concern for an increasing gap between the demand and supply for transplantable organs, our short-term data suggests that LT is a viable therapy for COVID-19 patients with sequelae refractory to conventional care.

CONCLUSION

Limited short-term data from April 2020 to March 31, 2022 for 353 patients who received lung transplants due to disease processes stemming from COVID-19 indicate that LT is a viable therapy for COVID-19 refractory to conventional care. As the SARS-CoV-2 pandemic continues to affect patients and families worldwide, treatment knowledge gaps persist,

including the role and effectiveness of LT. Our data suggests that COVID-19 LT patients with evidence of irreversible lung damage are older, more predominantly male, and less severely functionally compromised at time of transplant than non-COVID-19 ARDS LT recipients, and that COVID-19 patients with irreversible lung damage have comparable post-transplant outcomes to non-COVID-19 ARDS patients. As the number of COVID-19 lung transplant patient's increases and longer term follow up data becomes available, the role of LT in COVID-19 will become better defined and more completely understood. Future studies with longer follow-up can add granularity in identifying the variables that may influence outcomes following LT in the setting of COVID-19.

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WEBCAST

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Lung Transplantation in Patients with COVID-19- the Early National Experience

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SUPPLEMENTARY MATERIAL

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DISCUSSION

AATS 2022 Annual Meeting

Lung transplantation in patients with COVID-19- the early national experience

Presenter: Ms. Isabella Florissi

Invited Discussant: Dr Konrad Hoetzenecker



Dr Konrad Hoetzenecker (Vienna, Austria): Thank you very much for allowing me to discuss this very interesting paper, and I'd like to thank you, Isabella, for providing me with your manuscript and your slides well in advance.

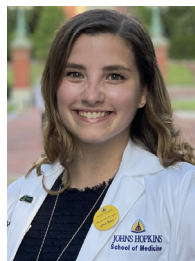
I'd like to congratulate you for this interesting study, because studies like this one are extremely important. Lung transplantation for COVID-19 is relatively new, and there are hardly any large-scale studies currently available. I remember the discussions we faced when we published our first case in Vienna, and there was, I can tell you, some fierce opposition against this practice from some of our colleagues. I have 3 questions, and I'll ask these separately. Based on the guidelines that were formulated by the 2 North American and the 2 European centers who first performed lung transplantation for COVID-19 acute respiratory distress syndrome (ARDS) back in 2020, we agreed that these patients should have exhausted all alternative treatment options and should have been treated by extracorporeal membrane oxygenation (ECMO) for at least 4-6 weeks before considering lung transplantation. So, I noticed that in the COVID cohort of the UNOS Database, there are 40% of patients who have not been on ECMO at the time of listing. I was wondering if you could comment on these patients. Is there anything that can be teased out of the database. What happened to these patients? Were they true ARDS patients? Yes or no?

Ms Isabella Soares Florissi (Baltimore, Maryland):

Yes. Thank you for your question. While we didn't look at the duration on ECMO before transplant, we noticed that 19 patients were taken off ECMO before receiving transplant while an additional 30 patients were initiated on ECMO before receiving transplant. So, it seems that while some patients were successfully weaned, others deteriorated clinically while awaiting transplant.

Dr Hoetzenecker:

Great. My second question relates to the complexity of the transplantation itself because, in the early days, we agreed that this type of transplantation should only be offered in centers who had sufficient experience in transplanting patients who were bridged for a prolonged period of time with ECLS to their transplantation. So, did you have a chance with over 300 patients in the database to look at the center volume effect?



Ms Florissi: Yes. These cases were performed across 53 centers with varying volume. The highest center performed 28 COVID lung transplants while 27 centers performed between 1 and 3 transplants, and the post-operative deaths that we noticed were few. There were 7 at 30 days and an additional 6 by 90 days, and we don't feel like we have enough information to study center volumes, but as center volumes continue to increase, we can establish these comparisons.

Dr Hoetzenecker:

Great. Hopefully, they won't increase. So, it's important once more to point out that the COVID group in your study is a very heterogeneous group of patients, right? And we know that COVID-19 ARDS - a true ARDS - is rare, and COVID-19 fibrosis patients might be miscoded as ARDS - even patients that were discharged from ICU, discharged from hospital but come back 6 months later with some type of lung fibrosis. So, those are 3 different disease entities, I guess. Could you comment on this in regard to your presentation?

Ms Florissi:

Yes. In previous iterations of our analysis, we had differentiated between COVID ARDS and COVID fibrosis patients, but we noticed that the distinction between these 2 diagnoses is up to the individual centers at which the case is performed, and there are no guidelines yet to determine when an ARDS case can be defined as fibrotic, so we were concerned that this bias would confound our results and chose instead to group these patients, but we acknowledge that it is a heterogeneous group of patients.

Dr Hoetzenecker:

Thank you. Once more, congratulations to this wonderful presentation. Thank you.