Should lung transplantation be performed for patients on mechanical respiratory support? The US experience

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Objective: The study objectives were to (1) compare survival after lung transplantation in patients requiring pretransplant mechanical ventilation or extracorporeal membrane oxygenation with that of patients not requiring mechanical support and (2) identify risk factors for mortality.

Methods: Data were obtained from the United Network for Organ Sharing for lung transplantation from October 1987 to January 2008. A total of 15,934 primary transplants were performed: 586 in patients on mechanical ventilation and 51 in patients on extracorporeal membrane oxygenation. Differences between nonsupport patients and those on mechanical ventilation or extracorporeal membrane oxygenation support were expressed as 2 propensity scores for use in comparing risk-adjusted survival.

Results: Unadjusted survival at 1, 6, 12, and 24 months was 83%, 67%, 62%, and 57% for mechanical ventilation, respectively; 72%, 53%, 50%, and 45% for extracorporeal membrane oxygenation, respectively; and 93%, 85%, 79%, and 70% for unsupported patients, respectively ($P < .0001$). Recipients on mechanical ventilation were younger, had lower forced vital capacity, and had diagnoses other than emphysema. Recipients on extracorporeal membrane oxygenation were also younger, had higher body mass index, and had diagnoses other than cystic fibrosis/bronchiectasis. Once these variables, transplant year, and propensity for mechanical support were accounted for, survival remained worse after lung transplantation for patients on mechanical ventilation and extracorporeal membrane oxygenation.

Conclusion: Although survival after lung transplantation is markedly worse when preoperative mechanical support is necessary, it is not dismal. Thus, additional risk factors for mortality should be considered when selecting patients for lung transplantation to maximize survival. Reduced survival for this high-risk population raises the important issue of balancing maximal individual patient survival against benefit to the maximum number of patients. (J Thorac Cardiovasc Surg 2010;139:765-73)

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Patients at the extreme of pulmonary failure who progress to respiratory failure and require respiratory support with mechanical ventilation or extracorporeal membrane oxygenation (ECMO) before lung transplantation (LTx) receive the highest priority for LTx by lung allocation score (LAS).¹

However, they seem to be at high risk for early postoperative mortality and organ wastage.²⁻⁴ Few publications describe the outcomes of this debilitated group of patients, with most focusing on those with cystic fibrosis⁵⁻¹¹; further, no single center has a large experience. Therefore, we queried the United Network for Organ Sharing registry to (1) identify factors predisposing patients to ventilatory support, (2) assess the impact of preoperative support on outcome after LTx, and (3) isolate risk factors for mortality that might help identify supported patients most likely to benefit from LTx.

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PATIENTS AND METHODS

Patients

From October 16, 1987, to January 1, 2008, 15,934 primary lung transplants were performed in the United States. Of these, 586 patients were on mechanical ventilation and 51 patients were on ECMO at the time of transplant. Age ranged from less than 1 year to 81 years, with a mean of 38 ± 21 years for the mechanical ventilation group, 39 ± 22 years for the ECMO group, and 48 ± 14 years for the unsupported group. Recipient, donor, and follow-up data were obtained from the United Network for Organ Sharing database. This registry includes compulsory data required by Organ Procurement and Transplantation Network policy and is audited continuously for accuracy.

Abbreviations and Acronyms

ECMO = extracorporeal membrane oxygenation

LAS = lung allocation score

LTx = lung transplantation

Follow-up

Median follow-up for all survivors was 2.9 years for those on mechanical ventilation, 2.0 years for those on ECMO, and 3.0 years for unsupported patients. Five percent of mechanically ventilated patients were followed more than 11 years, 5% of patients on ECMO were followed for more than 4 years, and 5% of unsupported patients were followed for more than 11 years.

Data Analysis**Factors predisposing patients to ventilatory support.**

Parsimonious models were developed to identify factors predisposing patients to mechanical ventilatory support and ECMO using bagging for variable selection.¹² Variables considered were only recipient variables related to demographics, diagnosis, lung function, pulmonary support, comorbidities, and serology (Appendix I). Sporadic missing values were replaced by 5-fold multiple imputation.¹³

Because the mechanical ventilation, ECMO, and unsupported groups differed in a number of characteristics (Tables 1 and 2), 2 propensity scores were developed by amplifying these parsimonious models into propensity models for risk-adjusted outcome comparison of mechanically ventilated versus unsupported patients and ECMO versus unsupported patients using polytomous logistic regression analysis.¹⁴ New variables added to the model are listed in Appendix 1. Propensity scores were then computed for each patient for use in matching and multivariable covariate adjustment of outcomes. A greedy matching algorithm¹⁵ was used to identify 566 unsupported patient matches for the 586 mechanically ventilated patients and 49 matches for the 51 patients on ECMO. The 22 unmatched supported patients were, in general, pediatric recipients (Table E1).

Outcome comparison. The 2 end points were retransplantation and death. Nonparametric estimates of freedom from retransplantation and survival were obtained by the Kaplan–Meier method, and parametric estimates were obtained by multiphase hazard modeling that resolved the number of phases of instantaneous risk of death (hazard function).¹⁶ (For additional details, see <http://www.clevelandclinic.org/heartcenter/hazard>.) Because both events were found to have an early high-risk phase and a later lower-risk phase, both unadjusted and risk-adjusted comparisons were made according to hazard phase.

Survival value of LTx for various combinations of risk factors for mortality in conjunction with mechanical ventilation or ECMO was explored by constructing nomograms from the multivariable risk factor analyses. The focus was on predicted 5-year survival according to certain risk factors, with others held constant.

Data Presentation

Continuous variables are summarized by mean $\pm$ standard deviation except for skewed variables, which are summarized by equivalent 15th, 50th (median), and 85th percentiles. Categorical data are summarized by frequency and percentage. All analyses were performed using SAS statistical software (SAS v9.1; SAS, Inc, Cary, NC). Survival estimates and hazard ratios are accompanied by 68% confidence limits equivalent to ± 1 standard error.

RESULTS**Factors Predisposing Patients to Ventilatory Support**

Younger patients who had poor pulmonary function, high oxygen requirement, and poor renal function, and who were considered more recently for LTx, were the most likely to receive ventilatory support, either by mechanical ventilation (Table 3) or ECMO (Table 4). These were moderately strong predictors, with C-statistics of .75 and .79, respectively. Figure 1 portrays some of these univariably.

TABLE 1. Lung transplant recipient and donor characteristics, details of transplantation, and in-hospital posttransplant events in ventilatory-supported and unsupported patients (categorical variables)

Variable	Mechanical ventilation (n = 586)		ECMO (n = 51)		Unsupported (n = 15,297)	
	n*	No. (%)	n*	No. (%)	n*	No. (%)
Recipient						
Demographic						
Female	586	284 (48)	51	26 (51)	15,297	7483 (49)
Diagnosis						
COPD/emphysema/alpha-1 antitrypsin deficiency	586	114 (19)	51	15 (19)	15,297	6960 (45)
Idiopathic pulmonary fibrosis	586	150 (26)	51	14 (27)	15,297	3369 (22)
Cystic fibrosis/bronchiectasis	586	166 (28)	51	6 (12)	15,297	2752 (18)
Sarcoidosis	586	25 (4.3)	51	1 (2)	15,297	417 (2.7)
Pulmonary arterial hypertension	586	28 (4.8)	51	5 (9.8)	15,297	731 (4.8)
Eisenmenger syndrome	586	7 (1.2)	51	0 (0)	15,297	176 (1.2)
Other	586	96 (16)	51	10 (20)	15,297	892 (5.8)
Surgical						
Double lung transplant	586	442 (76)	51	29 (57)	15,297	7481 (49)
Donor						
Female	586	267 (46)	51	21 (41)	15,297	5743 (38)
Smoker: >20 pack-y	500	104 (21)	42	7 (17)	13,057	3200 (25)

COPD, Chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation. *Patients with data available.

TABLE 2. Lung transplant recipient and donor characteristics, details of transplantation, and in-hospital posttransplant events in ventilatory-supported and unsupported patients (continuous variables)

Variable	Mechanical ventilation (n = 586)		ECMO (n = 51)		Unsupported (n = 15,297)		P
	n*	Mean ± SD or 15th/50th/ 85th percentiles	n*	Mean ± SD or 15th/50th/ 85th percentiles	n*	Mean ± SD or 15th/50th/ 85th percentiles	
Recipient							
Demographic							
Age (y)	586	38 ± 21	51	39 ± 22	15,297	48 ± 14	<.0001
BMI (kg/m ²)	529	23 ± 5.3	42	25 ± 4.9	14,839	24 ± 4.8	<.0001
Pulmonary function							
O ₂ requirement at rest (L/min)	433	1/3/10	43	0/2.5/10	11,843	0/2/4	<.0001
FEV ₁ (% of predicted)	453	34 ± 20	38	35 ± 21	13,975	34 ± 21	.3
FVC (% of predicted)	450	45 ± 17	39	52 ± 23	13,927	50 ± 18	<.0001
Hemodynamics							
Cardiac output (L/min)	266	5.4 ± 1.6	22	5.5 ± 1.3	8692	5.3 ± 1.5	.2
Mean P _{PA} (mm Hg)	294	30 ± 13	23	32 ± 12	9234	28 ± 13	<.0001
Creatinine (mg/dL)	521	0.8 ± 0.6	44	1.0 ± 0.4	13,227	0.9 ± 0.6	<.0001
LAS	221	54 ± 22	16	54 ± 21	3302	40 ± 11	<.0001
Surgical							
Maximum lung ischemic time (min)	491	285 ± 120	47	294 ± 110	13,559	277 ± 100	.05
Hospital stay (d)	404	11/26/66	38	9/24/55	9568	9/15/34	<.0001
Donor							
Age (y)	585	30 ± 18	51	26 ± 16	15,289	31 ± 14	.05
BMI (kg/m ²)	488	24 ± 5.4	42	25 ± 5.1	13,582	24 ± 4.5	.03

BMI, Body mass index; ECMO, extracorporeal membrane oxygenation; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; LAS, lung allocation score; PPA, pulmonary artery pressure; SD, standard deviation. *Patients with data available.

Survival Comparison

In addition to longer length of stay (Table 2), mechanical ventilation and ECMO were associated with reduced survival, particularly early after LTx. Unadjusted survival

at 1, 6, 12, and 24 months was 83%, 67%, 62%, and 57% for mechanical ventilation, respectively; 72%, 53%, 50%, and 45% for ECMO, respectively; and 93%, 85%, 79%, and 70% for unsupported patients, respectively

TABLE 3. Factors predisposing patients to mechanical ventilation

Factor	Coefficient ± SE	P	Reliability (%)*
Younger age†	0.47 ± 0.12	<.0001	83
Lower weight‡	0.13 ± 0.04	.0004	80
Lower FVC (% of predicted)§	0.43 ± 0.15	.01	60
Higher oxygen requirement at rest (L/min)	0.07 ± 0.01	<.0001	100
Creatinine (mg/dL)			
Higher creatinine¶	0.60 ± 0.15	<.0001	89
Higher creatinine**	0.53 ± 0.20	.008	89
Date of transplant (y)			
Later date††	1.52 ± 0.46	.001	99
Earlier date‡‡	-2.09 ± 0.70	.003	99
COPD/emphysema/alpha-1 antitrypsin deficiency	-0.66 ± 0.12	<.0001	99

COPD, Chronic obstructive pulmonary disease; FVC, forced vital capacity; SE, standard error. C-statistic = .75. *Percent of time factor appeared in 500 bootstrapped models. †Ln(age), logarithmic transformation. ‡(80/weight), inverse transformation. §Ln(FVC), logarithmic transformation. ||(Oxygen/2.7)², squared transformation. ¶(0.8/creatinine), inverse transformation. **Ln(creatinine), logarithmic transformation. ††Exp(transplant date|years since 1/1/1987|10), exponential transformation. ‡‡(Transplant date |years since 1/1/1987|10)², squared transformation.

TABLE 4. Factors predisposing patients to extracorporeal membrane oxygenation

Factor	Coefficient ± SE	P	Reliability (%)*
Age			
Younger age	-0.13 ± 0.03	<.0001	98
Older age†	2.42 ± 1.14	.03	98
Higher BMI‡	1.09 ± 0.50	.03	62
Cystic fibrosis/bronchiectasis	-1.30 ± 0.51	.01	71
Lower FEV ₁ (% of predicted)§	0.87 ± 0.23	.0003	55
Higher oxygen requirement	0.07 ± 0.02	.0001	79
Creatinine			
Lower creatinine¶	0.08 ± 0.02	.001	84
Higher creatinine**	0.96 ± 0.32	.003	84
More recent date of transplant††	0.35 ± 0.08	<.0001	98

BMI, Body mass index; FEV₁, forced expiratory volume in 1 second; SE, standard error. C-statistic = .79. *Percent of time factor appeared in 500 bootstrapped models. †(Age/50)², squared transformation. ‡(40/BMI), inverse transformation. §Ln(FEV₁), logarithmic transformation. ||(Oxygen/2.7)², squared transformation. ¶(0.8/creatinine)², inverse squared transformation. **Ln(creatinine), logarithmic transformation. ††Exp(transplant date |years since 1/1/1987|10), exponential transformation.

FIGURE 1. Relationship of lung transplant variables to the probability of requiring ventilatory support. *Filled circles* are averages within quintiles, and *solid lines* enclosed within 68% confidence limits show the loss estimate. **A.** Factors predisposing patients to mechanical ventilation. **B.** Factors predisposing patients to ECMO. *FVC*, forced vital capacity (expressed as percent of predicted); *FEV₁*, forced expiratory volume in 1 second (expressed as percent of predicted).

(Figure 2). These effects of mechanical ventilation and ECMO on survival persisted among propensity-matched patients (Figure 3). After adjustment for propensity score, the hazard ratio was 1.49 (68% confidence limits, 1.39–1.58; $P < .0001$) for mechanically ventilated patients compared with unsupported patients in the early hazard phase and 2.55 (68% confidence limits, 2.09–3.12; $P < .0001$) for patients on ECMO compared with unsupported

patients. After the high-risk early phase, survival of patients on ECMO was similar to that of unsupported patients, with hazards converging at approximately 9 months (Figure 2, B).

Risk Factors for Death

Preoperative mechanical ventilation and ECMO were strong risk factors for mortality after LTx in the multivariable analysis (Table 5). These were additive to other risk

FIGURE 2. Unadjusted mortality after LTx stratified by pretransplant requirement for ventilatory support. A, Survival. Each symbol represents a death; vertical bars are 68% confidence limits representing ± 1 standard error, and numbers in parentheses are patients remaining at risk. Solid lines are parametric estimates enclosed within dashed confidence limits. B, Hazard function (instantaneous risk) for death. Point estimates for each group are enclosed within 68% confidence limits. ECMO, Extracorporeal membrane oxygenation.

factors, including older recipient age (Figure 4), pulmonary arterial hypertension, lower pretransplant forced expiratory volume in 1 second, and longer ischemic time. There was no interaction identified between these other risk factors and mechanical ventilation or ECMO.

Retransplantation Comparison

Of 15,934 transplant recipients, 512 underwent retransplantation. There were 21, 4, and 487 retransplants in the mechanical ventilation, ECMO, and unsupported groups, respectively. In the mechanical ventilation group, the first retransplant occurred 3 days posttransplant. The first retransplant in the ECMO group was 9 days after primary transplant, and in the unsupported group, 4 patients underwent retransplantation within 1 day. Freedom from retransplant at 1 year was 97%, 91%, and 99% for the mechanical ventilation, ECMO, and unsupported groups, respectively (ECMO, $P = .06$; mechanical ventilation, $P = .9$) (Figure 5).

FIGURE 3. Survival for propensity-matched patients. A, Preoperative mechanical ventilation versus unsupported groups. B, ECMO versus unsupported groups. Format is as in Figure 2. ECMO, Extracorporeal membrane oxygenation.

DISCUSSION

Historically, transplant surgeons and pulmonologists have been reluctant to recommend LTx for patients on mechanical respiratory support.¹⁷⁻¹⁹ The prevailing sentiment was that these patients had become too sick and were no longer in the “transplant window”²⁰ because survival after LTx was unlikely.^{18,21} However, LTx has been performed selectively on supported patients and reported in a few small case series.^{11,22} The newly adopted LAS places a particular focus on these patients. Need for continuous mechanical ventilation is a heavily weighted factor in the LAS model (see http://www.unos.org/resources/frm_LAS_Calculator.asp?index=98). Patients requiring mechanical support in the United States now receive the highest LAS scores and have the greatest likelihood of undergoing transplantation, in part because of this weighting.³ To better understand the outcomes of these patients, this study evaluated all patients requiring mechanical support before LTx in the United States from 1987 to 2007. LTx was uncommon for patients on mechanical ventilation and extremely rare for those on ECMO. Most patients undergoing transplantation from mechanical ventilation or ECMO underwent operation in

TABLE 5. Incremental risk factors for death

Factor	Coefficient ± SE	P	Reliability (%)*
Early hazard phase			
Recipient			
ECMO at transplant	1.87 ± 0.24	<.0001	78
ECMO propensity score†	-0.12 ± 0.05	.02	
Mechanical ventilation at transplant	1.10 ± 0.11	<.0001	100
Mechanical ventilation propensity score†	0.39 ± 0.06	<.0001	
Older age	0.015 ± 0.003	<.0001	96
High weight/height ratio	2.11 ± 0.39	<.0001	98
COPD/emphysema/ alpha-1 antitrypsin deficiency	-0.37 ± 0.1	.0002	100
Pulmonary arterial hypertension	0.97 ± 0.12	<.0001	100
Cystic fibrosis/ bronchiectasis	-0.28 ± 0.12	.02	100
Eisenmenger syndrome	0.99 ± 0.17	<.0001	100
Higher serum creatinine	0.70 ± 0.12	<.0001	100
Lower serum creatinine‡	-0.033 ± 0.01	.0007	100
Lower FEV ₁ (% of predicted)	0.005 ± 0.002	.008	82
Longer ischemic time§	0.076 ± 0.02	<.0001	97
Year of transplant	-0.38 ± 0.04	<.0001	100
Year of transplant¶	0.18 ± 0.03	<.0001	100
Donor			
Older age**	0.095 ± 0.02	<.0001	76
Higher weight	0.009 ± 0.002	<.0001	92
Non-Caucasian	0.32 ± 0.08	.01	99
Living vs cadaveric	0.91 ± 0.19	<.0001	97
Head trauma as cause of death	0.23 ± 0.07	.001	78
Constant hazard phase			
Recipient			
ECMO at transplant	-0.39 ± 0.60	.7	20
ECMO propensity score†	-0.042 ± 0.01	.03	
Mechanical ventilation at transplant	-0.11 ± 0.12	.4	18
Mechanical ventilation propensity score†	0.006 ± 0.04	.9	
Younger age	-0.059 ± 0.01	<.0001	100
Older age††	1.87 ± 0.18	<.0001	100
Greater body surface area‡‡	0.52 ± 0.10	<.0001	86
Pulmonary arterial hypertension	-0.21 ± 0.07	.003	97
Diabetes	0.20 ± 0.05	<.0001	94
Oxygen requirement§§	0.018 ± 0.006	.001	98
Shorter ischemic time§	-0.039 ± 0.01	.005	94
Longer ischemic time	-0.010 ± 0.004	.02	94
Single lung transplant	0.21 ± 0.03	<.0001	100
Donor			
Non-Caucasian	0.11 ± 0.03	.0002	90

TABLE 5. Continued

Factor	Coefficient ± SE	P	Reliability (%)*
Smoker: >20 pack-y	0.10 ± 0.03	.002	63
Diabetic	0.29 ± 0.08	.0001	88
Anti-cytomegalovirus	0.14 ± 0.03	<.0001	100
Head trauma as cause of death	-0.081 ± 0.03	.003	65

COPD, Chronic obstructive pulmonary disease; *ECMO*, extracorporeal membrane oxygenation; *FEV₁*, forced expiratory volume in 1 second; *SE*, standard error. *Percent of time factor appeared in 500 bootstrapped models. †Expressed as logit. ‡(Creatinine/0.8)², squared transformation. §Exp(ischemic time/275), exponential transformation. ||(Transplant date [years since 1/1/1987]/10)², squared transformation. ¶(10/transplant date [years since 1/1/1987]), inverse transformation. **Exp(donor age/30), exponential transformation. ††(Age/50)², squared transformation. ‡‡(Body surface area), inverse transformation. §§(Oxygen/2.7)², squared transformation. |||(275/ischemic time)², inverse squared transformation.

recent years; their survival was considerably worse than that of patients not requiring mechanical support.

There were notable differences in recipient and transplant characteristics between the 2 groups. The most striking was that patients undergoing LTx while on mechanical support were considerably younger, more than a decade on average. This likely reflects the bias of treating physicians for accepting higher risk and attempting more extreme therapies in younger patients.²³ In addition, it might also reflect a belief that younger patients have greater functional reserve for withstanding a prolonged recovery. There were also differences in indications for LTx. Patients with emphysema were less likely and patients with cystic fibrosis were more likely to undergo transplantation from mechanical ventilation. The opposite finding held true for those on ECMO: Patients with cystic fibrosis were less likely to undergo transplantation, perhaps because of concerns over infectious complications. Patients undergoing LTx from mechanical support were more likely to undergo double LTx, although the reasons for this bias and the impact on posttransplant survival are unclear. Not surprisingly, postoperative length of stay was markedly longer for patients undergoing LTx on mechanical ventilation or ECMO than for unsupported patients.

Principal Findings

Survival. Patients supported preoperatively by mechanical ventilation or ECMO had markedly worse survival after LTx than those who did not require such support. This worse survival is not surprising. Patients requiring mechanical support before LTx are typically deconditioned from chronic progression to end-stage respiratory failure.^{24,25} Immobilization combined with corticosteroids causes rapid skeletal muscle wasting.²⁶ Even brief periods of mechanical support cause diaphragmatic weakness, critical to recovery after LTx.²⁷ Weaning from the ventilator after operation becomes more difficult, and delayed ambulation increases susceptibility to complications such as nosocomial pneumonia and thromboembolism.²⁸

FIGURE 4. Five-year survival after LTx according to recipient age. This is a nomogram of the multivariable equation in Table 5. Except for variables depicted, values for other risk factors were set as follows: *Recipient*: body surface area = 1.8 m², weight/height ratio = 0.4, pulmonary arterial hypertension, FEV₁ = 35%, oxygen requirement = 2.7 (L/min), nondiabetic, creatinine = 0.89 mg/dL, transplant year = 2007. *Donor*: age = 30 years, weight = 72 kg, head trauma as cause of death, nonsmoker, nondiabetic. *ECMO*, Extracorporeal membrane oxygenation.

The increase in mortality was evident only in the early phase after LTx. Patients surviving the first 6 months had comparable long-term survival to those not requiring preoperative mechanical support. This period of elevated risk likely represents prolonged recovery from surgery. There seems to be no lasting impact on survival after this recovery phase and no long-term injury to the graft.

For patients whose underlying pulmonary disease has progressed to respiratory failure, LTx is most likely the only hope for survival.²⁹ The LAS model was designed to balance individual waitlist urgency (likelihood of survival within 1 year without LTx) with expected posttransplant survival (likelihood of survival at 1 year after LTx).³ The results of our study support the validity of the LAS. Although survival is markedly reduced in this high-risk population, LTx is not futile.

Our study showed that patients on ECMO before LTx have the worst survival, even lower than that of patients on mechanical ventilation. Until now, there have been only a few reports on ECMO used as a “bridge to transplantation,” and they have demonstrated mixed results.³⁰⁻³⁶ Currently, ECMO is not a scoring factor in the LAS. Future consideration might be given to adding preoperative ECMO support as an LAS parameter on the basis of these data. Despite high mortality, our study shows that LTx for patients on preoperative ECMO can have successful outcomes.

Risk factors for mortality. In multivariable analysis, mechanical ventilation and ECMO were strong, independent risk factors for mortality after LTx. Others, including increased recipient age, older donors, pulmonary arterial hypertension, and longer ischemic time, have been well described.² However, there was no interaction among these

FIGURE 5. Freedom from retransplantation. *ECMO*, Extracorporeal membrane oxygenation.

risk factors and mechanical ventilation or ECMO. This points to a logical strategy for patient selection. Because mechanical ventilation and ECMO add important incremental risk to LTx, optimizing survival requires minimizing other known risk factors for mortality. Although some of these risk factors are modifiable, such as donor age and ischemic time, others, such as diagnosis and recipient age, are not.³⁷ These factors must be considered before proceeding with LTx and an objective decision made about the likelihood of success.

Retransplantation. In addition to survival, retransplantation is an important outcome after LTx. Retransplantation indicates severe graft failure resulting from immune and nonimmune-mediated injury and resultant organ loss.^{38,39} Prevalence of retransplantation among patients requiring preoperative mechanical ventilation or ECMO was higher than among unsupported patients. Patients receiving ECMO preoperatively had the highest prevalence of retransplantation. Clearly, mediators that negatively affect survival after LTx for mechanically supported patients also negatively affect graft survival and increase need for retransplantation.

Limitations. This study has the advantage of being able to compare survival using large numbers of patients, including a wide range of donor, recipient, and transplant variables. Its limitations include lack of data collection for detailed recipient factors, some of which may be important predictors of mortality in these patients. These include signs of infection (eg, fever or elevated white blood cell count), indicators of nutritional status (eg, albumin and prealbumin),^{40,41} and length of pre-LTx intubation time.¹¹ In addition, it does not consider the acute or chronic nature of respiratory decompensation or subjective factors, such as patient motivation and family support. Finally, some pretransplant patient data gathered before the LAS are difficult to compare with that gathered after the LAS, which requires continuously updated information with changes in a patient's clinical condition.

CONCLUSIONS

Although survival after LTx is worse when preoperative mechanical support is necessary, it is not dismal. Those surviving the initial period after LTx have long-term survival comparable to those not requiring mechanical support. Reduced survival for this high-risk population raises an important ethical issue: balancing maximal individual patient survival against benefit to the maximum number of patients.

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APPENDIX 1. Variables considered in analyses

Recipient

Demographics:

Age (y), weight (kg), height (cm), weight/height ratio, body surface area (m²), body mass index (kg/m²), gender, race

Diagnosis:

Idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease/emphysema + alpha-antitrypsin deficiency, primary arterial hypertension Eisenmenger syndrome, sarcoidosis, cystic fibrosis + bronchiectasis

Lung function:

FEV₁ % of predicted, FVC % of predicted

Support:

Oxygen requirement, mechanical ventilation, ECMO

Comorbidities:

Diabetes, smoking history, drug-treated hypertension, creatinine

Serology:

ABO blood groups, panel-reactive antibodies

Donor

Demographics:

Age (y), body mass index (kg/m²), gender, race

Type:

Cadaveric

Comorbidities:

Smoking history, diabetes, hypertension, creatinine, clinical infection

Cause of death:

Anoxia, head trauma, stroke

Serology:

ABO compatibility, cytomegalovirus antibodies

Surgical

Double LTx, ischemic time, year of transplantation

FEV₁, Forced expiratory volume in 1 second; *FVC*, forced vital capacity; *ECMO*, extracorporeal membrane oxygenation; LTx, lung transplantation.

TABLE E1. Characteristics of respiratory-supported recipients who were not propensity matched (n = 22)

Characteristic	n*	No. (%) or Mean $\pm$ SD
Age (mo)	22	12/12/29†
Female	22	12 (55)
African-American	22	3 (14)
Height (cm)	22	69 $\pm$ 24
Weight (kg)	22	8.3 $\pm$ 9.1
Body surface area (m ²)	22	0.40 $\pm$ 0.25
Body mass index (kg/m ²)	22	16 $\pm$ 4.5
Diagnosis		
Idiopathic pulmonary fibrosis	22	2 (9.1)
Primary arterial hypertension	22	3 (14)
Other‡	22	17 (77)
Oxygen requirement at rest (L/min ¹)	19	9.8 $\pm$ 2.5
Diabetes	21	1 (4.8)
Serum creatinine (mg/dL ¹)	21	0.39 $\pm$ 0.33

SD, Standard deviation. *Patients with data available. †15th, 50th, and 85th percentiles. ‡Chronic pneumonitis of infancy (1), surfactant protein B deficiency (1), other congenital (6), non-retransplant obliterative bronchiolitis (2), pulmonary arterial disease (1), secondary pulmonary hypertension (1), nonspecified (5).