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ORIGINAL RESEARCH

Association of Pulmonary Artery Pressure Change With Post-Lung Transplantation Survival

Retrospective Analysis of China Registry

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ABSTRACT

BACKGROUND Extracorporeal membrane oxygenation (ECMO) has been used as intraoperative hemodynamic support in patients with end-stage lung diseases and pulmonary hypertension undergoing lung transplantation (LT).

OBJECTIVES The aim of this study was to identify the association of pulmonary artery pressure change during ECMO and post-LT survival.

METHODS The study investigators collected and analyzed the data from Chinese Lung Transplantation Registry. Patients who have severe pulmonary hypertension with intraoperative ECMO support were enrolled. Post-LT mortality and morbidity were further collected and compared.

RESULTS A total of 208 recipients were included in the study, during which 53 deaths occurred post-LT. All the patients had severe pulmonary hypertension and were supported by intraoperative ECMO. Using eXtreme Gradient Boosting, or XGboost, model method, 20 variables were selected and ranked. Changes of mean pulmonary artery pressure at the time of ECMO support and ECMO wean-off (ΔmPAP) were related to post-LT survival, after adjusting for potential confounders (recipient age, New York Heart Association functional class status before LT, body mass index, pre-LT hypertension, pre-LT steroids, and pre-LT ECMO bridging). A nonlinear relationship was detected between ΔmPAP and post-LT survival, which had an inflection point of 35 mm Hg. Recipients with ΔmPAP ≦35 mm Hg had higher mortality rate calculated through the Kaplan-Meier estimator ($P = 0.041$). Interaction analysis showed that recipients admitted in LT center with high case volume (≥50 cases/year) and ΔmPAP >35 mm Hg had better long-term survival. The trend was reversed in recipients who were admitted in LT center with low case volume (<50 cases/year).

CONCLUSIONS The relationship between ΔmPAP and post-LT survival was nonlinear. Optimal perioperative ECMO management strategy with experienced team is further warranted. (JACC: Asia 2022;2:819-828) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

ECMO = extracorporeal membrane oxygenation

LT = lung transplantation

mPAP = mean pulmonary artery pressure

P/F ratio = ratio of arterial oxygen concentration to the fraction of inspired oxygen

PH = pulmonary hypertension

XGboost = eXtreme Gradient Boosting

Patients with end-stage lung disease always had group 3 pulmonary hypertension (PH), defined as a mean pulmonary artery pressure (mPAP) of >20 mm Hg at rest measured during right heart catheterization.[1] Patients with PH had worse survival.[2] PH in candidates for lung transplantation (LT) who have chronic obstructive pulmonary disease and pulmonary fibrosis ranged between 23%-84.3% and 31.4%-46.1%, respectively.[3,4] PH might lead to secondary right heart dysfunction and tricuspid valve regurgitation.[5] High pulmonary vascular resistance also elevated risk to require intraoperative extracorporeal support because of the risk of right heart failure as well as reduced oxygenation capacities in patients in critical condition.[6]

Prophylactic use of extracorporeal membrane oxygenation (ECMO) intraoperatively and prolonged in the postoperative period in patients with severe PH have been demonstrated to improve perioperative and long-term results in LT.[7] ECMO has been used as bridging and intraoperative hemodynamic support during LT. Pre-LT peripheral venovenous ECMO bridging could be switched to central venoarterial ECMO to further provide hemodynamic support.[8] It has been reported that patients with systolic PAP over 50 mm Hg using intraoperative ECMO support could have a change of mPAP around 37 mm Hg compared before and after ECMO support.[9] However, post-LT mortality rate was still high even though the patients have been supported with ECMO.[10,11] Thus, optimal ECMO support strategy in perioperative management is further needed, and impacting factors related to post-LT survival have not been fully illustrated.

In China, a high proportion of patients with end-stage lung diseases and severe PH have received bilateral LT with ECMO support.[12] Based on CLuTR (Chinese Lung Transplantation Registry) data, we have summarized and analyzed the data from patients with primary and secondary PH who are supported by perioperative ECMO. Factors possibly affecting long-term outcome were presented, and cutoff values of preoperative known hemodynamic indicators that may be associated with complications and survival were further explored.

METHODS

DATA SOURCE. Patients with severe PH, who received LT between January 1, 2016, and September 1, 2021, were enrolled, and their data were collected and further analyzed (Table 1). mPAP over 35 mm Hg was recognized as indicating the presence of severe PH.[5]

Data were collected from CLuTR, which enrolled recipients from all the LT centers in China. All patients' data were retrospectively reviewed. The Institutional Ethics Committee waived the need for further patient consenting to this study because all patients agreed to the use of their data for retrospective studies at the time of signing the informed consent to transplantation. Variables with more than 20% observations missing were not included to facilitate and ensure the accuracy of the review.

CLINICAL MANAGEMENT AND DATA COLLECTION. The indication for intraoperative cardiopulmonary support is usually confirmed on test clamping of the pulmonary artery before pneumectomy and implantation of the donor lung as well as after test clamping of the contralateral pulmonary artery for implantation of the second side.[6] Criteria of ECMO support followed the national guidelines and were reported elsewhere.[13] Retrospectively collected data included routine pretransplant variables, primary diagnoses indicating LT, duration of extracorporeal circulatory support during and after transplantation, as well as the length of stay in the intensive care unit and long-term survival outcome. In the registry data, difference of mPAP at time of ECMO support and ECMO wean-off (ΔmPAP) was recorded from invasive hemodynamic measurement (right heart catheterization). We further explored the association of ΔmPAP and post-LT survival. To select impact factors based on the variables collected from the registry, we performed eXtreme Gradient Boosting (XGboost) model[14] to analyze the contribution (gain) of each variable to long-term survival; variables were selected with a threshold of $P < 0.05$.[15]

STATISTICAL ANALYSIS. Patients were initially divided into 2 groups—dead or alive, and variables were displayed and compared between groups. Regression analysis to determine the impact of confounders on survival up to September 30, 2021, were performed. Categorical data were summarized as counts and percentages. Continuous variables were presented as median (IQR). One-way analysis of variance (normal distribution), Kruskal-Wallis *H* (skewed distribution) test, and chi-square test (categorical variables) were used to determine any significant differences between the means and proportions of the groups. The univariate regression model was used to evaluate the associations between ΔmPAP and survival outcome. According to the recommendation of the STROBE (Strengthening the Reporting of

Observational Studies in Epidemiology) statement, data of unadjusted, minimally adjusted, and fully adjusted analyses were further presented.[16] Covariates selected a priori based on guidance from International Society for Heart and Lung Transplantation models reported, clinical judgment, XGboost-based variables screening, and availability within the data set, as well as estimated variables change of at least 10% of potential confounding effects.[17] The survival function was plotted with the Kaplan-Meier estimator, and differences between groups were quantified by the log-rank test. Generalized additive models were used to identify nonlinear relationships between survival and ΔmPAP. After nonlinear correlation was observed, a 2-piecewise linear regression model was performed to calculate the threshold effect of the ΔmPAP on survival in terms of the smoothing plot. Recursive method further calculated the inflection point, where the maximum model likelihood will be used.[18] The modifications and interactions of subgroups were inspected by likelihood ratio tests. All of the analyses were performed with the statistical software package R (The R Foundation) and Empower-Stats (X and Y Solutions). *P* values <0.05 (2-sided) were considered statistically significant.

RESULTS

VARIABLE SELECTION AND BASELINE CHARACTERISTICS. A total of 208 patients were included in our study, including 155 survivors and 53 deaths up to the date we collected all the data. **Figure 1** is a flowchart describing the procedure for subject selection. As shown in Supplemental Figure 1, the most important features, identified by the results of XGboost analysis and strongly associated with mortality, included recipient age, mPAP at time of ECMO support, donor age, recipient ratio of arterial oxygen concentration to the fraction of inspired oxygen (P/F ratio), ΔmPAP, donor P/F ratio, ejection fraction, body mass index, creatinine, and LT center volume (<50 cases/year vs ≥50 cases/year). Comparisons of the baseline characteristics, vital signs, laboratory parameters between the nonsurvivors and the survivors based on the variables selected by XGboost were summarized in **Table 1**.

For patients with end-stage lung disease and severe PH, death occurred in recipients who were older ($P = 0.047$), were transplanted with grafts from older donors ($P = 0.007$), used steroids pre-LT ($P = 0.042$), were admitted to a less-experienced LT center with case volume <50 cases/year ($P = 0.010$), and had ΔmPAP ≦35 mm Hg ($P = 0.05$). No statistically significant difference was observed between groups of survivors and death for body mass index, diagnosis, admission status before LT, New York Heart Association functional class status before LT, proportion of pre-LT ECMO bridging, pre-LT hypertension, recipient or donor P/F ratio, pre-LT ejection fraction, pre-LT creatinine, LT type, intraoperative or post-LT ECMO mode, mPAP on listing, and mPAP at time of ECMO support. Significantly higher rate of heart failure occurrence, longer time of intensive care unit stay, and time on intubation post-LT were observed in the death group.

NONLINEAR ASSOCIATION BETWEEN ΔmPAP AND POST-LT SURVIVAL. We observed that death occurred more in patients with ΔmPAP ≦35 mm Hg during ECMO support. However, for those patients with higher ΔmPAP, extremely high mPAP before LT was also related to increased mortality. To explore whether the benefit brought by ECMO-supported mPAP would be compromised by high pre-LT mPAP level, we tentatively analyzed the nonlinear relationship between mPAP and survival probability. As demonstrated in Supplemental Figure 2A, a threshold effect was observed with sharp decrease of survival time. A further calculation showed inflection point was 35 mm Hg (**Table 2**) after adjusting for recipient age, New York Heart Association functional class status before LT, body mass index, pre-LT hypertension, pre-LT steroids, and pre-LT ECMO bridging. There was a positive association between ΔmPAP and post-LT survival on the right side of the inflection point ($P = 0.0139$). If further stratified by LT center experience, patients who received LT in a less-experienced center with <50 cases/year had shorter post-LT survival time, although ΔmPAP was increased (Supplemental Figure 2B). To further demonstrate the survival outcome, survival curves were plotted and compared (**Central Illustration**). -Patients with ΔmPAP ≦35 mm Hg had inferior long-term survival, compared to patients with ΔmPAP >35 mm Hg (log-rank $P = 0.041$).

UNIVARIATE AND MULTIVARIATE ANALYSES USING COX PROPORTIONAL-HAZARDS REGRESSION MODEL. The results of univariate analysis showed that donor age, pre-LT steroids use, pre-LT hypertension, low LT center case volume, pre-LT ECMO bridging, and ΔmPAP ≦35 mm Hg could be possibly related to post-LT morbidity ($P < 0.10$). LT center ≥50 cases/year, pre-LT ECMO bridging, and ΔmPAP >35 mm Hg had significant effects on post-LT survival ($P < 0.05$) (**Table 3**, Supplemental Table 1). The test for interactions for LT center case volume and ΔmPAP category was significant ($P = 0.0314$). The

TABLE 1 Baseline Characteristics of Recipients of LT

	Survival (n = 155)	Death (n = 53)	*P* Value
Recipient age, y	55 (46-62)	57 (50- 65)	0.047
Donor age, y	41.00 (30.25, 48.00)	47.00 (39.00- 51.50)	0.007
BMI, kg/m^2	20.06 (17.58- 23.62)	21.30 (19.26- 23.88)	0.058
Diagnosis			0.345
IPF	51 (32.90)	26 (49.06)	
Non-IPF ILD	33 (21.29)	8 (15.09)	
IPAH	2 (1.29)	0 (0.00)	
Pneumoconiosis	25 (16.13)	7 (13.21)	
COPD	17 (10.97)	3 (5.66)	
Others	27 (17.42)	9 (16.98)	
Admission status before LT			0.565
Not admitted	20 (12.90)	7 (13.21)	
General ward admission	118 (76.13)	38 (71.70)	
ICU admission	15 (9.68)	8 (15.09)	
Not specified	2 (1.29)	0	
NYHA functional class status before LT			0.323
II	5 (3.23)	1 (1.89)	
III	98 (63.23)	29 (54.72)	
IV	49 (31.61)	23 (43.40)	
Not specified	3 (1.94)	0	
Pre-LT ECMO bridging	3 (2.22)	4 (7.84)	0.072
Pre-LT steroids use	41 (27.15)	22 (42.31)	0.042
Pre-LT hypertension	16 (10.53)	10 (19.61)	0.093
Recipient P/F ratio	232.47(171.74- 304.76)	214.49 (163.00- 283.33)	0.737
Donor P/F ratio	420.00 (369.00- 480.90)	426.00 (366.75- 471.75)	0.649
Ejection fraction, %	63.00 (60.50- 67.50)	64.00 (60.00- 67.00)	0.789
Creatinine, μmol/L	60.00 (50.70- 70.38)	61.00 (49.00- 68.42)	0.791
LT center volume type, cases/y			0.010
<50	46 (29.68)	26 (49.06)	
≥50	109 (70.32)	27 (50.94)	
Cold ischemic time, h	7.50 (6.00- 9.12)	7.00 (5.00- 8.50)	0.057
LT type			0.229
Bilateral LT	85 (54.84)	24 (45.28)	
Unilateral LT	70 (45.16)	29 (54.72)	
Intraoperative ECMO mode			0.695
V-V	82 (52.90)	25 (47.17)	
V-A	63 (40.65)	26 (49.06)	
V-AV	6 (3.87)	1 (1.89)	
Not specified	4 (2.58)	1 (1.89)	
Post-LT ECMO mode			0.234
V-V	57 (36.77)	17 (32.08)	
V-A	32 (20.65)	14 (26.42)	
V-AV	2 (1.29)	3 (5.66)	
Not specified	64 (41.29)	19 (35.85)	

Continued on the next page

effect sizes of ΔmPAP on survival were different in LT centers with high or low case volume. ΔmPAP >35 mm Hg and LT center ≥50 cases/year were positively associated with patients' long-term survival (HR: 0.20; $P = 0.0345$), after adjustment for demographic and pre-LT variables. We further performed multivariate analyses based on Cox model stratified by LT center case volume.

In adjusted model 1, when we only adjusted for demographic variables, ΔmPAP >35 mm Hg showed increased risk of post-LT morbidity (HR: 3.21; $P = 0.0457$) in low case volume (<50 cases/year) LT center. However, ΔmPAP >35 mm Hg was associated with reduced risk of post-LT morbidity (HR: 0.23; $P = 0.0514$) in high case volume (≥50 cases/year) LT center. When we adjusted more variables

TABLE 1 Continued

	Survival (n = 155)	Death (n = 53)	*P* Value
mPAP on listing, mm Hg	35.00 (25.50- 45.50)	38.00 (29.00- 44.00)	0.538
mPAP at time of ECMO support, mm Hg	55.00 (40.50- 70.00)	50.00 (37.00- 68.00)	0.238
mPAP at time of ECMO support, mm Hg			0.954
≦75	137 (88.39)	47 (88.68)	
>75	18 (11.61)	6 (11.32)	
ΔmPAP, mm Hg	20.00 (11.00- 35.00)	23.00 (10.00-, 30.00)	0.344
ΔmPAP, mm Hg			
≦35	118 (76.13)	47 (88.68)	0.05
>35	37 (23.87)	6 (11.32)	
Heart failure post-LT			<0.001
No	144 (92.90)	39 (73.58)	
Yes	11 (7.10)	14 (26.42)	
ICU stay, h	136.00 (89.75- 200.25)	285.00 (216.00- 480.00)	<0.001
Time on intubation post-LT, h	48.00 (35.00- 89.00)	185.00 (70.00- 264.00)	<0.001
Time on ECMO post-LT, h	20.00 (8.00- 34.00)	20.00 (0.00- 50.00)	0.875
Primary graft dysfunction			
No	134 (86.45)	36 (67.92)	0.003
Yes	21 (13.55)	17 (32.08)	

Values are median (IQR) or n (%).

ΔmPAP = difference of mean pulmonary artery pressure at time of extracorporeal membrane oxygenation support and extracorporeal membrane oxygenation wean-off; BMI = body mass index; COPD = chronic obstructive pulmonary disease; ECMO = extracorporeal membrane oxygenation; ICU = intensive care unit; ILD = interstitial lung disease; IPAH = idiopathic pulmonary arterial hypertension; IPF = idiopathic pulmonary fibrosis; mPAP = mean pulmonary artery pressure; NYHA = New York Heart Association functional class; P/F ratio = ratio of arterial oxygen concentration to the fraction of inspired oxygen; V-A = venoarterial; V-AV = hybrid venovenous and venoarterial; V-V = venovenous.

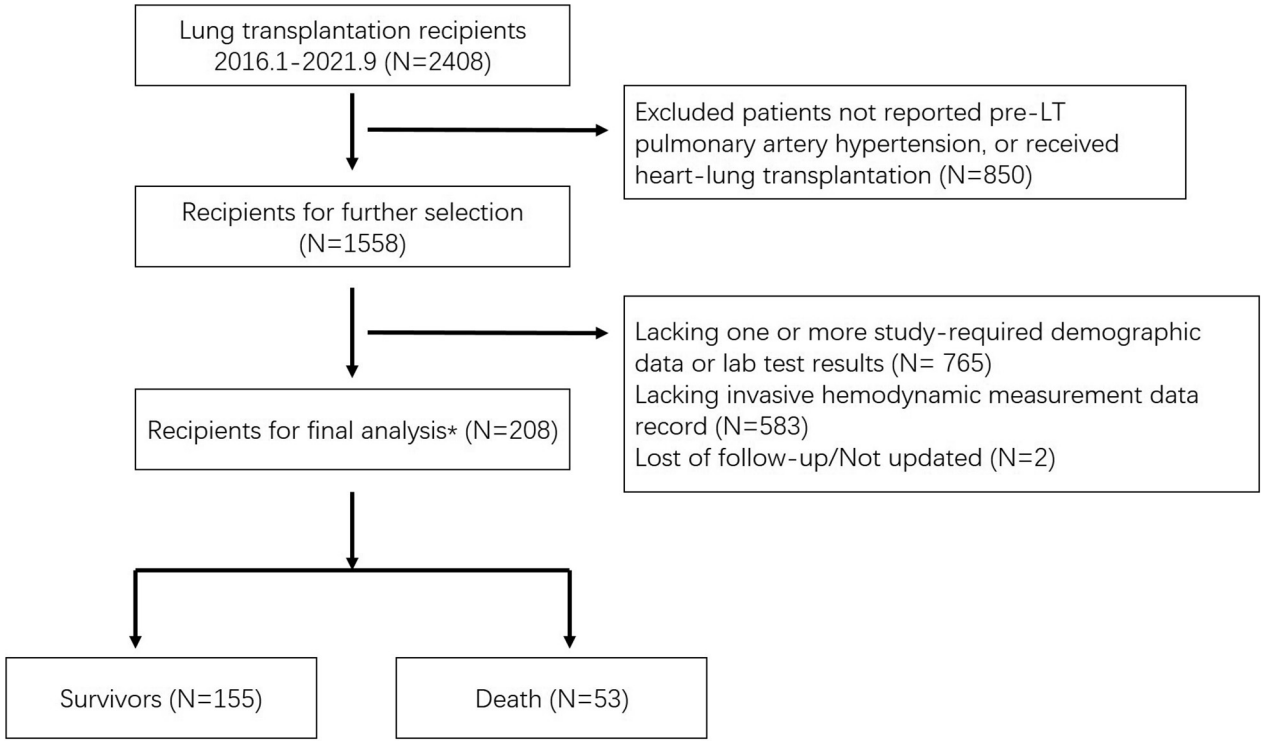
including pre-LT status, sensitivity analysis showed the same trend of risk discrepancy. However, when we observed ΔmPAP as a continuous variable and mPAP at time of ECMO support, the correlation was not significant irrespective of LT center case volume (Table 4).

DISCUSSION

For patients with PH, double LT is presently the procedure preferred over heart-lung transplantation.[10] During follow-up post-LT, right ventricle remodeling and regression of tricuspid valve regurgitation occurred.[19] Usually, LT in patients with PH is performed with cardiopulmonary bypass as an intraoperative hemodynamic support.[7] ECMO is becoming more promising with advantages over cardiopulmonary bypass in terms of intraoperative and postoperative morbidity and mortality.[20] Patients with severe PH are unstable during transplantation with high risk of cardiac dysfunction and gained risk of pulmonary reperfusion edema.[9] With ECMO support, in recipients with preoperative extremely severe PH, their pulmonary artery pressure decreased significantly as soon as the donated lungs were transplanted and reperfused. Patients with PH are at higher risk for developing primary graft dysfunction than other transplant indications.[21] Reduction of the incidence of primary graft dysfunction and thus the rate of in-hospital mortality could explain the survival benefit of ECMO use.

ECMO-supported lung transplantation has been widely used in patients with end-stage lung disease and PH among LT centers in China. A better biocompatibility and a reduced intraoperative and postoperative morbidity has been observed globally.[22] The benefits of using intraoperative and post-LT support, compared with cardiopulmonary bypass, included lower priming volume, lesser inflammatory activation, and feasible coagulation strategy. With the advancement of ECMO technique, pre-LT peripheral ECMO could be switched to intraoperative central ECMO support. Reports from Aigner et al [23] and Salman et al[24] have illustrated that in patients with severe PH, use of prophylactic venoarterial ECMO could reduce in-hospital mortality and primary graft dysfunction incidence. For patients with extremely high preoperative mPAP, high risk of postoperative heart failure events occurred, and prolonged ECMO use was adopted in these patients. Factors such as cardiopulmonary function and ECMO mode have been associated with perioperative pulmonary artery pressure

FIGURE 1 Flowchart of Recipient Enrollment and Data Extraction



Data were collected from CLuTR (China Lung Transplantation Registry), which enrolled recipients from all the lung transplantation (LT) centers in China. Patients with severe pulmonary hypertension who received LT between January 2016 and September 2021 were enrolled, and their data were collected and further analyzed. A total of 208 patients were included in our study, including 155 survivors and 53 deaths up to the date we collected all the data. *These recipients had recorded PH, and their mean pulmonary artery pressure at time of extracorporeal membrane oxygenation support was over 35 mm Hg.

change. In our study, nonlinear relationship of ΔmPAP and post-LT outcome was revealed with an inflection point of 35 mm Hg (**Central Illustration**). Risk factors related to outcome included New York Heart Association functional class III/IV, mechanical ventilation period, multiorgan dysfunction, among others. However, the criteria for selecting optimal strategy and predicting its benefit, varied in LT centers with different case experience, reflecting by the complex conditions of patients and post-LT complications management.

TABLE 2 Nonlinear Relationship of ΔmPAP and Post-LT Survival

Inflection Point of ΔmPAP (mm Hg)	HR (95% CI)	*P* Value
≦35	1.03 (1.00-1.06)	0.0978
>35	0.86 (0.76-0.97)	0.0139

Abbreviations as in Table 1.

National registry-based analysis in our study has revealed the LT center experience could significantly affect the intraoperative ECMO support outcome in patients with severe PH. Institutional protocol discrepancy included selection of ECMO support mode (venovenous, venoarterial, or hybrid) and access (peripheral, central), intraoperative anesthesiology management, determination if prolonged ECMO used in postoperative period, management strategy of ECMO-related or non-ECMO-related complication. ECMO-related postoperative bleeding, thrombosis, neurologic injury, and acute renal injury were recognized to affect patients' outcome (Supplemental Table 2).

The top 3 experienced LT centers in China, included Wuxi center, China-Japan Friendship Hospital, and First Affiliate Hospital of Guangzhou Medical University, which had largest group of LT recipients.[12] In Wuxi LT center, with the largest

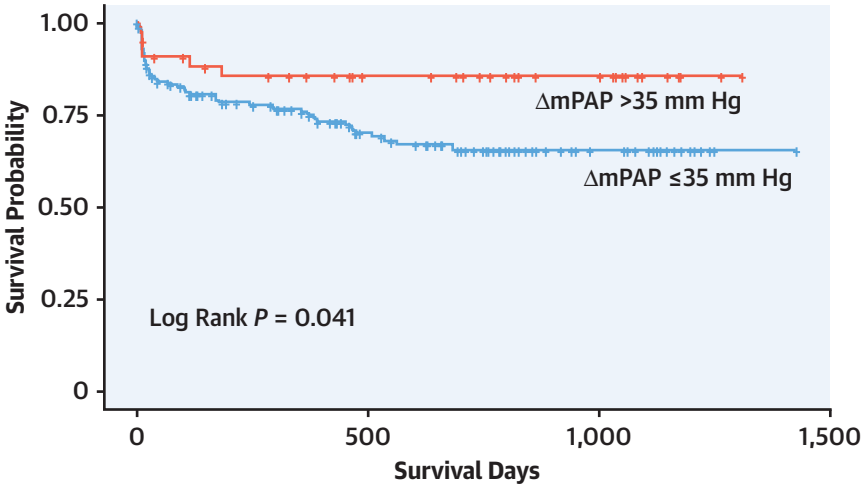
CENTRAL ILLUSTRATION **Kaplan-Meier Plots of Recipient Survival Rates Categorized by Difference in Mean Pulmonary Artery Pressure Between Time of Support and Time of Wean-Off**

Enrolled 208 severe PH patients with intraoperative ECMO support from Chinese Lung Transplantation Registry.

Data collected consecutively from January 2016 to September 2021 with a median follow-up duration of 467 days.

All-cause mortality was calculated. The inflection point of ΔmPAP (35 mm Hg) was calculated by using a 2-piecewise linear regression model. Difference of mPAP at time of ECMO support and ECMO wean-off (ΔmPAP) was recorded.

Patients with ΔmPAP ≤35 mm Hg has inferior long-term survival, comparing to patients with ΔmPAP >35 mm Hg (log rank P = 0.041).



Number at risk				
ΔmPAP ≤35 mm Hg	165	64	18	0
ΔmPAP >35 mm Hg	43	26	15	0

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The survival function was plotted with the Kaplan-Meier estimator and differences between groups were quantified by the log-rank test. ΔmPAP is the difference of mean pulmonary artery pressure (mPAP) at time of extracorporeal membrane oxygenation (ECMO) support and ECMO wean-off. PH = pulmonary hypertension.

TABLE 3 Univariate Analysis of Factors Associated With Post-LT Survival

	HR (95% CI)/ β (95% CI)	*P* Value
Age, y	1.02 (0.99-1.05)	0.2527
Donor age, y	1.04 (1.00-1.08)	0.0647
BMI, kg/m^2	1.08 (0.98-1.19)	0.1426
Cold ischemic time, h	0.96 (0.80-1.15)	0.6415
Admission status before LT		
Not admitted	Ref	
General ward admission	0.93 (0.41-2.08)	0.8588
ICU admission	1.50 (0.54-4.13)	0.4369
Pre-LT steroids use		
No	Ref	
Yes	1.69 (0.97-2.93)	0.0621
Pre-LT hypertension		
No	Ref	
Yes	1.81 (0.91-3.62)	0.0922
LT center volume ≥50 cases/y		
No	Ref	
Yes	0.46 (0.27-0.79)	0.0049
NYHA functional class status before LT		
II	Ref	
III	1.48 (0.20-10.90)	0.6984
IV	2.42 (0.33-17.92)	0.3885
Pre-LT ECMO bridging		
No	Ref	
Yes	3.39 (1.21-9.48)	0.0202
mPAP at time of ECMO support, mm Hg	0.98 (0.97-1.00)	0.3885
ΔmPAP, mm Hg		
≦35	Ref	
>35	0.42 (0.18-0.99)	0.0481

Ref = reference; other abbreviations as in Table 1.

case volume in China, ECMO support was set up before anesthesia induction in patients with severe PH.[25] When stratifying the outcome by center experience level, discrepancy of long-term outcome could be revealed, thus, indicating the need of further training and optimizing peri-LT strategy. Our study might reflect the unbalanced status of LT development, indicating that the techniques and protocols required should be homogenized and promoted nationwide, even further in Asian-wide developing LT programs.

Recently, novel machine learning techniques have been used to screen variables and construct prediction models.[15] XGboost has been widely recognized in a number of machine learning and data mining challenges, with the remarkable features of processing the missing data.[26] We used XGboost method in the initial variables screening, thus providing reference for further model construction and adjustment.

STUDY LIMITATIONS. The main limitation is the retrospective nature of this study and the limited number of patients used. A certain degree of measurement variability may be presumed because data were reported from teams of different centers. When deciding ECMO support strategy, selection bias regarding the postoperative course was not avoidable. As years of experience is gained in different centers, patient outcome may change, thus limited the efficacy of this study. Limitation of variables collected as well as missing data, especially in patient populations with different diagnoses, such as idiopathic pulmonary arterial hypertension, in CLuTR further reduced the insightfulness of the sensitivity analysis. In this LT registry, limited variables related to cardiac function evaluation were collected. Further study will be needed to illustrated how to make best use of ECMO in patients with end-stage lung disease who have severe PH based on risk-stratification analysis.

TABLE 4 Multivariable Analysis of Factors Associated With Post-LT Survival in Different Models

	LT Center Volume Type <50 Cases/y			LT Center Volume Type ≥50 Cases/y		
	Crude Model	Model 1	Model 2	Crude Model	Model 1	Model 2
ΔmPAP, mm Hg	1.02 (0.99-1.06), 0.2172	1.02 (0.99-1.06), 0.1917	1.02 (0.99-1.06), 0.2161	0.98 (0.96-1.01), 0.1472	0.99 (0.96-1.02), 0.4335	0.98 (0.96-1.01), 0.2794
ΔmPAP, mm Hg						
≦35	Ref	Ref	Ref	Ref	Ref	Ref
>35	3.24 (1.09-9.63), 0.0340	3.21 (1.02-10.08), 0.0457	3.43 (1.07-11.00), 0.0382	0.19 (0.04-0.80), 0.0239	0.23 (0.05-1.01), 0.0514	0.20 (0.04-0.89), 0.0345
mPAP at time of ECMO support	1.01 (0.98-1.04), 0.4695	1.01 (0.99-1.04), 0.2730	1.02 (0.99-1.05), 0.2513	0.99 (0.96-1.01), 0.2507	0.99 (0.96-1.02), 0.4883	0.41 (0.09-2.00), 0.2734
≦75 mm Hg	Ref	Ref	Ref	Ref	Ref	Ref
>75 mm Hg	4.15 (1.42-12.17), 0.0094	1.01 (0.99-1.04), 0.2730	1.02 (0.99-1.05), 0.2513	0.48 (0.11-2.02), 0.3168	0.99 (0.96-1.02), 0.4883	0.99 (0.96-1.01), 0.3541

Values are HR (95% CI), *P* value. Crude model: no variable was adjusted. Adjusted model 1: recipient age, NYHA functional class status before LT, BMI, and pre-LT hypertension were adjusted. Adjusted model 2: recipient age, NYHA functional class status before LT, BMI, pre-LT hypertension, pre-LT steroids, and pre-LT ECMO bridging were adjusted.

Abbreviations as in Tables 1 and 2.

CONCLUSIONS

In patients with end-stage lung disease who have severe PH, using optimized ECMO support protocol based on hemodynamic parameters will benefit their post-LT survival. Although the postoperative course was complicated in terms of discrepancy of team experience, to reduce the waiting list mortality and enhance long-term survival of these patients who are in critical conditions warrants further investigation.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: ECMO has been used as intraoperative hemodynamic support in patients with end-stage lung disease and PH undergoing LT. The association of pulmonary artery pressure change with ECMO support and post-LT survival was nonlinear.

COMPETENCY IN PATIENT CARE: In patients with end-stage lung disease and severe PH, optimized ECMO support protocol based on hemodynamic parameters will benefit their post-LT survival.

TRANSLATIONAL OUTLOOK: Although the postoperative course was complicated in terms of discrepancy of team experience, to reduce the waiting list mortality and enhance long-term survival of these patients who are in critical condition warrants further investigation. Optimal perioperative ECMO management strategy with experienced team is demonstrated to benefit LT recipients with severe PH.

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APPENDIX For supplemental figures and tables, please see the online version of this paper.