A risk score for predicting extracorporeal membrane oxygenation support before lung transplantation

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Background: Extracorporeal membrane oxygenation (ECMO) has been increasingly used as life support for lung transplantation. However, there are no clinical risk models to predict whether ECMO support is required for lung transplantation. This study developed a simple risk score to predict the need for intraoperative ECMO in patients undergoing lung transplantation, identify high-risk patients who need ECMO support, and guide clinical interventions.

Methods: Patients, who underwent lung transplantation between January 1, 2016 and July 31, 2021, were systematically reviewed. All enrolled patients were divided in a ratio of 7:3 to establish the development and validation datasets. A risk score model was established using stepwise logistic regression and verified using bootstrapping and the split-sample method.

Results: A total of 248 patients who underwent lung transplants were enrolled. Multivariate analysis showed that the primary disease diagnosis, pulmonary artery systolic pressure, sex, surgical type, creatine kinase isoenzyme-MB, and pro-B-type natriuretic peptide were risk factors for intraoperative ECMO during lung transplantation. The risk score was established and calibrated according to these six factors, ranging from 0 to 41, with the associated prediction of intraoperative use of ECMO ranging from 1.5% to 99.7% (Hosmer-Lemeshow χ^2=5.624; P=0.689). Good discrimination was verified by developing and validating the datasets (C-statistics =0.850 and 0.842, respectively). Based on the distribution of the scores, the three levels were classified as low-risk (0–10], moderate-risk (10–20], and high-risk (20–41].

Conclusions: This simple risk score model effectively predicts the need for intraoperative ECMO and stratifies high-risk patients who require ECMO support.

Keywords: Extracorporeal membrane oxygenation (ECMO); risk score; lung transplantation; prediction

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Introduction

Background

Lung transplantation was first introduced in 1963 (1), and the first successful lung transplantation was performed in Toronto in 1983 (2). Lung transplantation is recognized worldwide as an effective method for treating end-stage lung disease, improving the quality of life, and prolonging patient survival (3). However, due to preoperative respiratory failure, pulmonary hypertension, and cardiac dysfunction, critically ill patients often require cardiopulmonary support to manage hemodynamic fluctuations and maintain oxygenation during lung transplantation (4,5).

Extracorporeal membrane oxygenation (ECMO) has been implemented in clinical practice since 1972 (6), which has become an indispensable auxiliary support technology in the clinical treatment of critically ill patients (7-10) to provide both blood flow support and *in vitro* gas exchange. However, ECMO is an invasive procedure that is associated with significant complications. Patients receiving ECMO have a higher risk of secondary bleeding due to systemic anticoagulation and lack of coagulation factors. Blood transfusion may increase the incidence of primary graft dysfunction (PGD) in patients undergoing lung transplant patients (11-13). Other complications include cardiac tamponade, infection, thrombosis, and gas embolism, which may delay postoperative recovery and increase mortality (14-16).

Highlight box

Key findings
- Establishing a reliable and practical risk score for predicting intraoperative extracorporeal membrane oxygenation (ECMO) support before lung transplantation.

What is known and what is new?
- ECMO has been used more and more in lung transplantation. Implementing ECMO without planning or choosing the wrong patients for ECMO implementation could waste medical resources, raise medical costs, and increase the risk of postoperative complications and mortality.
- Our results reveal this simple risk score model as an effective predictor for the need of intraoperative ECMO and stratify high-risk patients who require ECMO support.

What is the implication, and what should change now?
- Before lung transplantation, it is essential to identify the risk factors linked to intraoperative ECMO requirements and promptly intervene in high-risk patients.

Rationale and knowledge gap

Implementation of ECMO during transplantation without prediction or improper patient selection may lead to wastage of medical resources, increased medical costs, and an increased incidence of postoperative complications and mortality (17,18). Therefore, it is necessary to identify the risk factors associated with intraoperative ECMO requirements before lung transplantation and provide timely intervention in high-risk patients. However, only a few studies have addressed this issue. Currently, no clinical risk model can predict ECMO support for lung transplantation.

Objective

This study's primary outcome is identifying risk factors for predicting ECMO support at lung transplantation and developing an accurate and convenient risk score to identify high-risk patients who need intraoperative ECMO support. We present this article in accordance with the TRIPOD reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-452/rc).

Methods

Study design

This large single-center retrospective cohort study included patients who underwent lung transplantation at the Guangzhou Institute of Respiratory Diseases between January 1, 2016, and July 31, 2021. Patients enrolled in this study had indications for lung transplantation after careful evaluation and were ≥18 years old. Patients with multiple organ transplantation or retransplantation, those who had received ECMO as a bridge to transplantation in the intensive care unit (ICU), those who received urgent intraoperative ECMO after receiving a lung transplant on one side, and those younger than 18 were excluded from this study.

Patients were excluded if their preoperative examination results were invalid or unavailable, or their perioperative medical records were incomplete. The data collector was blinded to the primary outcomes.

Ethical declaration

This study was approved by the Medical Ethics Committee of The First Affiliated Hospital of Guangzhou Medical University on December 14, 2021 (No. GYFYY-

2021-K-45). The requirement for informed consent was waived because of its retrospective nature. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Main procedures of anesthesia and surgery

In addition to routine monitoring, the radial artery was punctured to monitor the invasive arterial pressure. Anesthesia was induced sequentially using midazolam, sufentanil, etomidate, and rocuronium. A double-lumen bronchial catheter was inserted into the right place under fiberoptic bronchoscopy guidance. The tidal volume (VT), breath rate, and fraction of inspired oxygen (FiO$_2$) were set at 6–8 mL/kg, 12–16 breaths/min, and 100% respectively. A central and pulmonary catheter was inserted into the internal jugular vein, and a pulse-indicating continuous cardiac output (PiCCO) catheter was inserted into the femoral artery.

Anesthesia was maintained bispectral index values between 40 and 60 with dexmedetomidine 0.5–1 µg/kg/h, propofol target-controlled infusion 2–3 µg/mL, and remifentanil 0.05–0.2 µg/kg/min.

Based on the preoperative clinical evaluation, the surgeon decides whether the patient will undergo single-lung or double-lung transplantation. After the primary lung was removed, the donor lungs were implanted. The trachea, pulmonary artery, and pulmonary vein were anastomosed. At the end of the surgery, the patient was transferred to the ICU after the double-lumen bronchial tube was replaced with a single-lumen tube.

Primary outcome and candidate predictors

Data of patients who underwent lung transplantation at our hospital were systematically reviewed. The primary outcome was the provision of ECMO support during lung transplantation. The criteria for intra-operative ECMO support were as follows: hemodynamic instability, severe hypoxemia (impaired gas exchange, hyperperfusion, and inability to tolerate single lung ventilation) after optimization of patient cardiopulmonary conditions, or a combination of the following conditions: hypercapnia [partial pressure of carbon dioxide in arterial blood (PaCO$_2$) >60 mmHg, pH <7.2], arterial oxygen saturation (SaO$_2$) <85%, and cardiac index (CI) levels <2 L/min/m^2 (15).

The preoperative characteristics and post-anesthesia variables were included as the candidate predictors, including age, body mass index (BMI), sex, primary diagnosis, surgical type, the physical status of the American Society of Anesthesiologists, comorbidities, the result of pulmonary ventilation-perfusion scan, pro-B-type natriuretic peptide (pro-BNP), creatine kinase isoenzyme-MB (CKMB), cardiac troponin I, myocardial enzyme, left ventricular ejection fraction, the results of hepatic and renal function, hemocytes examination, procalcitonin concentration, and arterial blood gas analysis, the saturation of pulse oximetry, invasive mean arterial pressure, central venous pressure (CVP), heart rate, pulmonary artery systolic pressure (PASP), and peak airway pressure.

Statistical analysis

Data were analyzed using SAS version 9.4. All analyses were in line with the complete case input. All patients enrolled in the study were divided in a ratio of 7:3 to establish the development and validation datasets. According to the development datasets, risk and risk score models were created. A risk model was constructed following the univariate analysis with candidate predictors (P<0.05). The bootstrap method was used to select the best subset of risk factors. The scoring method of the risk-scoring model was based on the development a risk model that resembled the previous scoring method (19). Continuous variables were defined as clinically meaningful for scoring. The degree of correlation between the score level and the risk of using ECMO was assessed using Pearson's contingency coefficient, and the trend was examined using the Cochran-Armitage test.

The prediction accuracy of the risk model and risk score model was assessed using C-statistics and calibrated using Hosmer-Lemeshow χ^2 statistics and calibration plots. The split-sample method was used to verify the risk-scoring model and assess its stability. DeLong's nonparametric method (20) was used to compare the area under the receiver operating characteristic (ROC) curve.

Results

This study enrolled 248 lung transplant patients (*Figure 1*).

The development of the risk model and risk score

Of the enrolled 248 patients, 103 (41.5%) received intraoperative ECMO support. The development datasets included 166 patients, of whom 69 (41.6%) received

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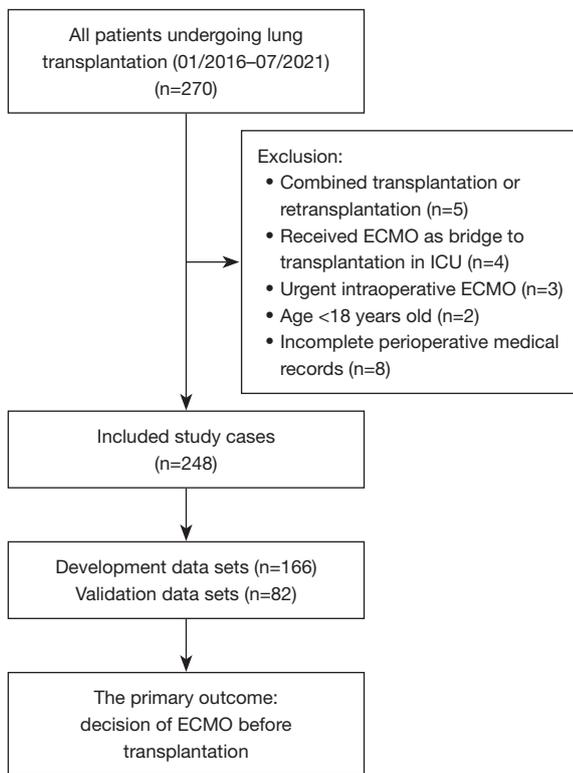
Figure 1 The flow chart of this study. ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit.

intraoperative ECMO support, in contrast, the validation datasets included 82 patients, of whom 34 (41.5%) received intraoperative ECMO support. (Table S1). The Bootstrap technique was used to select variables in the developmental dataset. Primary disease diagnosis, PASP, sex, surgical type, CKMB, and pro-BNP were screened out to establish the risk model, the best subset of risk factors (*Table 1*). The risk scores for all predictive variables are shown in *Table 2*.

Risk score validation

Based on the development data sets, the risk score model was used for discrimination, with a high χ^2 statistic calibration of 5.624 (P=0.689) and a C-statistic of 0.850 [95% confidence interval (CI): 0.792–0.908] (*Figure 2*). When the risk score model was applied to the split sample from the validation datasets, the validation results were the same as those from the development datasets, accompanied by a high χ^2 statistic calibration of 4.584 (P=0.801) and a C-statistic of 0.842 (95% CI: 0.759–0.924) (*Figure 2*). The ROC curves for the development and validation datasets

were similar (*Figure 2*), and the percentage of intraoperative ECMO support use had no significant difference between the two groups.

Clinical significance of the risk score model

According to the risk score model, the risk scores were divided into three levels suitable for clinical application according to the risk score model (*Figures 3,4*). Based on the score distribution of intraoperative ECMO use, three levels were classified as low-risk (0–10], moderate-risk (10–20], and high-risk (20–41] (Table S2), with total risk scores ranging from 0 (lowest risk) to 41 (highest risk) (*Table 2*). The associated predictions of intraoperative ECMO use ranged from 1.5% to 99.7%. The correlation between the risk level and predicted risk probability was successively defined as low-risk (1.5–12.2%), moderate-risk (15.1–62.2%), and high-risk (67.8–99.7%) (*Table 3*).

Discussion

Key findings

ECMO can provide cardiopulmonary support to patients with heart and respiratory failures through external gas exchange and power pumps (6,8,21). Intraoperative ECMO can overcome right heart failure, excessive pulmonary hypertension or hypercapnia, and global hypoxia during one-lung ventilation, effectively improving the oxygenation state of the body, maintaining the systemic blood supply and hemodynamics in a relatively stable state, improving the success rate of lung transplantation, and improving the prognosis of lung transplant recipient (22-25). Our institute is one of China's largest lung transplantation centers (26).

However, when considering the implementation of ECMO during lung transplantation, the judgment is frequently based on previous experience. Therefore, there is an urgent need to establish a scientific evaluation model for clinical decision-making. This study established and validated a risk score model according to six available factors (primary disease diagnosis, PASP, sex, surgical type, CKMB, and pro-BNP levels) that can predict the need for intraoperative ECMO before lung transplant. We classified low-, moderate-, and high-risk levels that clinicians can easily consult.

This study aimed to predict the need for intraoperative ECMO in patients undergoing lung transplantation based on preoperative characteristics and variables after

Table 1 Univariate and multivariable logistic regression analysis of risk factors that were selected to develop the risk model for predicting the use of intraoperative ECMO (development data sets, n=166)

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Primary disease diagnosis						
COPD	Ref			Ref		
NSIP	10.636	3.596–31.460	<0.0001	6.045	1.773–20.617	0.004
Silicosis	9.000	1.918–42.235	0.005	6.399	0.976–41.934	0.053
Bronchiectasis	18.000	3.958–81.861	<0.0001	3.207	0.521–19.764	0.209
IPF	14.250	4.409–46.052	<0.0001	10.887	2.747–43.156	0.001
Lymphangiomyoma	6.000	1.501–23.990	0.011	1.468	0.243–8.872	0.676
PASP	1.057	1.027–1.088	<0.0001	1.050	1.011–1.090	0.012
Female *vs.* male	4.227	1.726–10.353	0.002	5.905	1.582–22.040	0.008
Surgical type						
Double-LTx	Ref			Ref		
Right-LTx	0.199	0.087–0.456	<0.0001	0.215	0.074–0.625	0.005
Left-LTx	0.343	0.161–0.731	0.006	0.375	0.131–1.073	0.067
Log CKMB[†]	1.087	0.624–1.894	0.769	1.678	0.783–3.599	0.183
Log pro-BNP[†]	1.402	1.143–1.719	0.001	1.418	1.090–1.845	0.009

[†], the natural logarithmic transformations of CKMB and pro-BNP were made because of their extreme positive skewness. ECMO, extracorporeal membrane oxygenation; OR, odds ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; NSIP, nonspecific interstitial pneumonia; IPF, idiopathic pulmonary fibrosis; PASP, pulmonary artery systolic pressure; LTx, lung transplantation; CKMB, creatine kinase isoenzyme-MB; pro-BNP, pro-B-type natriuretic peptide.

anesthesia. This simple and effective risk score can immediately identify high-risk patients and grade their risk, ultimately prompting clinicians to initiate early treatment.

Strengths and limitations

This study had some limitations. Firstly, the number of patients undergoing lung transplantation was relatively small. Because of the insufficient number of donor lung organs, it was impossible to obtain a large sample size. Second, this retrospective study was conducted at a single center, which might have led to some bias. Although clinical practice between different transplant centers influences the administration of ECMO due to different policies or preferences, our transplantation center implemented transplantation according to the guidelines of the International Society for Heart and Lung Transplantation; therefore, the risk model is still adaptable to other centers. Thirdly, a split-sample method was used to verify the

model. This is an easy method to test for overfitting without ensuring the generality of the individual queues. Fourth, pulmonary function values were not included in the analysis due to the many patients with preoperative end-stage lung disease, leading to failure to complete the pulmonary function examination. If they had been included in the analysis, many patients without pulmonary function examinations might have been excluded, leading to deviations in the results. Pulmonary function was assessed by arterial blood gas analysis instead of a pulmonary function test.

Comparison with similar researches

ECMO is a reliable and effective strategy for supporting lung function; however, severe PGD significantly impacts early and late outcomes (27). The timing of intraoperative ECMO may also affect postoperative outcomes. Fessler *et al.* reported that patients who received emergency

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Table 2 The risk scores for all predicting variables

Risk factors	Score
Surgical type	
Double-LTx	6
Right-LTx	0
Left-LTx	2
Primary disease diagnosis	
COPD	0
NSIP	7
Silicosis	8
Bronchiectasis	5
IPF	10
Lymphangiomyoma	2
Gender	
Female	7
Male	0
PASP	
≤30 mmHg	0
31–50 mmHg	4
51–70 mmHg	8
>70 mmHg	12
CKMB	
≤12 U/L	0
13–24 U/L	1
>24 U/L	2
Pro-BNP	
≤125 pg/mL	0
126–450 pg/mL	1
451–900 pg/mL	2
901–1,800 pg/mL	3
>1,800 pg/mL	4

LTx, lung transplantation; COPD, chronic obstructive pulmonary disease; NSIP, nonspecific interstitial pneumonia; IPF, idiopathic pulmonary fibrosis; PASP, pulmonary artery systolic pressure; CKMB, creatine kinase isoenzyme-MB; pro-BNP, pro-B-type natriuretic peptide.
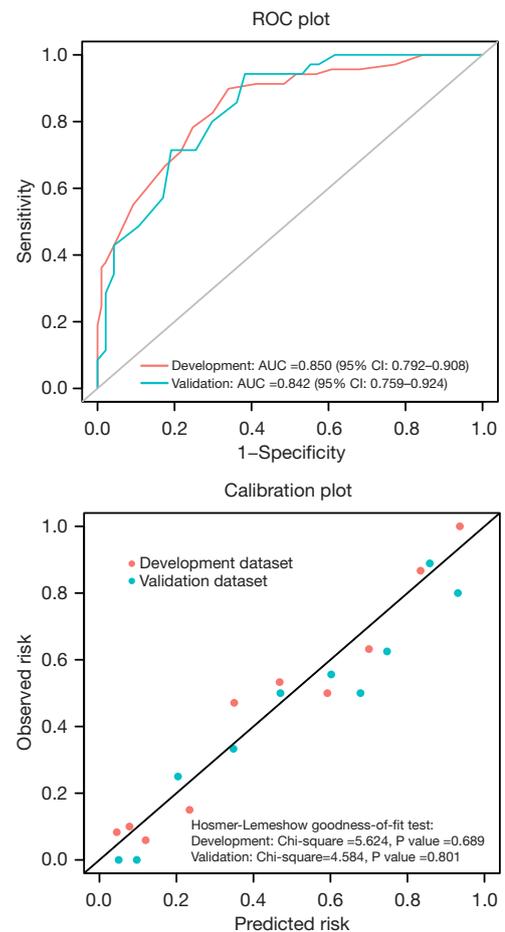
Figure 2 The area under the ROC curves and calibration plot with the Hosmer-Lemeshow test for goodness-of-fit result for the risk score. ROC, receiver operator characteristic; AUC, area under the curve; CI, confidence interval.
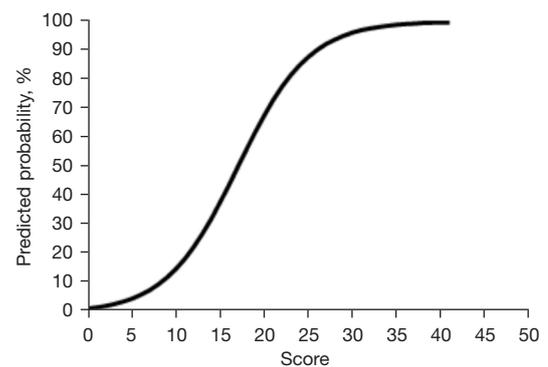
Figure 3 The score and corresponding predicted probability.
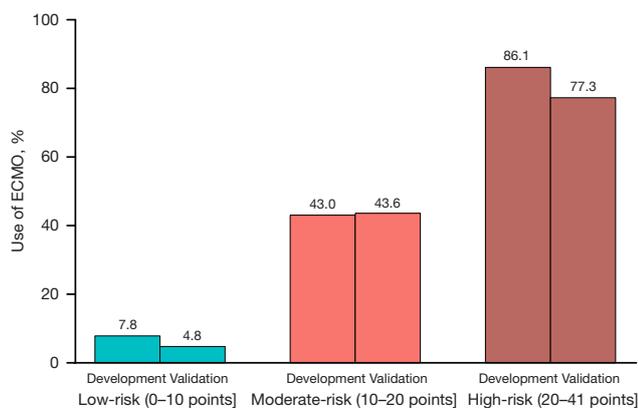
Figure 4 The correlation between the risk level and the risk score range. ECMO, extracorporeal membrane oxygenation.

Table 3 The relationship between risk level and predicted risk of the use of intraoperative ECMO

Risk level	Risk score level (points)	Predicted risk (%)
Low-risk	(0–10]	1.5–12.2
Moderate-risk	(10–20]	15.1–62.2
High-risk	(20–41]	67.8–99.7

ECMO, extracorporeal membrane oxygenation.

intraoperative ECMO support due to complications had a worse prognosis than those who did not need it (28). ECMO can improve survival when used preemptively at the start of transplantation in patients with significant extracorporeal life support needs and surgically in patients with cardiopulmonary instability following cross-clapping of the pulmonary artery.

Vienna found that intraoperative ECMO-supported lung transplantation had a higher survival rate than transplants without intraoperative support, and recommended that ECMO can be extended until the early period after surgery (29). Hoetzenecker *et al.* suggested that routine intraoperative ECMO could reduce the incidence of primary PGD and lead to good graft function and interim outcomes in lung transplant recipients (30).

In addition, it has been found that recipients requiring ECMO support during lung transplantation tend to have more serious pulmonary hypertension (31,32). Patients with severe pulmonary hypertension are at high risk of pulmonary reperfusion edema in the early post-transplantation period due to acute right heart failure caused by an increased right heart load during surgery.

CKMB and pro-BNP are commonly used indices to evaluate cardiac function, the higher the values, the higher the possibility of cardiac insufficiency. In lung transplant patients, increased CVP caused by cardiac insufficiency can lead to increased blood perfusion pressure, increased risk of pulmonary edema, postoperative renal failure, and failure of other failures.

Increased CVP can, in turn, aggravate pulmonary vascular resistance, cause interstitial edema, further increase airway resistance, decrease SaO_2, and form a hemodynamic vicious circle. ECMO-assisted diversion can effectively reduce pulmonary hypertension and blood perfusion pressure in new lungs, stabilize patients' blood circulation system, and reduce perioperative cardiac failure (29,33,34). Salman reported that routine prophylactic application of ECMO support during lung transplantation for patients with primary pulmonary hypertension can reduce perioperative mortality and improve cardiac function recovery 1 year after surgery (24).

Patients receiving ECMO support may have higher mortality rates. Bermudez retrospectively assessed and reported that the 1-year survival rate of patients with and without ECMO support was 80.9% and 86.1% respectively (35). Munich reported 11.1% perioperative mortality and 81.5% 1-year survival rate with ECMO support, compared to 4.5% and 81.8% without ECMO support, respectively (36). Ius reported that the overall survival rates at 1- and 4-year were 83% and 68% for patients who underwent ECMO preoperatively, 82% and 69% when ECMO was administered intraoperatively, and 93% and 73% for those who did not receive ECMO (37).

However, several other retrospective single-center observational studies have shown that the survival rates of patients receiving ECMO-bridging transplantation are comparable to those of patients who do not (38-40). A systematic review found that the survival rate of patients supported by ECMO varied from 10% to 50% after surgery, and from 50% to 90% 1 year after transplantation (41). The success rate of ECMO at different stages highlights the need for careful patient selection, especially considering the potential role of disease processes on prognosis (42).

Explanations of findings

In this study, the recommended risk scores showed a high level of variability and good calibration in the development and validation datasets, and the risk scores were more accurate in predicting the need for intraoperative ECMO.

The risk score model established in this study, combined with the six preoperative and operative factors, has a more comprehensive prediction ability, which can provide more scientific guidance for the clinical decision to use ECMO. At low-risk (score ≤10), patients can complete lung transplantation without ECMO, perioperative management becomes simple, ECMO-related complications can be avoided, medical resources can be saved, and the economic burden of patients can be reduced.

The risk level is moderate if the score is between 10–20. In this case, more real-time clinical information, such as patient volume status, degree of hemodynamic fluctuation, amplitude of pulmonary artery pressure increase when clapping pulmonary artery, and oxygenation during single-lung ventilation, should be combined to evaluate whether patients should use ECMO. The risk level is high when the score is >20 points.

Implications and actions needed

Patients undergoing lung transplantation are advised to receive ECMO before surgery to improve their overall survival or even use ECMO bridging transplantation (43,44). There is no unified evaluation index for intraoperative ECMO support, and most centers use this index based on their own experiences according to the patient's preoperative and postoperative conditions. Establishing this risk-scoring model is an auxiliary method to further support decisions based on experience. This would be a useful tool to avoid unnecessary intraoperative ECMO, which is costly and carries the risk of complications, and to avoid urgent intraoperative cannulations by identifying patients requiring extracorporeal life support during transplantation.

Conclusions

This simple risk-scoring model, established based on six available factors (primary disease diagnosis, PASP, sex, surgical type, CKMB, and pro-BNP), effectively predicts the need for intraoperative ECMO. This can help clinicians discriminate between high-, moderate-, and low-risk patients and perform appropriate early interventions while optimizing the allocation of healthcare resources.

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Footnote

Reporting Checklist: The authors have completed the TRIPOD reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-452/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-452/dss

Peer Review File: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-452/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-452/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Medical Ethics Committee of The First Affiliated Hospital of Guangzhou Medical University on December 14, 2021 (No. GYFYY-2021-K-45). The requirement for informed consent was waived because of its retrospective nature.

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Supplementary

Table S1 The comparisons of variables between the validation data set and development data set

Variables	Development data set	Validation data set	$\chi^2/t/Z$	P
ECMO			<0.001	0.988
Yes	69 (41.6)	34 (41.5)		
No	97 (58.4)	48 (58.5)		
Gender			0.750	0.386
Male	139 (83.7)	65 (79.3)		
Female	27 (16.3)	17 (20.7)		
CHD	9 (5.4)	8 (9.8)	1.615	0.204
DM	13 (7.8)	13 (15.9)	3.764	0.052
Hypertension	10 (6.0)	11 (13.4)	3.868	0.049
Smoking	103 (62.0)	47 (57.3)	0.514	0.473
Diagnosis			1.198	0.945
COPD	50 (30.1)	24 (29.3)		
NSIP	48 (28.9)	28 (34.1)		
Silicosis	10 (6.0)	5 (6.1)		
Bronchiectasis	12 (7.2)	5 (6.1)		
IPF	31 (18.7)	15 (18.3)		
Lymphangiomyoma	15 (9.0)	5 (6.1)		
Surgical type			0.123	0.940
Double-LTx	62 (37.3)	32 (39.0)		
Right-LTx	50 (30.1)	23 (28.0)		
Left-LTx	54 (32.5)	27 (32.9)		
Log pro-BNP	5.19±1.64	5.34±1.54	−0.683	0.495
Log CKMB	2.42±0.56	2.47±0.48	−0.767	0.444
Log c-TnI	−5.13±2.39	−5.18±2.62	0.136	0.892
ALT (U/L)	24.88±27.52	25.21±29.74	−0.086	0.931
ALB (g/L)	36.15±5.58	35.10±4.41	1.604	0.110
TBIL (µmol/L)	10.10±4.66	11.06±5.58	−1.433	0.153
BUN (mmol/L)	5.93±5.95	5.60±3.58	0.545	0.586
SCr (µmol/L)	67.93±20.10	65.92±19.29	0.751	0.454
WBC (10^9/L)	9.87±8.39	9.16±3.30	0.96	0.338
NEUT	71.72±12.83	73.64±11.74	−1.142	0.255
Hb (g/L)	119.63±23.51	122.66±21.54	−0.981	0.328
PCT (ng/mL)	0.45±2.66	0.22±0.30	1.086	0.279
pH	7.37±0.06	7.38±0.05	−0.726	0.468
$PaCO_2$ (mmHg)	53.30±12.44	50.11±11.45	1.954	0.052
PaO_2 (mmHg)	116.04±49.74	105.35±39.00	1.849	0.066
HR (beats/minute)	91.35±14.04	90.13±15.23	0.628	0.531
MAP (mmHg)	91.92±11.87	94.52±14.34	−1.419	0.158
SpO_2 (%)	97.01±4.23	95.36±7.07	1.95	0.054
PASP (mmHg)	43.60±12.83	45.33±13.09	−0.995	0.321
P_{PEAK} (mmHg)	26.25±6.38	26.50±6.29	−0.288	0.774

Data are presented as mean ± standard deviation or n (%). ECMO, extracorporeal membrane oxygenation; CHD, coronary heart disease; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; NSIP, nonspecific interstitial pneumonia; IPF, idiopathic pulmonary fibrosis; LTx, lung transplantation; pro-BNP, pro-B-type natriuretic peptide; CKMB, creatine kinase isoenzyme-MB; c-TnI, cardiac troponin I; ALT, alanine aminotransferase; ALB, albumin; TBIL, total bilirubin; BUN, blood urea nitrogen; SCr, serum creatinine; WBC, white blood cell; NEUT, neutrophil ratio; Hb, hemoglobin; PCT, procalcitonin; pH, potential of hydrogen; $PaCO_2$, partial pressure of carbon dioxide in artery; PaO_2, arterial partial pressure of oxygen; HR, heart rate; MAP, mean arterial pressure; SpO_2, saturation of pulse oximetry; PASP, pulmonary artery systolic pressure; P_{PEAK}, peak airway pressure.

Table S2 The comparisons of variables between the low-, moderate-, and high-risk groups

variables	Low-risk groups	Moderate-risk groups	High-risk groups	χ^2/t/Z	P
ECMO				75.980	<0.001
Yes	5 (6.9)	51 (43.2)	48 (82.8)		
No	67 (93.1)	67 (56.8)	10 (17.2)		
Gender				47.594	<0.001
Male	71 (98.6)	102 (86.4)	31 (53.4)		
Female	1 (1.4)	16 (13.6)	27 (46.6)		
CHD	8 (11.1)	7 (5.9)	2 (3.4)	3.254	0.196
DM	4 (5.6)	12 (10.2)	10 (17.2)	4.698	0.095
Hypertension	12 (16.7)	7 (5.9)	2 (3.4)	8.460	0.015
Smoking	65 (90.3)	69 (58.5)	16 (27.6)	53.203	<0.001
Diagnosis				194.007	<0.001
COPD	63 (87.5)	11 (9.3)	0 (0)		
NSIP	6 (8.3)	47 (39.8)	23 (39.7)		
Silicosis	0 (0)	12 (10.2)	3 (5.2)		
Bronchiectasis	0 (0)	7 (5.9)	10 (17.2)		
IPF	0 (0)	28 (23.7)	18 (31.0)		
Lymphangiomyoma	3 (4.2)	13 (11.0)	4 (6.9)		
Surgical type				63.709	<0.001
Double-LTx	6 (8.3)	44 (37.3)	44 (75.9)		
Right-LTx	34 (47.2)	35 (29.7)	4 (6.9)		
Left-LTx	32 (44.4)	39 (33.1)	10 (17.2)		
Log pro-BNP	4.94±1.13	5.03±1.50	6.03±1.79	9.841	<0.001
Log CKMB	2.56±0.51	2.36±0.52	2.45±0.58	3.414	0.034
Log c-TnI	−5.24±2.40	−5.56±2.36	−4.20±2.51	6.278	0.002
ALT (U/L)	23.57±18.34	24.38±23.08	28.00±43.87	0.446	0.641
ALB (g/L)	37.44±5.05	35.47±5.57	34.43±4.23	5.978	0.003
TBIL (µmol/L)	9.66±3.91	10.80±5.34	10.57±4.99	1.211	0.300
BUN (mmol/L)	5.67±3.34	6.19±6.95	5.27±2.67	0.634	0.531
SCr (µmol/L)	67.18±17.75	68.71±19.87	64.45±22.07	0.897	0.409
WBC (10^9/L)	9.83±10.46	9.46±5.82	9.74±3.67	0.068	0.934
NEUT	73.92±11.68	70.81±13.41	73.56±11.28	1.752	0.176
Hb (g/L)	117.72±19.00	122.16±24.66	121.14±23.56	0.858	0.425
PCT (ng/mL)	0.19±0.30	0.54±3.17	0.24±0.30	0.713	0.491
pH	7.37±0.05	7.38±0.05	7.38±0.07	0.868	0.421
$PaCO_2$ (mmHg)	55.89±13.89	50.05±11.07	52.19±11.23	5.310	0.006
PaO_2 (mmHg)	110.28±33.79	119.88±53.15	100.27±44.05	3.624	0.028
HR (beats/minute)	91.29±14.15	90.17±14.34	92.12±15.06	0.383	0.682
MAP (mmHg)	96.77±13.14	93.05±12.88	87.274±9.98	9.556	<0.001
SpO_2 (%)	97.70±3.90	96.82±4.80	94.21±7.20	7.624	0.001
PASP (mmHg)	36.74±8.59	44.63±10.11	52.47±16.76	29.474	<0.001
P_{PEAK} (mmHg)	25.03±6.78	26.13±6.08	28.36±5.86	4.681	0.010

Data are presented as mean ± standard deviation or n (%). ECMO, extracorporeal membrane oxygenation; CHD, coronary heart disease; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; NSIP, nonspecific interstitial pneumonia; IPF, idiopathic pulmonary fibrosis; LTx, lung transplantation; pro-BNP, pro-B-type natriuretic peptide; CKMB, creatine kinase isoenzyme-MB; c-TnI, cardiac troponin I; ALT, alanine aminotransferase; ALB, albumin; TBIL, total bilirubin; BUN, blood urea nitrogen; SCr, serum creatinine; WBC, white blood cell; NEUT, neutrophil ratio; Hb, hemoglobin; PCT, procalcitonin; pH, potential of hydrogen; $PaCO_2$, partial pressure of carbon dioxide in artery; PaO_2, arterial partial pressure of oxygen; HR, heart rate; MAP, mean arterial pressure; SpO_2, saturation of pulse oximetry; PASP, pulmonary artery systolic pressure; P_{PEAK}, peak airway pressure.