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Effects of single versus bilateral lung transplantation on primary graft dysfunction after transplantation

LIU Zijuan, XU Hongyang

Department of Critical Care Medicine, The Affiliated Wuxi People's Hospital of Nanjing Medical University, Wuxi People's Hospital, Wuxi Medical Center, Nanjing Medical University, Wuxi, Jiangsu 214000, China

Corresponding author: XU Hongyang, E-mail: xhy1912@aliyun.com

Abstract: **Objective** To investigate the differences in primary graft dysfunction (PGD) within 72 h post-surgery between recipients of single lung transplantation and bilateral lung transplantation, and to evaluate the risk factors for the development of PGD. **Methods** A retrospective cohort study was conducted to systematically collect and analyze clinical data from 175 lung transplant patients who underwent surgery at Wuxi People's Hospital, Affiliated to Nanjing Medical University, from January to December 2023. Patients were divided into single lung transplantation group (n=58) and bilateral lung transplantation group (n=17) based on transplantation type. Baseline demographic characteristics (such as age, gender, underlying disease), perioperative key indicators [including surgery duration, donor lung cold ischemia time, and extracorporeal membrane oxygenation (ECMO) application], and early postoperative inflammatory markers. Univariate and multivariate logistic regression analyses were used to identify factors influencing the occurrence of PGD. Univariate and multivariate logistic regression analyses were performed to identify factors influencing the occurrence of PGD. Kaplan-Meier method was used for survival analysis, and Log-rank test was applied for significance testing of cumulative survival rates. **Results** The overall incidence rate of 175 lung transplant recipients was 25.14% (44/175). The incidence of PGD was significantly lower in the bilateral lung transplant group than in the single lung transplant group [66.67% (78/117) *vs* 86.21% (50/175), χ^2=7.537, P=0.006], while there was no statistically significant difference in the incidence of severe PGD (31.03% *vs* 22.22%, χ^2=1.600, P=0.206). Significant differences were observed between the two groups in terms of age, surgery duration, donor lung cold ischemia time, intraoperative and postoperative ECMO application, and postoperative inflammatory markers(P<0.05). Univariate and multivariate logistic regression analyses showed that compared with single lung transplantation, bilateral lung transplantation reduced the risk of PGD occurrence (OR=0.160, 95%CI:0.058-0.441, P<0.001). **Conclusion** The incidence of PGD was lower in the double lung transplantation group than in the single lung transplantation group. Compared with single lung transplantation, double lung transplantation can reduce the overall risk of PGD.

Keywords: Primary graft dysfunction; Lung transplantation; Acute lung injury; Bilateral lung transplantation; Extracorporeal membrane oxygenation

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Lung transplantation is the ultimate treatment for end-stage lung disease. However, the survival rate of lung transplant recipients still lags behind that of recipients of other solid organ transplants. Primary graft dysfunction (PGD) is a critical factor contributing to short-term mortality after lung transplantation, affecting nearly one-third of patients[1]. As an acute lung injury clinical syndrome occurring within 72 hours after lung transplantation, PGD is characterized by persistent hypoxemia and bilateral diffuse alveolar infiltrates on chest imaging[2-3]. The underlying mechanism involves lung injury caused by innate immune activation, impaired epithelial and endothelial cell barrier function, and cytokine release during ischemia-reperfusion[4].Lung transplantation can be performed as single or bilateral lung transplantation, and the selection strategy remains controversial. For patients with non-suppurative lung diseases, both bilateral-and single lung transplantation are reasonable options, each with staunch proponents[5]. Single lung transplantation helps alleviate donor shortages, reduces waiting times, and lowers associated morbidity and mortality, making it more suitable for elderly patients with multiple comorbidities. In contrast, bilateral lung transplantation may improve long-term survival and lung function, although evidence remains inconclusive[6].Since the impact of choosing unilateral versus bilateral lung transplantation on postoperative PGD remains undetermined, this study retrospectively analyzed the clinical data of lung transplant recipients at Wuxi People's Hospital Affiliated to Nanjing Medical University in 2023. The aim was to compare the incidence of PGD within 72 h after surgery between unilateral and bilateral lung transplant recipients and evaluate the risk factors for PGD.

1 Materials and methods

1.1 Study subjects

A retrospective analysis was performed on clinical data of patients who underwent lung transplantation at Wuxi People's Hospital Affiliated to Nanjing Medical University from January 2023 to December 2023.

Inclusion criteria: (1) Adult recipients who underwent lung transplantation between January 2023 and December 2023; (2) ICU stay ≥24 hours. **Exclusion criteria:** (1) Re-transplantation; (2) Preoperative use of extracorporeal membrane oxygenation (ECMO); (3) Incomplete or missing clinical data affecting primary outcomes. This study adhered to the ethical standards established by the Research Ethics Committee of Wuxi People's Hospital Affiliated to Nanjing Medical University, and informed consent was waived.

1.2 Study methods

Clinical data of eligible subjects were collected, including baseline data: gender, age, primary disease, underlaying diseases including diabetes, hypertension, pulmonary hypertension, history of coronary atherosclerotic heart disease (CHD)]; preoperative data: preoperative respiratory support, routine preoperative laboratory indicators; intraoperative data: transplant type, operation duration, ECMO application, ECMO mode including veno-venous (VV), venous-arterial (VA), veno-arterio-venous (VAV), and veno-veno-arterial (VVA) modes, donor lung cold ischemia time, intraoperative blood loss, and volume reduction surgery; postoperative data: routine laboratory indicators, postoperative ECMO application, ECMO duration, mechanical ventilation time, sequential ventilation mode, 28-day postoperative mortality, etc.The primary outcome was the development of PGD. Secondary outcomes included 28-day postoperative mortality, ECMO use, and mechanical ventilation duration. PGD was graded according to the criteria of the International Society for Heart and Lung Transplantation (ISHLT). Patients with normal arterial oxygen partial pressure (PaO2)/fractional inspired oxygen (FiO2) and no diffuse pulmonary edema on chest radiography were scored as grade 0. For patients with diffuse pulmonary edema on chest radiography, the grading was as follows: PaO_2/FiO_2 > 300 mmHg as grade 1, 200–300 mmHg as grade 2, and < 200 mmHg as grade 3. Patients requiring continued ECMO after lung transplantation with pulmonary infiltrates were classified as PGD grade 3[7]. Severe PGD was defined as PGD grade.

1.3 Statistical methods

This study conducted using the Zstats software (www.zstats.net), and R version 4.3.3. Continuous variables with a normal distribution were expressed as $\bar{x} \pm s$, and comparisons between two groups were performed using independent samples t-test. Skewed continuous variables were presented as $M(Q_1,Q_3)$ and analyzed using the Mann-Whitney U test (two independent samples rank sum test). Two-group comparisons of ordinal data were performed using the Wilcoxon rank-sum test. Categorical variables were described as n(%) and compared using the chi-square test or Fisher's exact test. Logistic regression analysis was performed with the development of PGD as the primary outcome variable. Variables with a P value < 0.2 in univariate analysis were included in the multivariate logistic regression model, and variables were selected using the stepwise backward elimination method. Kaplan-Meier survival curves were plotted for the two groups, and the log-rank test was used to compare cumulative survival rates. A P-value < 0.05 was considered statistically significant.

2 Results

2.1 General data

This retrospective study initially screened 203 patients who underwent lung transplantation. After excluding 11 cases of retransplantation, 6 cases aged <18 years, and 11 cases with preoperative ECMO use, 175 adult patients were finally included in the analysis. Patients were grouped by transplantation type: 58 cases (33.14%) in the Single lung transplantation group and 117 cases (66.86%) in the bilateral lung transplantation group.

2.1.1 Preoperative baseline data

Baseline data of patients are presented in **Table 1**. Male patients accounted for 81.14%, with a mean age of (53.54 ± 12.41) years. Among primary diseases, idiopathic pulmonary fibrosis (IPF) was the most common (53.76%), followed by silicosis, chronic obstructive pulmonary disease (COPD), and interstitial lung disease (ILD). Compared with the Single lung transplantation group, patients in the bilateral lung transplantation group were significantly younger (P=0.002). There were no statistically significant differences between the two groups in gender, preoperative liver/kidney function, blood routine indicators, or comorbidities such as diabetes, hypertension, coronary heart disease, pulmonary hypertension, and respiratory failure (P>0.05).

2.1.2 Intraoperative conditions

For bilateral lung transplantation, cold ischemia time was defined as that of the second transplanted lung. The bilateral lung transplantation group had significantly longer cold ischemia time (P<0.01), operative duration, and intraoperative blood loss compared to the Single lung group (P<0.01). Most patients received intraoperative ECMO support, with VV-ECMO being the most common modality, and its use was more frequent in the bilateral lung group. There were no significant differences in surgical incision type (clam-shell incision) or lung volume reduction between groups (P>0.05).

Tab.1 Comparison of baseline characteristics and perioperative data between single and bilateral lung transplantation groups

Variable	Single lung transplantation group (*n*=58)	Bilateral lung transplantation group (*n*=117)	$\chi^2/t/Z$ Value	*P* Value
General data				
Gender [a]			0.632	0.426
Male	49 (84.48)	93 (79.49)		
Female	9 (15.52)	24 (20.51)		
Age (years) [b]	57.72 ± 10.75	51.47 ± 12.70	2.961	0.002
Weight (kg) [b]	57.71 ± 10.46	58.45 ± 12.99	0.377	0.711
Diabetes [a]	11 (18.97)	13 (11.11)	2.022	0.155
Hypertension [a]	9 (15.52)	21 (17.95)	0.161	0.927
Coronary heart disease [a]	8 (13.79)	6 (5.13)	3.956	0.138
Pulmonary hypertension [a]	23 (39.66)	44 (37.61)	0.069	0.966
Respiratory failure [a]	33 (56.90)	70 (59.83)	0.138	0.933
Primary disease [a]				0.043[c]
Interstitial lung disease	6 (10.53)	5 (4.31)		
Diopathic pulmonary fibrosis	37 (64.91)	56 (48.28)		
COPD	4 (7.02)	19 (16.38)		
Silicosis	10 (17.54)	19 (16.38)		
Bronchiectasis	0	5 (4.31)		
Bronchiolitis obliterans	0	7 (6.03)		
Primary pulmonary hypertension	0	1 (0.86)		
Pulmonary veno-occlusive disease	0	3 (2.59)		
Pulmonary lymphangioleiomyomatosis	0	1 (0.86)		
Other diseases	1（1.72）	1（0.86）		
Preoperative				
Creatinine (μmol/L) [a]	63.62 ± 17.65	58.24 ± 17.78	1.889	0.061
Urea nitrogen (mmol/L) [a]	6.31 ± 2.30	5.97 ± 2.17	0.956	0.356
Albumin (g/L) [a]	38.64 ± 4.57	38.63 ± 4.59	0.014	0.983
White blood cell count (×10⁹/L) [a]	9.77 ± 2.79	10.35 ± 3.79	1.005	0.316
Hemoglobin (g/L) [a]	134.95 ± 15.93	134.16 ± 19.94	0.264	0.792
Platelet count (×10⁹/L) [a]	243.53 ± 87.68	241.05 ± 74.35	0.195	0.845
Preoperative calcium (mmol/L) [c]	2.24 (2.16, 2.31)	2.25 (2.19, 2.31)	0.583	0.560
Preoperative CRP (mg/dL) [c]	5.40 (1.40, 10.35)	4.90 (0.50, 11.50)	0.607	0.544
Intraoperative				
Intraoperative blood loss (mL) [c]	600.00(500.00, 800.00)	1 000.00(800.00, 1300.00)	6.207	<0.001
Donor lung cold Ischemia time (min) [b]	424.31 ± 85.46	568.43 ± 103.28	9.179	<0.001
Operative time (min) [b]	272.66 ± 70.44	434.93 ± 84.57	12.602	<0.001
Intraoperative ECMO [a]	47 (81.03)	113 (96.58)	10.058	0.002
ECMO mode [a]			17.361	<0.001
None	11 (18.97)	4 (3.42)		
VV	32 (55.17)	95 (81.20)		
VA	12 (20.69)	12 (10.26)		
VAV/VVA	3 (5.17)	6 (5.13)		
Clam-shell incision [a]	0	2 (1.71)		1.000
Lung volume reduction [a]	3 (5.17)	15 (12.82)	2.458	0.117

Variable	Single lung transplantation group (*n*=58)	Bilateral lung transplantation group (*n*=117)	$\chi^2/t/Z$ Value	*P* Value
Postoperative				
PGD grade [a]			7.846	0.049
Grade 0	8 (13.79)	39 (33.33)		
Grade 1	23 (39.66)	35 (29.91)		
Grade 2	9 (15.52)	17 (14.53)		
Grade 3	18 (31.03)	26 (22.22)		
Postoperative ECMO mode [a]			15.750	0.001
None	11 (18.97)	5 (4.27)		
VV	36 (62.07)	97 (82.91)		
VA	10 (17.24)	9 (7.69)		
VAV/VVA	1 (1.72)	6 (5.13)		
Sequential ventilation [a]			3.204	0.524
Failure to wean	5 (8.62)	15 (12.82)		
High-flow nasal cannula	23 (39.66)	39 (33.33)		
Non-invasive ventilation	5 (8.62)	12 (10.26)		
Nasal cannula	1 (1.72)	0		
Alternating high-flow/non-invasive	24 (41.38)	51 (43.59)		
SIRI (×10⁹/L) [c]	4.04 (1.71, 10.10)	12.24 (5.93, 22.43)	5.460	<0.001
WBC (×10⁹/L) [b]	9.75 ± 5.47	12.95 ± 6.79	3.114	0.002
MO (×10⁹/L) [c]	0.36 (0.20, 0.59)	0.53 (0.33, 0.79)	3.032	0.002
LYM (×10⁹/L) [c]	0.67 (0.45, 1.18)	0.49 (0.32, 0.76)	3.121	0.002
WBC (×10⁹/L) [b]	11.04 ± 6.32	14.19 ± 7.31	2.809	0.006
Hemoglobin (g/L) [b]	109.48 ± 16.43	108.29 ± 18.12	0.422	0.673
Hematocrit (%) [b]	33.36 ± 5.19	32.89 ± 5.61	0.544	0.587
Platelet count (×10⁹/L) [b]	184.76 ± 69.65	157.08 ± 63.94	2.617	0.010
Total bilirubin (μmol/L) [b]	26.36 ± 12.79	33.90 ± 19.68	2.652	0.009
Albumin (g/L) [b]	42.18 ± 5.80	39.81 ± 5.59	2.608	0.010
CRP (mg/dL) [c]	5.40 (4.90, 10.90)	7.40 (5.00, 16.50)	1.520	0.127
Urea nitrogen (mmol/L) [c]	5.40 (4.30, 6.60)	5.60 (4.80, 6.80)	1.216	0.224
Calcium (mmol/L) [c]	2.09 (2.00, 2.22)	2.15 (2.00, 2.22)	0.270	0.787
BNP (ng/L) [c]	164.40(89.25, 262.75)	146.00 (89.00, 334.80)	0.328	0.743
SII [b]	2 488.25(992.90, 3 887.15)	3 505.88(1 942.15, 5 948.51)	3.197	0.001
ECMO duration (h) [c]	21.00 (14.25, 57.25)	21.00 (15.00, 60.00)	1.104	0.270
Mechanical Ventilation time (h) [c]	43.50 (26.25, 109.25)	62.00 (39.00, 138.00)	1.764	0.078
Hospital stay (days) [c]	33.50 (24.00, 59.75)	46.00 (28.00, 63.00)	1.282	0.200
ICU stay (days) [c]	5.00 (4.00, 8.00)	5.00 (4.00, 8.00)	0.280	0.780
ICU-free days within 28 d [c]	23.00 (20.00, 24.00)	23.00 (20.00, 24.00)	0.280	0.780
28-d survival days [c]	28.00 (28.00, 28.00)	28.00 (28.00, 28.00)	1.365	0.172
Reintubation within 48 hours [a]	1 (1.72)	1 (0.85)		1.000[c]
Postoperative CRRT [a]	2 (3.45)	15 (12.82)	3.884	0.049
28-d all-cause mortality [a]	6 (10.34)	18 (15.38)	0.832	0.362
WBC (×10⁹/L) [b]	11.04 ± 6.32	14.19 ± 7.31	2.809	0.006
Hemoglobin (g/L) [b]	109.48 ± 16.43	108.29 ± 18.12	0.422	0.673

Note: a, presented as n (%); b, presented as $\bar{x} \pm s$; c, presented as $M(Q_1,Q_3)$; d presented as Fisher's exact test.

2.1.3 Postoperative outcomes

The incidence of severe PGD in this cohort was 25.14%. PGD grades were distributed as follows: grade 1 (58 cases, 33.14%), grade 2 (26 cases, 14.86%), and grade 3 (44 cases, 25.14%). The bilateral lung transplantation group had a significantly lower PGD incidence than the Single lung group (66.67% *vs* 86.21%, χ^2=41.330, *P*<0.01), while the difference in severe PGD incidence was not significant (31.03% *vs* 22.22%, χ^2=1.600, *P*>0.05). Postoperatively, the bilateral lung group exhibited higher levels of neutrophils (NEUT), white blood cells (WBC), systemic inflammatory response index (SIRI), systemic immune inflammation index (SII), monocytes (MO), and total bilirubin, along with lower platelet counts, albumin, and lymphocytes (LYM) (*P*<0.05). Postoperative ECMO was continued in 90.86% of recipients, with more frequent use in the bilateral lung group (predominantly VV-ECMO). The bilateral lung group also had higher utilization of continuous renal replacement therapy (CRRT). There were no significant differences in postoperative ECMO duration, mechanical ventilation time, hospital stay, ICU stay, ICU-free days within 28 days, or 28-day all-cause mortality (*P*>0.05). **[Table.1]**

2.2 Factors associated with the development of PGD

Factors that may influence outcomes were included in univariate logistic regression analysis to identify factors associated with the development of PGD. Univariate analysis showed that compared with Single lung transplantation, bilateral lung transplantation reduced the risk of PGD (*P*=0.008). Additionally, preoperative creatinine, preoperative white blood cell count (WBC), postoperative lymphocyte count (LYM), were identified as risk factors for PGD occurrence (*P* < 0.05), while the sequential use of non-invasive assisted ventilation alternating with nasal high-flow ventilation after extubation was identified as a protective factor (*P*=0.028). **[Table 2]**

Variables with P < 0.2 in the univariate analysis were included in the multivariate logistic regression analysis, and variables were selected using a stepwise backward method. The final model included three independent influencing factors: preoperative WBC, intraoperative blood loss, and transplant type. Among these, double lung transplantation reduced the risk of PGD, while preoperative WBC and intraoperative blood loss were independent risk factors (P < 0.028). **[Table 3]**

Tab.2 Univariate logistic regression analysis of factors affecting PGD

Variable	*β*	*SE*	*P* value	*OR*(95%*CI*)	Variable	*β*	*SE*	*P* value	*OR*(95%*CI*)
Female	0.376	0.465	0.419	1.457(0.586-3.623)	**Volume reduction**	-0.347	0.532	0.514	0.707(0.249-2.005)
Age	-0.001	0.014	0.918	0.999(0.972-1.026)	**Operation time**	-0.002	0.002	0.185	0.998(0.995-1.001)
Body weight	0.027	0.015	0.068	1.027(0.998-1.058)	**Donor lung cold ischemia time**	0	0.001	0.877	1.000(0.997-1.003)
Primary disease					**Intraoperative blood loss**	0	0	0.137	1.000(1.000-1.001)
ILD				1	**Postoperative**				
IPF	0.191	0.720	0.791	1.210(0.295-4.959)	**ECMO mode**				
COPD	-0.894	0.795	0.261	0.409(0.086-1.945)	**None**				1
Silicosis	0.363	0.818	0.657	1.438(0.290-7.138)	**VV**	-0.623	0.668	0.351	0.537(0.145-1.986)
Bronchiectasis	-1.386	1.137	0.223	0.250(0.027-2.319)	**VA**	-0.145	0.853	0.865	0.865(0.163-4.602)
Bronchiolitis obliterans	-0.065	1.076	0.952	0.938(0.114-7.728)	**VAV/VVA**	15.100	906.943	0.987	3 611 852.490(0.000-Inf)
Primary pulmonary hypertension	15.585	2 399.545	0.995	5869260.297(0.000-Inf)	**Sequential ventilation**				
Pulmonary veno-occlusive disease	15.585	1 385.378	0.991	5869 260.296(0.000-Inf)	**Failed weaning**				1
Pulmonary lymphangiomatosis	15.585	2 399.545	0.995	5869 260.297(0.000-Inf)	**High-flow nasal cannula**	-1.888	1.066	0.077	0.151(0.019-1.223)
Diabetes mellitus	1.057	0.643	0.100	2.879(0.817-10.144)	**Non-invasive ventilation**	-1.766	1.175	0.133	0.171(0.017-1.710)
Hypertension	0.455	0.492	0.355	1.577(0.601-4.138)	**Nasal cannula**	11.622	882.744	0.989	111 483.157(0.000-Inf)
Coronary heart disease	0.845	0.784	0.281	2.328(0.501-10.814)	**Alternating high-flow/non-invasive**	-2.311	1.054	0.028	0.099(0.013-0.783)
Pulmonary hypertension	-0.001	0.351	0.998	0.999(0.502-1.988)	**SIRI**	-0.015	0.01	0.137	0.985(0.966-1.005)
Respiratory failure	-0.41	0.356	0.249	0.664(0.330-1.332)	**SII**	0	0	0.558	1.000(1.000-1.000)
Preoperative creatinine	0.027	0.011	0.015	1.028(1.005-1.051)	**NEUT**	0.011	0.027	0.684	1.011(0.959-1.065)
Preoperative urea nitrogen	0.010	0.078	0.901	1.010(0.867-1.176)	**MO**	-0.125	0.404	0.756	0.882(0.400-1.946)
Preoperative calcium	-0.010	0.014	0.497	0.990(0.963-1.018)	**LYM**	0.846	0.408	0.038	2.330(1.048-5.180)
Preoperative albumin	-0.026	0.038	0.492	0.974(0.904-1.050)	**WBC**	0.012	0.025	0.627	1.012(0.964-1.062)
Preoperative white blood cell	0.13	0.057	0.024	1.139(1.018-1.274)	**Hemoglobin**	0.012	0.01	0.213	1.013(0.993-1.033)
Preoperative hemoglobin	0.005	0.009	0.597	1.005(0.987-1.023)	**Hematocrit**	0.043	0.032	0.184	1.044(0.980-1.112)
Preoperative platelets	0.002	0.002	0.306	1.002(0.998-1.007)	**Platelet count**	0.001	0.003	0.626	1.001(0.996-1.006)
Preoperative CRP	0.002	0.009	0.817	1.002(0.985-1.020)	**CRP**	0.007	0.01	0.443	1.007(0.989-1.027)
Transplant type					**Total bilirubin**	-0.006	0.009	0.498	0.994(0.977-1.012)
Single lung transplant				1	**Albumin**	0.003	0.03	0.926	1.003(0.946-1.063)
bilateral lung transplant	-1.139	0.428	0.008	0.320(0.138-0.741)	**Urea nitrogen**	-0.026	0.02	0.212	0.975(0.937-1.015)
Intraoperative ECMO	-0.417	0.669	0.533	0.659(0.178-2.447)	**Calcium**	-0.114	0.871	0.896	0.893(0.162-4.920)
Clam-shell incision	14.58	1 029.121	0.989	2147755.591(0-Inf)	**BNP**	0	0	0.259	1.000(1.000-1.001)

2.3 Survival Analysis

The 28-day mortality rate for the entire cohort was 13.71%, with no statistically significant difference observed between the single-lung transplantation group and the double-lung transplantation group ($P > 0.05$). The Kaplan-Meier survival analysis results were consistent with this finding, as shown in **Fig. 1**. Additionally, the severity of PGD was associated with short-term mortality, and compared to no PGD, PGD grade 1, and PGD grade 2, PGD grade 3 significantly increased the risk of short-term mortality ($P < 0.05$). See **Fig. 2.**

Tab.3 Multivariate logistic regression analysis of factors affecting PGD

Variable	*β*	*SE*	*P* value	*OR (95%CI)*
Body weight	0.03	0.017	0.071	1.030 (0.997-1.065)
Preoperative creatinine	0.018	0.013	0.151	1.019 (0.993-1.044)
Preoperative WBC	0.171	0.063	0.007	1.186 (1.048-1.343)
bilateral lung transplantation	-1.831	0.516	<0.001	0.160 (0.058-0.441)
Intraoperative blood loss	0.001	<0.001	0.03	1.001 (1.001-1.002)

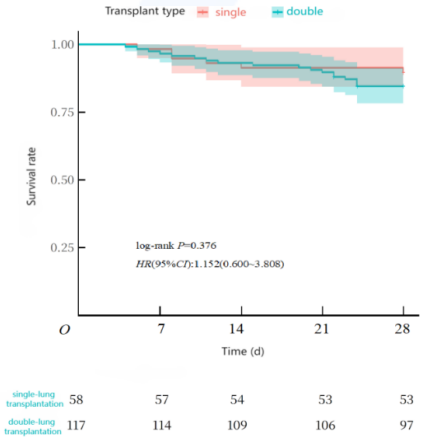

Fig.1 Kaplan-Meier survival curves for patients with different type of lung transplantation

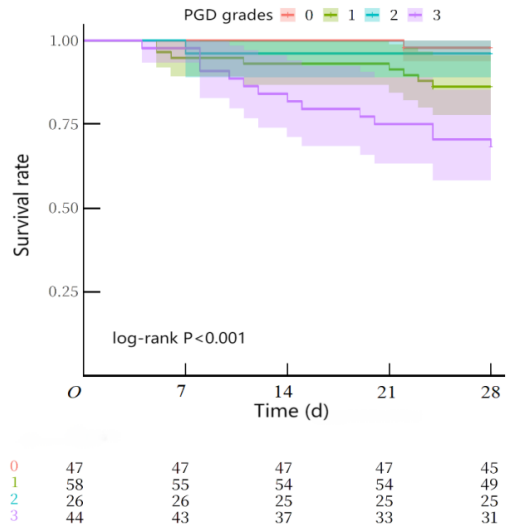

Fig.2 Kaplan-Meier survival curves for different PGD patients

3 Discussion

Lung transplantation is an irreplaceable ultimate treatment option for patients with end-stage lung disease [8]. However, PGD, as the main form of acute lung injury after lung transplantation, seriously threatens patient prognosis. Its pathological features include pulmonary edema, decreased lung compliance, gas exchange disorders, and increased pulmonary vascular resistance. The 2012 Berlin Definition of Acute Respiratory Distress Syndrome (ARDS) mentions that PGD can be regarded as an independent phenotype of ARDS, where lung transplantation is the clinical injury factor leading to this phenotype [9]. With the increasing number of lung transplants, attention should be paid to the differential impact of different transplant types on PGD, which is crucial for optimizing perioperative management strategies.

This study included 175 lung transplant recipients (58 in the Single lung transplantation group and 117 in the bilateral lung transplantation group), with an overall incidence of grade PGD of 25.14%, consistent with the internationally reported range of 25% to 30% [10-11]. The study found that the total incidence of PGD in the bilateral lung transplantation group was significantly lower than that in the Single lung transplantation group, but there was no statistically significant difference in the incidence of severe PGD between the two groups. Multivariate analysis showed that compared with Single lung transplantation, bilateral lung transplantation could reduce the risk of PGD. The possible mechanisms include the following three aspects.

(1) Hemodynamic changes and reperfusion injury: after Single lung transplantation, the native lung coexists with the transplanted lung. If the native lung has COPD or IPF, its pulmonary vascular resistance is usually significantly higher than that of the transplanted lung. During mechanical ventilation, blood flow is preferentially perfused to the transplanted lung with lower resistance, leading to ventilation/perfusion mismatch, overinflation of the native lung, increased capillary pressure, endothelial damage, and edema, which exacerbates reperfusion injury and PGD risk [12-13]. (2) differences in inflammatory response: bilateral lung transplantation completely removes end-stage diseased lungs (such as chronic inflammatory foci in COPD and IPF), reducing the impact of residual infection or inflammation on the transplanted lung. (3) protective effect of ECMO: The usage rate of intraoperative and postoperative VV-ECMO was higher in the bilateral lung transplantation group, which can provide stable oxygenation and ventilation, effectively reduce mechanical ventilation stress injury to the transplanted lung, lower pulmonary artery pressure and right heart load, and provide "rest" conditions for the lungs, thereby alleviating ischemia-reperfusion injury [14].

The 2019 Annual Report of the International Society for Heart and Lung Transplantation showed that long-term survival rates of bilateral lung transplant recipients are better than those of Single lung transplant recipients [8], but this advantage disappears in recipients over 60 years old [15]. In this study, the age in the Single lung group was significantly higher than that in the bilateral lung group [(57.72±10.75) years *vs* (51.47±12.70) years, P=0.002], which is consistent with our center's strategy of preferentially selecting Single lung transplantation for elderly and high-risk patients. Although this study did not find differences in short-term survival prognosis between the two groups in different age groups, the results of Weingarten *et al.* [6] showed that Single lung transplantation may result in lower morbidity and better short-term survival for elderly patients, but 5-year survival rates are still lower than bilateral lung transplantation. This indicates that Single lung transplantation is acceptable for elderly patients at higher risk of

not tolerating bilateral lung transplantation. Similarly, Leong *et al.* [16] suggested that the benefits of bilateral lung transplantation over Single lung transplantation diminish with increasing age, indicating that Single lung transplantation may still be a viable option for elderly patients.

Casillan *et al.* [17] found that donor lung cold ischemia time exceeding 6 h increases 30-day and 1-year mortality after first bilateral lung transplantation, but has no significant impacts on Single lung transplantation. In this study, cold ischemia time and intraoperative blood loss in the bilateral lung group were significantly higher than those in the Single lung group. Univariate analysis found that both were risk factors for PGD, while only intraoperative blood loss was an independent risk factor after stepwise regression analysis. This may indicate that surgical trauma-related inflammatory responses are more critical for PGD development [18]. Although the bilateral lung transplantation group showed stronger signs of systemic inflammatory response postoperatively, this did not translate into higher PGD risk. Possible explanations are that ECMO support mitigates the direct impact of inflammatory responses on transplanted lung oxygenation function; or bilateral lung transplantation provides greater physiological reserve, enabling patients to maintain adequate ventilation even in inflammatory states [15].

Indications and prognosis differ between Single lung and bilateral lung transplantation. For COPD patients, Benvenuto *et al.* [19] suggested that right Single lung transplantation and bilateral lung transplantation have similar short-term and long-term survival rates, while bilateral lung transplantation may provide more durable survival benefits. For ILD patients, Watanabe *et al.* [20] found that long-term survival rates of Single lung transplantation are similar to non-ILD patients. This study found no significant difference in short-term survival rates between the two groups, but grade 3 PGD significantly increased short-term mortality risk (P<0.05). Christie *et al.* [21] also suggested that grade 3 PGD is associated with increased morbidity and mortality after lung transplantation and prolongs mechanical ventilation and hospital stay. These results indicate that surgical approach selection requires individualized assessment, and preventing severe PGD is crucial for improving prognosis.

As lung transplantation technology enters the era of precision medicine, innovations in surgical techniques and optimization of perioperative management provide more possibilities for shortening cold ischemia time and reducing PGD risk. This single-center retrospective study found that bilateral lung transplantation can reduce PGD risk, which may be related to younger patients, routine application of VV-ECMO to mitigate reperfusion injury, and the impact of native lung in Single lung transplantation. Meanwhile, preoperative white blood cells and intraoperative blood loss were identified as independent risk factors for PGD. It should be noted that although bilateral lung transplantation reduces overall PGD risk, there were no significant differences in severe PGD incidence and 28-day mortality between the two groups. Due to limitations such as limited sample size, potential selection bias, and confounding factors, conclusions should be extrapolated with caution. Future multicenter large-sample studies are needed to more comprehensively evaluate the impact of different transplant types on PGD and other complications and provide more reliable evidence for clinical decision-making.

Conflict of interest None

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·论　著·

单侧肺移植与双侧肺移植对术后原发性移植物功能障碍的影响

刘紫娟，　许红阳

南京医科大学无锡医学中心　南京医科大学附属无锡人民医院重症医学科，　江苏 无锡 214000

摘要：目的　探讨单肺移植和双肺移植对肺移植受者术后 72 h 发生原发性移植物功能障碍（PGD）的差异性，并评估影响 PGD 的危险因素。**方法**　采用回顾性队列研究，系统收集并分析 2023 年 1 月至 12 月南京医科大学附属无锡市人民医院接受肺移植手术 175 例患者的临床资料，根据移植类型分为单肺移植组（n=58）和双肺移植组（n=117），比较两组间基线人口学特征（如年龄、性别、原发病）、围手术期关键指标［包括手术时长、供肺冷缺血时间、体外膜肺氧合（ECMO）应用情况］及术后早期炎症指标。使用单因素和多因素 logistic 回归筛选影响 PGD 发生的因素，并采用 Kaplan-Meier 法进行生存分析，log-rank 法进行累积生存率的显著性检验。**结果**　175 例患者重度 PGD 发生率为 25.14%（44/175）。双肺移植组 PGD 发生率显著低于单肺移植组［66.67%（78/117）*vs* 86.21%（50/58），χ^2=41.330，P < 0.01］，而双肺和单肺移植重度 PGD 的发生率差异无统计学意义（31.03% *vs* 22.22%，P > 0.05）。两组年龄、手术时间、供肺冷缺血时间、术中及术后 ECMO 的应用、术后炎症指标方面差异均有统计学意义（P<0.05）。单因素和多因素 logistic 回归分析均显示，相较于单肺移植，双肺移植降低 PGD 发生风险（OR=0.160，95%CI：0.058~0.441，P<0.01）。整个队列 28 d 病死率为 13.71%，单肺移植组与双肺移植组 28 d 病死率差异无统计学意义（P>0.05）。生存分析显示，PGD 严重程度与短期死亡率相关，且相较于无 PGD、PGD1 级、PGD2 级，PGD3 级会显著增加短期死亡风险（P<0.05）。**结论**　双肺移植组 PGD 发生率低于单肺移植组，与单肺移植相比，双肺移植能降低总体 PGD 风险。

关键词：原发性移植物功能障碍；肺移植；急性肺损伤；双肺移植；体外膜肺氧合

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Effects of single versus bilateral lung transplantation on primary graft dysfunction after lung transplantation

LIU Zijuan, XU Hongyang

Department of Critical Care Medicine, The Affiliated Wuxi People's Hospital of Nanjing Medical University, Wuxi Medical Center, Nanjing Medical University, Wuxi, Jiangsu 214000, China

Corresponding author: XU Hongyang, E-mail: xhy1912@aliyun.com

Abstract: Objective　To investigate the differences in primary graft dysfunction (PGD) within 72 h post-surgery between recipients of single lung transplantation and bilateral lung transplantation, and to evaluate the risk factors for the development of PGD. **Methods**　A retrospective cohort study was conducted to systematically collect and analyze clinical data from 175 lung transplant patients who underwent surgery at the Affiliated Wuxi People's Hospital of Nanjing Medical University, from January to December 2023. Patients were divided into single lung transplantation group (n=58) and bilateral lung transplantation group (n=117) based on transplantation type. Baseline demographic characteristics (such as age, gender and underlying disease), perioperative key indicators [including surgery duration, donor lung cold ischemia time, application of extracorporeal membrane oxygenation (ECMO)], and early postoperative inflammatory markers were compared between two groups. Univariate and multivariate logistic regression analyses were

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通信作者：许红阳，E-mail：xhy1912@aliyun.com

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used to identify factors influencing the development of PGD. Kaplan-Meier method was used for survival analysis, and log-rank test was applied for significance testing of cumulative survival rates. **Results** The incidence of severe PGD among 175 lung transplant recipients was 25.14% (44/175). The incidence of PGD was significantly lower in the bilateral lung transplant group than that in the single lung transplant group [66.67% (78/117) *vs* 86.21% (50/58), χ^2=41.330, $P<0.01$], while there was no statistically significant difference in the incidence of severe PGD between the bilateral and single groups (31.03% *vs* 22.22%, $P>0.05$). Significant differences were observed between the two groups in terms of age, surgery duration, donor lung cold ischemia time, intraoperative and postoperative ECMO application, and postoperative inflammatory markers (P<0.05). Univariate and multivariate logistic regression analyses showed that compared with single lung transplantation, bilateral lung transplantation reduced the risk of PGD development (*OR*=0.160, 95%*CI*: 0.058-0.441, P<0.01). The 28-day mortality of the entire cohort was 13.71%. There was no statistically significant difference in 28-day mortality between the single lung transplantation group and the bilateral lung transplantation group (P>0.05). Survival analysis showed that the severity of PGD was associated with short-term mortality, and compared with no PGD, PGD grade 1, and PGD grade 2, PGD grade 3 significantly increased the risk of short-term death (P<0.05). **Conclusion** The incidence of PGD is lower in the bilateral lung transplantation group than that in the single lung transplantation group. Compared with single lung transplantation, bilateral lung transplantation can reduce the overall risk of PGD.

Keywords: Primary graft dysfunction; Lung transplantation; Acute lung injury; Bilateral lung transplantation; Extracorporeal membrane oxygenation

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肺移植是终末期肺疾病的最终治疗手段，肺移植受者的存活率仍落后于其他实体器官移植受者。原发性移植物功能障碍(primary graft dysfunction，PGD)是肺移植术后短期死亡的重要因素，影响近三分之一的患者[1]。PGD作为肺移植后72 h内出现的急性肺损伤临床综合征，其典型表现为持续性低氧血症、胸部影像学双侧弥漫性肺泡浸润[2-3]，潜在机制是缺血再灌注期间由先天免疫激活、上皮和内皮细胞屏障功能受损以及细胞因子释放引起的肺损伤[4]。

肺移植可为单侧和双侧肺移植，选择策略仍存在争议。对于非化脓性肺病患者，双肺移植和单肺移植都是合理选项，每种策略都有其坚定的支持者[5]。单肺移植有助于缓解供体短缺问题，缩短等待时间，减少相关发病率及死亡率，更适合高龄、共病多的患者。而双肺移植可能改善长期生存率和肺功能，但证据尚不明确[6]。

由于单侧与双侧肺移植的选择对术后72 h PGD的影响尚无定论，本研究回顾性分析2023年南京医科大学附属无锡人民医院的肺移植受者临床资料，旨在比较单侧和双侧肺移植对肺移植受者术后72 h发生PGD的差异，并评估PGD的危险因素。

1 对象与方法

1.1 *研究对象* 对2023年1月至2023年12月在南京医科大学附属无锡人民医院接受肺移植手术的患者临床资料进行回顾性分析。纳入标准：(1) 在2023年1月至2023年12月接受肺移植的成年受者；(2) 住ICU时间≥24 h。排除标准：(1) 二次移植；(2) 术前应用体外膜肺氧合(extracorporeal membrane oxygenation，ECMO)；(3) 影响主要结果的临床资料不全或缺失。本研究遵循南京医科大学附属无锡人民医院科研伦理委员会所制定的伦理学标准(批件号：KY25120)。

1.2 *研究方法* 收集符合纳入标准研究对象的临床资料，基线资料包括性别、年龄、原发病、基础疾病[糖尿病、高血压、肺动脉高压、冠状动脉粥样硬化性心脏病(冠心病)病史]；术前资料包括术前呼吸支持、术前常规实验室指标；术中资料包括移植类型、手术时间、是否应用ECMO、ECMO模式[包括静脉-静脉(veno-venous，VV)、静脉-动脉(venous-arterial，VA)、静脉-动脉-静脉(veno-arterio-venous，VAV)和静脉-静脉-动脉(veno-veno-arterial，VVA)模式]、供肺冷缺血时间、术中失血量、是否进行减容手术；术后资料包括常规实验室指标、术后是否应用ECMO、ECMO时间、机械通气时间、序贯通气方式、术后28 d病死率等。

主要结局是PGD的发生，次要结局是术后28 d病死率、ECMO、机械通气应用情况。根据国际心肺移植学会(International Society for Heart and Lung

Transplantation, ISHLT)的标准对PGD进行分级。动脉血氧分压(arterial oxygen partial pressure, PaO_2)/吸入氧浓度(fractional inspired oxygen, FiO_2)正常且X线胸片上无弥漫性肺水肿的患者评分为0。X线胸片上显示弥漫性肺水肿患者的分级:PaO_2/FiO_2>300 mmHg为1级,200~300 mmHg为2级,<200 mmHg为3级。肺移植后继续进行ECMO的患者,如果表现出肺部浸润,则被归类为PGD 3级[7]。重度PGD指PGD 3级。

1.3　统计学方法　本研究采用Zstats软件(www.zstats.net)和R version 4.3.3完成。其中正态分布的连续变量采用$\bar{x}\pm s$表示,两组间的比较采用独立样本t检验;偏态分布的连续变量采用$M(Q_1, Q_3)$表示,采用两独立样本的秩和检验;等级资料的两组比较采用Wilcoxon秩和检验。分类变量采用例(%)表示,采用χ^2检验或Fisher确切概率法。以PGD的发生作为主要结局变量进行logistic回归分析,将单因素分析中P<0.2的变量纳入多因素logistic回归模型,并采用逐步向后法筛选变量。采用Kaplan-Meier法绘制两组的生存曲线,log-rank法进行累积生存率的显著性检验。P<0.05为差异有统计学意义。

2　结　果

2.1　一般资料　本次回顾性研究筛选了203例接受肺移植手术的患者,排除二次移植11例、年龄小于18岁6例、术前应用ECMO 11例,最终纳入175例接受肺移植手术的成年患者进行分析,根据移植类型进行分组,单肺移植组有58例,占比33.14%,双肺移植组有117例,占比66.86%。

2.1.1　术前一般情况　患者的基线资料见表1。男性占比81.14%,年龄为(53.54 ± 12.41)岁。原发病中,以肺间质纤维化(idiopathic pulmonary fibrosis, IPF)最常见(53.14%),其次是矽肺、慢性阻塞性肺疾病(chronic obstructive pulmonary disease, COPD)、间质性肺病(interstitial lung disease, ILD)。与单肺移植组相比,双肺移植组患者更年轻(P=0.002)。两组性别、体质量、术前肝肾功能、血常规指标、糖尿病、高血压、冠心病、肺动脉高压、呼吸衰竭等基础疾病方面差异无统计学意义(P>0.05)。

2.1.2　术中情况　将双肺移植的供肺冷缺血时间定义为第二侧移植肺的冷缺血时间,双肺移植组的供肺冷缺血时间显著长于单肺移植组(P<0.01)。相较于单肺移植组,双肺移植组的手术时间长、术中失血量也更多(P<0.01)。大多数患者术中应用ECMO辅助,且双肺移植组术中使用ECMO占比更高,其中VV-ECMO最多见(P<0.01)。两组在手术切口(是否为clam-shell切口)、肺减容方面差异无统计学意义(P>0.05)。见表1。

2.1.3　术后情况　该队列重度PGD发生率为25.14%。PGD 1级共58例(33.14%),2级26例(14.86%),3级44例(25.14%)。双肺移植组PGD发生率显著低于单肺移植组(66.67% *vs* 86.21%, χ^2=41.330, P < 0.01),而双肺和单肺移植组重度PGD发生率差异无统计学意义(31.03% *vs* 22.22%, P > 0.05)。双肺移植组术后中性粒细胞计数(NEUT)、白细胞计数(WBC)、全身炎症反应指数(systemic inflammatory response index, SIRI)、全身免疫反应指数(systemic immune inflammation index, SII)、单核细胞计数(MO)、总胆红素更高,血小板计数、白蛋白、淋巴细胞计数(LYM)更低(P<0.05)。术后90.86%的受者继续使用ECMO,双肺移植组ECMO应用更多,且同样以VV-ECMO最多见。双肺移植组术后连续性肾脏替代治疗(continuous renal replacement therapy, CRRT)的应用更多(P<0.05)。两组在术后ECMO应用时间、机械通气时间、住院天数、ICU天数、28 d内无ICU天数、28 d全因死亡率方面差异无统计学意义(P>0.05)。见表1。

2.2　影响PGD发生的相关因素分析　将可能对PGD产生影响的因素纳入单因素logistic回归分析,筛选出与PGD发生相关的因素。单因素分析显示,相较于单肺移植,双肺移植降低PGD风险(P= 0.008)。此外,术前肌酐、术前WBC、术后LYM是PGD发生的危险因素(P<0.05),术后脱机拔管后序贯使用无创辅助通气交替经鼻高流量通气是其保护因素(P=0.028)。见表2。

将单因素分析中P<0.2的变量纳入多因素logistic回归分析,并采用逐步向后法筛选变量,最终包含术前WBC、术中失血量、移植类型3个独立影响因素。其中,双肺移植能降低PGD发生风险,术前WBC和术中失血量高是独立危险因素(P<0.05)。见表3。

2.3　生存分析　整个队列28 d病死率为13.71%,单肺移植组与双肺移植组28 d病死率差异无统计学意义(P > 0.05)。Kaplan-Meier生存分析结果与之一致,见图1。此外,PGD严重程度与短期死亡率相关,且相较于无PGD、PGD1级、PGD2级,PGD3级会显著增加短期死亡风险(P<0.05)。见图2。

表1 两组患者基线特征及围手术期资料比较

Tab.1 Comparison of baseline characteristics and perioperative data between single and bilateral lung transplantation groups

变量	单肺移植组（n=58）	双肺移植组（n=117）	$\chi^2/t/Z$值	P值
一般资料				
性别[a]				
男	49（84.48）	93（79.49）	0.632	0.426
女	9（15.52）	24（20.51）		
年龄（岁）[b]	57.72±10.75	51.47±12.70	3.219	0.002
体质量（kg）[b]	57.71±10.46	58.45±12.99	0.377	0.711
糖尿病[a]	11（18.97）	13（11.11）	2.022	0.155
高血压[a]	9（15.52）	21（17.95）	0.161	0.927
冠心病[a]	8（13.79）	6（5.13）	3.956	0.138
肺动脉高压[a]	23（39.66）	44（37.61）	0.069	0.966
呼吸衰竭[a]	33（56.90）	70（59.83）	0.138	0.933
原发病[a]				
ILD	6（10.34）	5（4.27）		
IPF	37（63.79）	56（47.86）		
COPD	4（6.90）	19（16.24）		
矽肺	10（17.24）	19（16.24）		
支气管扩张	0	5（4.27）		0.053[d]
闭塞性细支气管炎	0	7（5.98）		
原发性肺动脉高压	0	1（0.85）		
肺静脉闭塞症	0	3（2.56）		
肺淋巴管瘤病	0	1（0.85）		
其他疾病	1（1.72）	1（0.85）		
术前				
肌酐（μmol/L）[a]	63.62±17.65	58.24±17.78	1.889	0.061
尿素氮（mmol/L）[a]	6.31±2.30	5.97±2.17	0.956	0.340
白蛋白（g/L）[a]	38.64±4.57	38.63±4.59	0.014	0.983
白细胞计数（×10⁹/L）[a]	9.77±2.79	10.35±3.79	1.034	0.302
血红蛋白（g/L）[a]	134.95±15.93	134.16±19.94	0.264	0.792
血小板计数（×10⁹/L）[a]	243.53±87.68	241.05±74.35	0.195	0.845
术前钙（mmol/L）[c]	2.24（2.16，2.31）	2.25（2.19，2.31）	0.583	0.560
术前CRP（mg/dL）[c]	5.40（1.40，10.35）	4.90（0.50，11.50）	0.607	0.544
术中				
术中失血量（mL）[c]	600.00（500.00，800.00）	1 000.00（800.00，1300.00）	6.207	<0.001
供肺冷缺血时间（min）[b]	424.31±85.46	568.43±103.28	9.179	<0.001
手术时间（min）[b]	272.66±70.44	434.93±84.57	12.602	<0.001
术中ECMO[a]	47（81.03）	113（96.58）	10.058	0.002
ECMO模式[a]				
无	11（18.97）	4（3.42）		
VV	32（55.17）	95（81.20）	17.630	<0.001
VA	12（20.69）	12（10.26）		
VAV/VVA	3（5.17）	6（5.13）		
Clam-shell切口[a]	0	2（1.71）		1.000[d]
减容[a]	3（5.17）	15（12.82）	2.458	0.117
术后				
PGD分级[a]				
0	8（13.79）	39（33.33）		
1	23（39.66）	35（29.91）	2.231	0.026[e]
2	9（15.52）	17（14.53）		
3	18（31.03）	26（22.22）		
术后ECMO模式[a]				
无	11（18.97）	5（4.27）		
VV	36（62.07）	97（82.91）	15.750	0.001
VA	10（17.24）	9（7.69）		
VAV/VVA	1（1.72）	6（5.13）		
序贯通气[a]				
无法脱机	5（8.62）	15（12.82）		
经鼻高流量	23（39.66）	39（33.33）		
无创辅助通气	5（8.62）	12（10.26）	3.204	0.524
鼻导管吸氧	1（1.72）	0		
高流量与无创交替	24（41.38）	51（43.59）		
SIRI（×10⁹/L）[c]	4.04（1.71，10.10）	12.24（5.93，22.43）	5.460	<0.001
NEUT（×10⁹/L）[b]	9.75±5.47	12.95±6.79	3.114	0.002
MO（×10⁹/L）[c]	0.36（0.20，0.59）	0.53（0.33，0.79）	3.032	0.002
LYM（×10⁹/L）[c]	0.67（0.45，1.18）	0.49（0.32，0.76）	3.121	0.002
WBC（×10⁹/L）[b]	11.04±6.32	14.19±7.31	2.809	0.006
血红蛋白（g/L）[b]	109.48±16.43	108.29±18.12	0.422	0.673
红细胞压积（%）[b]	33.36±5.19	32.89±5.61	0.544	0.587
血小板计数（×10⁹/L）[b]	184.76±69.65	157.08±63.94	2.617	0.010
总胆红素（μmol/L）[b]	26.36±12.79	33.90±19.68	2.652	0.009
白蛋白（g/L）[b]	42.18±5.80	39.81±5.59	2.608	0.010
CRP（mg/dL）[c]	5.40（4.90，10.90）	7.40（5.00，16.50）	1.520	0.127
尿素氮（mmol/L）[c]	5.40（4.30，6.60）	5.60（4.80，6.80）	1.216	0.224
血钙（mmol/L）[c]	2.09（2.00，2.22）	2.15（2.00，2.22）	0.270	0.787
BNP（ng/L）[c]	164.40（89.25，262.75）	146.00（89.00，334.80）	0.328	0.743
SII[b]	2 488.25（992.90，3 887.15）	3 505.88（1 942.15，5 948.51）	3.197	0.001
ECMO时间（h）[c]	21.00（14.25，57.25）	21.00（15.00，60.00）	1.104	0.270
机械通气时间（h）[c]	43.50（26.25，109.25）	62.00（39.00，138.00）	1.764	0.078
住院天数（天）[c]	33.50（24.00，59.75）	46.00（28.00，63.00）	1.282	0.200
ICU时间（天）[c]	5.00（4.00，8.00）	5.00（4.00，8.00）	0.280	0.780
28 d无ICU时间（天）[c]	23.00（20.00，24.00）	23.00（20.00，24.00）	0.280	0.780
28 d存活天数（天）[c]	28.00（28.00，28.00）	28.00（28.00，28.00）	1.365	0.172
48 h再插管[a]	1（1.72）	1（0.85）		1.000[d]
术后CRRT[a]	2（3.45）	15（12.82）	3.884	0.049
术后28 d死亡[a]	6（10.34）	18（15.38）	0.832	0.362

注：[a]为数据以例（%）表示；[b]为数据以$\bar{x}\pm s$表示；[c]为数据以$M(Q_1,Q_3)$表示；[d]为采用Fisher确切概率法；[e]为采用等级资料比较的Wilcoxon秩和检验。CRP（C反应蛋白）；BNP（B型利钠肽）。

表 2　影响 PGD 的单因素 logistic 回归分析

Tab.2　Univariate logistic regression analysis of factors affecting PGD

变量	β	SE	P 值	OR(95%CI)	变量	β	SE	P 值	OR(95%CI)
性别为女	0.376	0.465	0.419	1.457(0.586~3.623)	减容	−0.347	0.532	0.514	0.707(0.249~2.005)
年龄	−0.001	0.014	0.918	0.999(0.972~1.026)	手术时间	−0.002	0.002	0.185	0.998(0.995~1.001)
体质量	0.027	0.015	0.068	1.027(0.998~1.058)	供肺冷缺血时间	0	0.001	0.877	1.000(0.997~1.003)
原发病					术中失血量	0	0	0.137	1.000(1.000~1.001)
ILD				1	术后				
IPF	0.191	0.720	0.791	1.210(0.295~4.959)	ECMO 模式				
COPD	−0.894	0.795	0.261	0.409(0.086~1.945)	无				1
矽肺	0.363	0.818	0.657	1.438(0.290~7.138)	VV	−0.623	0.668	0.351	0.537(0.145~1.986)
支气管扩张	−1.386	1.137	0.223	0.250(0.027~2.319)	VA	−0.145	0.853	0.865	0.865(0.163~4.602)
闭塞性细支气管炎	−0.065	1.076	0.952	0.938(0.114~7.728)	VAV/VVA	15.100	906.943	0.987	3 611 852.490(0~Inf)
原发性肺动脉高压	15.585	2 399.545	0.995	5 869 260.297(0~Inf)	序贯通气				
肺静脉闭塞症	15.585	1 385.378	0.991	5 869 260.296(0~Inf)	无法脱机				1
肺淋巴管瘤病	15.585	2 399.545	0.995	5 869 260.297(0~Inf)	经鼻高流量	−1.888	1.066	0.077	0.151(0.019~1.223)
糖尿病	1.057	0.643	0.100	2.879(0.817~10.144)	无创辅助通气	−1.766	1.175	0.133	0.171(0.017~1.710)
高血压	0.455	0.492	0.355	1.577(0.601~4.138)	鼻导管吸氧	11.622	882.744	0.989	111 483.157(0~Inf)
冠心病	0.845	0.784	0.281	2.328(0.501~10.814)	高流量与无创交替	−2.311	1.054	0.028	0.099(0.013~0.783)
肺动脉高压	−0.001	0.351	0.998	0.999(0.502~1.988)	SIRI	−0.015	0.010	0.137	0.985(0.966~1.005)
呼吸衰竭	−0.410	0.356	0.249	0.664(0.330~1.332)	SII	0	0	0.558	1.000(1.000~1.000)
术前肌酐	0.027	0.011	0.015	1.028(1.005~1.051)	NEUT	0.011	0.027	0.684	1.011(0.959~1.065)
术前尿素氮	0.010	0.078	0.901	1.010(0.867~1.176)	MO	−0.125	0.404	0.756	0.882(0.400~1.946)
术前血钙	−0.010	0.014	0.497	0.990(0.963~1.018)	LYM	0.846	0.408	0.038	2.330(1.048~5.180)
术前白蛋白	−0.026	0.038	0.492	0.974(0.904~1.050)	WBC	0.012	0.025	0.627	1.012(0.964~1.062)
术前 WBC	0.130	0.057	0.024	1.139(1.018~1.274)	血红蛋白	0.012	0.010	0.213	1.013(0.993~1.033)
术前血红蛋白	0.005	0.009	0.597	1.005(0.987~1.023)	红细胞压积	0.043	0.032	0.184	1.044(0.980~1.112)
术前血小板	0.002	0.002	0.306	1.002(0.998~1.007)	血小板计数	0.001	0.003	0.626	1.001(0.996~1.006)
术前 CRP	0.002	0.009	0.817	1.002(0.985~1.020)	CRP	0.007	0.010	0.443	1.007(0.989~1.027)
移植类型					总胆红素	−0.006	0.009	0.498	0.994(0.977~1.012)
单肺移植				1	白蛋白	0.003	0.030	0.926	1.003(0.946~1.063)
双肺移植	−1.139	0.428	0.008	0.320(0.138~0.741)	尿素氮	−0.026	0.020	0.212	0.975(0.937~1.015)
术中 ECMO	−0.417	0.669	0.533	0.659(0.178~2.447)	血钙	−0.114	0.871	0.896	0.893(0.162~4.920)
Clam-shell 切口	14.58	1 029.121	0.989	2 147 755.591(0~Inf)	BNP	0	0	0.259	1.000(1.000~1.001)

表 3　影响 PGD 的多因素 logistic 回归分析

Tab.3　Multivariate logistic regression analysis of factors affecting PGD

变量	β	SE	P 值	OR (95%CI)
体质量	0.030	0.017	0.071	1.030 (0.997~1.065)
术前肌酐	0.018	0.013	0.151	1.019 (0.993~1.044)
术前 WBC	0.171	0.063	0.007	1.186 (1.048~1.343)
双肺移植	−1.831	0.516	<0.001	0.160 (0.058~0.441)
术中失血量	0.001	<0.001	0.030	1.001 (1.001~1.002)

3　讨　论

肺移植是终末期肺疾病患者不可替代的终极治疗选择[8]。然而，PGD 作为肺移植术后急性肺损伤的主要形式，严重威胁患者预后。其病理特征包括肺

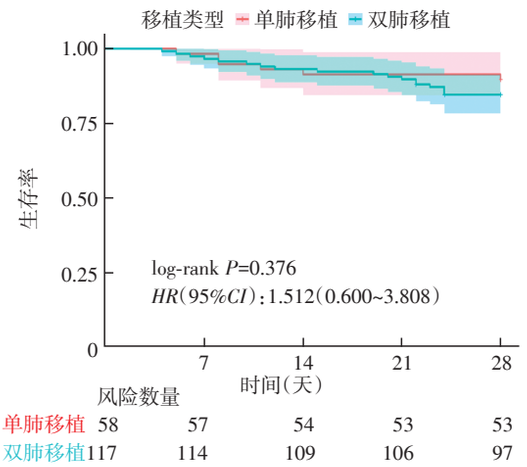

图 1　不同肺移植类型患者的 Kaplan-Meier 生存曲线

Fig.1　Kaplan-Meier survival curves for patients with different type of lung transplantation

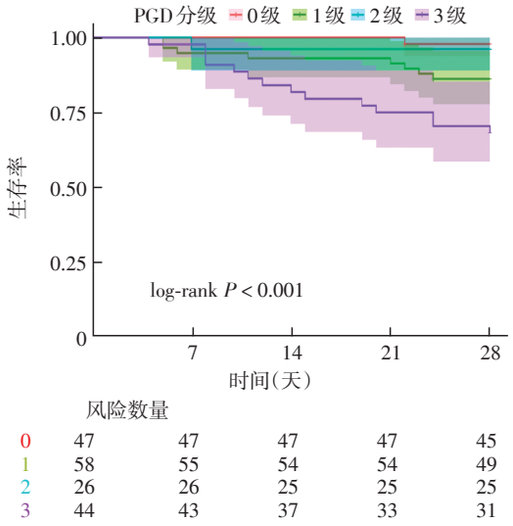

图2　不同PGD分级患者的Kaplan- Meier生存曲线

Fig.2　Kaplan-Meier survival curves for different PGD patients

水肿、肺顺应性下降、气体交换障碍及肺血管阻力升高。2012年急性呼吸窘迫综合征(acute respiratory distress syndrome, ARDS)柏林标准提到，PGD可视为ARDS的一个独立表型，其中肺移植是导致该表型的临床损伤因素[9]。随着肺移植数量增加，不同移植类型对PGD的影响差异需引起重视，这对优化围术期管理策略相当重要。

本研究纳入175例肺移植受者(单肺移植组58例，双肺移植组117例)，总体重度PGD发生率为25.14%，与国际报道的25%~30%一致[10-11]。研究发现，双肺移植组PGD总发生率显著低于单肺移植组，但两组重度PGD发生率差异无统计学意义。多因素分析显示，相较于单肺移植，双肺移植可降低PGD发生的风险。可能的机制包括以下三个方面。(1) 血流动力学改变与再灌注损伤：单肺移植后，自体肺与移植肺并存，若自体肺存在COPD或IPF，其肺血管阻力通常显著高于移植肺。机械通气时血流优先灌注阻力较低的移植肺，导致通气/灌注比不匹配、自体肺过度膨胀、毛细血管压力升高、内皮损伤和水肿，加剧再灌注损伤和PGD风险[12-13]。(2) 炎症反应差异：双肺移植彻底清除终末期病肺(如COPD、IPF的慢性炎性病灶)，减少残留感染或炎症对移植肺的影响。(3) ECMO保护作用：双肺移植组术中、术后VV-ECMO的使用率更高，其能提供稳定的氧合和通气，有效减轻移植肺机械通气应力损伤，降低肺动脉压力和右心负荷，为肺提供“休息”条件，从而减轻缺血再灌注损伤[14]。

国际心肺移植学会2019年度报告显示，双肺移植受者的长期生存率优于单肺移植[8]，但这一优势在60岁以上受者中消失[15]。本研究中单肺组年龄显著大于双肺组[(57.72 ± 10.75)岁 *vs* (51.47 ± 12.70)岁，*P*=0.002]，这与本中心对老年及高危患者优先选择单肺移植的策略一致。尽管本研究在短期生存预后上暂未发现两组患者在不同年龄段的差异，Weingarten等[6]的研究结果表明，单肺移植对老年患者可能带来较低的发病率和较好的短期生存，但5年生存率仍低于双肺移植。这表明，对于有较高风险无法耐受双肺移植的老年患者来说，单肺移植是可接受的。无独有偶，Leong等[16]认为双肺移植相对于单肺移植的益处在年龄增加时减弱，提示了单肺移植可能仍是老年患者的可行选择。

Casillan等[17]研究发现供肺冷缺血时间超过6 h会增加首次双肺移植术后30天和1年死亡率，但对单肺移植无显著影响。本研究中，双肺组冷缺血时间和术中失血量均显著高于单肺组，单因素分析发现二者均为PGD的危险因素，而逐步回归分析后仅术中失血量是独立危险因素。这可能表明手术创伤相关的炎症反应对PGD发生更关键[18]。尽管双肺移植组术后表现出更强烈的全身炎症反应迹象，但这并未转化为更高的PGD风险。可能的解释是ECMO支持减轻炎症反应对移植肺氧合功能的直接影响；或双肺移植能为患者提供更大的生理储备，使其在炎症状态下也能维持良好通气[15]。

单肺移植与双肺移植适应证与预后存在差异。对于COPD患者，Benvenuto等[19]认为右单肺移植与双肺移植的短期和长期生存率相近，而双肺移植可能提供更持久的生存获益。对于ILD患者，Watanabe等[20]则发现单肺移植的长期生存率与非ILD患者相似。而本研究未发现两组短期生存率存在显著差异，但PGD 3级显著增加短期死亡风险(*P*<0.05)。Christie等[21]也认为PGD 3级与肺移植术后发病率和死亡率增加相关并延长机械通气和住院时间。这些结果提示术式选择需要个体化评估，而预防重度PGD对改善预后至关重要。

随着肺移植技术进入精准医学时代，手术方式革新和围术期管理优化为缩短冷缺血时间、降低PGD风险提供了更多可能。本研究为单中心回顾性研究，发现双肺移植能降低PGD发生风险，这一效应可能与患者更年轻、常规应用VV-ECMO减轻再灌注损伤及单肺移植自体肺影响有关。同时，术前白细胞与术中失血量高被确认为PGD独立危险因素。需要注意的是虽然双肺移植降低总体PGD风险，但两组间重度PGD发生率及28 d病死率无显著差异。由于研究样本量有限、潜在选择偏倚、混杂因

素干扰等局限性，结论外推需谨慎。未来需开展多中心大样本研究，以更全面评估不同移植类型对PGD及其他并发症的影响，并为临床决策提供更可靠的依据。

利益冲突　无

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