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Pulmonary Embolism as a Cause of Death in Lung Transplant Recipients: Data From a Nationwide Registry

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ABSTRACT

Pulmonary embolism (PE) is a leading cause of mortality in lung transplant recipients, with early cases associated with particularly poor outcomes. Identified risk factors include elevated BMI, renal dysfunction, ABO mismatch, donor malignancy, and specific immunosuppressive agents. Tailored risk assessments and targeted interventions are essential to mitigating PE-related mortality.

Pulmonary embolism (PE) is a serious complication in lung transplant recipients, compromising allograft function due to poorly developed collateral bronchial circulation and impacting survival [1, 2]. This study aimed to investigate PE as a cause of death in lung transplant recipients and identify modifiable risk factors to improve recipient outcomes.

Data from 1987 to 2023 on adult lung transplant recipients were collected from the multicenter OPTN/UNOS database. PE incidence was determined from cause-of-death records, as living cases with PE were not identifiable. Exclusions included recipients with prior or multi-organ transplants, those alive at last follow-up, and individuals without documented cause-of-death information. The final cohort consisted of adult first-time lung transplant recipients with known causes of death, categorized into two groups: the "PE mortality cohort" (deaths due to PE) and the "non-PE mortality cohort" (deaths from other causes). Pre-, intra-, and post-operative variables were compared, and Firth logistic regression was used to assess risk factors for PE mortality and early PE mortality (within 30 days posttransplant).

The study included 27,372 mortality cases among lung transplant recipients. The PE mortality cohort ($n = 313$, mean age 56.19 ± 0.69 years, female 39.30%, White 83.07%, lung allocation score [LAS] 43.07 ± 1.19) had baseline characteristics largely comparable to the non-PE mortality cohort ($n = 27{,}059$, mean age 54.96 ± 0.08 years, female 43.18%, White 85.20%, LAS 42.51 ± 0.12). However, differences were observed in body mass index (BMI) (25.75 ± 0.27 vs. 24.94 ± 0.03, $p = 0.003$), idiopathic interstitial pneumonia (IIP) as the transplant indication (40.26% vs. 34.40%, $p = 0.03$), thyroid cancer history (0.64% vs. 0.11%, $p = 0.01$), transplant waiting time (194.99 ± 16.34 vs. 252.06 ± 2.23 days, $p = 0.01$), and survival time (837.89 ± 61.31 vs. 1652.56 ± 9.97 days, $p < 0.001$). Donors for the PE mortality cohort were more likely to have a history of genitourinary cancer (0.96% vs. 0.31%, $p = 0.04$) but had a similar cancer-free interval (9.67 ± 3.48 vs. 7.84 ± 0.47 years, $p = 0.59$).

The PE mortality cohort had significantly shorter median survival (450 days, interquartile range [IQR] 87–1164.5) and 1-year survival rate (54.31%, 95% confidence interval [CI] 48.63%–59.64%) compared to the non-PE mortality cohort (median survival 1160 days, IQR 374–2463; 1-year survival rate 72.11%, 95% CI 71.57%–72.64%). Within the PE mortality cohort, early PE mortality ($n = 34$) had a median survival of 11 days (IQR 7.75–20.25), while late PE mortality (occurring

more than 30 days posttransplant, $n = 279$) had a median survival of 1149 days (IQR 371–2451).

Pretransplant predictive factors for PE mortality identified in the multivariate analysis included recipient BMI ≥ 25 (adjusted odds ratio [aOR] 1.03, 95% CI 1.01–1.06, $p = 0.02$), thyroid cancer (aOR 7.36, 95% CI 2.01–26.98, $p = 0.003$), serum creatinine ≥ 1.0 mg/dL (aOR 1.06, 95% CI 1.01–1.12, $p = 0.03$) (Table 1). IIP was associated with PE mortality in univariate analysis only (OR 1.29, 95% CI 1.03–1.61, $p = 0.03$). Donor-related factors for PE mortality included a history of breast cancer (aOR 7.10, 95% CI 1.33–37.80, $p = 0.02$) and genitourinary cancer (aOR 3.59, 95% CI 1.22–10.54, $p = 0.02$). Additionally, everolimus induction (aOR 25.56, 95% CI 1.04–630.60, $p = 0.05$) and tacrolimus maintenance therapy (aOR 2.96, 95% CI 1.01–8.65, $p = 0.05$) were associated with increased risk of death due to PE.

For early PE mortality, multivariate analysis identified the following pretransplant predictive factors: higher recipient BMI (aOR 1.16, 95% 1.06–1.28, $p = 0.002$), ABO blood group mismatch (aOR 325.32, 95% CI 14.78–7161.04, $p < 0.001$), human immunodeficiency virus (HIV) infection (aOR 26.91, 95% CI 1.48–488.32, $p = 0.03$), and pre-existing malignancies, including gastrointestinal (aOR 494.43, 95% CI 16.38–14923.18, $p < 0.001$), genitourinary (aOR 7.01, 95% CI 1.15–42.88, $p = 0.04$), and neurologic cancers (aOR 527.13, 95% CI 23.36–11893.53, $p < 0.001$) (Table 1). Pretransplant procedural factors, such as lung surgery (aOR 2.97, 95% CI 1.01–8.73, $p = 0.05$)—specifically pneumonectomy before transplant (aOR 47.33, 95% CI 1.58–1413.63, $p = 0.03$)—inotrope use (aOR 268.59, 95% CI 10.25–7035.53, $p = 0.001$), and intra-aortic balloon pump (IABP) use (aOR 59.23, 95% CI 2.45–1433.64, $p = 0.01$) were also associated with premature death due to PE, along with elevated serum creatinine levels (aOR 1.12, 95% CI 1.04–1.20, $p = 0.002$). Donor-related factors included a history of head and neck cancer (aOR 106.18, 95% CI 1.55–7283.75, $p = 0.03$) and breast cancer (aOR 38.11, 95% CI 1.04–1396.28, $p = 0.05$).

Among immunosuppressive regimens, sirolimus induction (aOR 78.33, 95% CI 3.21–1911.53, $p = 0.01$), everolimus induction (aOR 948.26, 95% CI 34.37–26159.27, $p < 0.001$), rituximab induction (aOR 10.64, 95% CI 1.87–60.50, $p = 0.01$), rabbit antithymocyte globulin maintenance (aOR 312.13, 95% CI 11.99–8128.12, $p = 0.001$), everolimus maintenance (aOR 201.33, 95% CI 7.04–5754.85, $p = 0.002$), alemtuzumab antirejection therapy (aOR 58.11, 95% 2.89–1167.83, $p = 0.01$), and sirolimus antirejection therapy (aOR 110.24, 95% CI 4.23–2876.28, $p = 0.01$) were associated with increased risk of early PE mortality (Table 1). Conversely, steroid maintenance therapy was a protective factor (aOR 0.16, 95% CI 0.07–0.40, $p < 0.001$).

Other variables, including recipient female sex, lung cancer, lobectomy, pulmonary capillary wedge pressure > 15 mmHg, along with posttransplant interventions (e.g., extracorporeal membrane oxygenation, dialysis, mycophenolate mofetil maintenance), were associated with early PE mortality in univariate analysis only (Table 1). Donor-related factors, specifically living donor status and donor malignancies (thyroid, gastrointestinal, genitourinary, hematologic cancers), showed similar univariate-only associations. Conversely, factors like race/ethnicity, ABO blood type, HLA mismatch, smoking status, performance status, other transplant indications (non-IIP interstitial lung disease subtypes, chronic obstructive pulmonary disease, alpha-1 antitrypsin deficiency, primary pulmonary hypertension, and cystic fibrosis), intensive care unit admission, mechanical ventilation, tracheostomy, transfusion, central venous catheter use, and the year (whether before or after the implementation of LAS in 2005) or type of lung transplant, showed no significant association with early PE mortality.

These findings highlight PE as a significant cause of mortality in lung transplant recipients, particularly in the early posttransplant period. The bleeding risks associated with early anticoagulation underscore the importance of timely risk assessment and targeted preventive strategies for high-risk patients [3]. Evidence suggesting that 90-day enoxaparin prophylaxis may not reduce thromboembolic incidence further emphasizes the need for alternative preventive measures [4].

Pretransplant recipient characteristics, such as elevated BMI and serum creatinine, emerged as significant predictors of PE mortality. Higher BMI likely reflects a pro-inflammatory and hypercoagulable state, increasing susceptibility to thrombotic complications following transplantation [5]. Similarly, higher serum creatinine levels, indicative of impaired renal function, may exacerbate systemic and vascular inflammation, further elevating PE risk [6]. ABO blood group mismatch and HIV infection were strong predictors of early PE mortality, highlighting the importance of pretransplant evaluations for immune compatibility and systemic conditions [7, 8]. Optimizing pretransplant weight and renal function while carefully addressing immune and systemic risks may help minimize PE-related complications.

Donor-related factors, such as histories of breast, genitourinary, and head and neck cancers, were strongly associated with increased PE mortality in recipients, suggesting that prior malignancy in donors may introduce pro-thrombotic factors either systemically or within the graft [9]. Using donors with a history of malignancy can address organ shortages, but enhanced screening and risk stratification are crucial. Although donor history of PE was not linked to recipient PE mortality in this study, prior research has shown that donor lungs with incidentally detected PE may contribute to higher rates of acute cellular rejection and reduced chronic lung allograft dysfunction-free survival [10]. Furthermore, genetic predispositions in donors may exacerbate thrombotic risks, emphasizing the need for comprehensive evaluation of donor profiles to optimize recipient outcomes [11].

Pretransplant interventions, such as prior lung surgery, inotrope use, and IABP support, were strongly associated with early PE mortality, with pneumonectomy posing an exceptionally high risk due to hemodynamic and vascular disruptions [12]. Vigilant perioperative monitoring, early detection of thrombotic events through imaging or biomarkers, and personalized anticoagulation strategies can help reduce both clotting and bleeding risks.

TABLE 1 | Univariate and multivariate predictors of overall and early pulmonary embolism mortality.

	Pulmonary embolism mortality						Early pulmonary embolism mortality					
	Univariate			Multivariate[a]			Univariate			Multivariate[a]		
Factor	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Recipient demographics												
Age ≥ 55	1.01	1.00–1.02	0.10				1.01	0.98–1.04	0.48			
Female	0.85	0.68–1.07	0.17				0.42	0.19–0.91	**0.03**	0.65	0.30–1.15	0.15
Race or ethnicity												
White	1						1					
Black	0.68	0.22–2.07	0.49				0.39	0.02–8.15	0.57			
Hispanic	0.61	0.19–1.94	0.40				0.61	0.03–12.82	0.75			
Asian	0.47	0.11–2.11	0.33				0.48	0.01–24.20	0.71			
Body mass index ≥ 25	1.04	1.01–1.06	**0.003**	1.03	1.01–1.06	**0.02**	1.17	1.09–1.24	**< 0.001**	1.16	1.06–1.28	**0.002**
ECOG Performance status ≥ 2	1.05	0.83–1.34	0.68				0.79	0.40–1.56	0.49			
Smoking	0.87	0.69–1.10	0.25				1.03	0.53–2.03	0.92			
ABO blood group												
O	1						1					
A	1.00	0.78–1.27	0.99				0.77	0.36–1.63	0.49			
B	1.06	0.73–1.52	0.77				1.59	0.64–3.94	0.32			
AB	0.99	0.55–1.77	0.98				1.01	0.19–5.35	1.00			
ABO blood group mismatch	6.64	0.37–118.12	0.20				60.94	3.37–1102.87	**0.01**	325.32	14.78–7161.04	**< 0.001**
HLA mismatch	0.59	0.04–9.74	0.71				0.06	0.00–1.08	0.06			
Transplant indication												
COPD	0.88	0.69–1.12	0.31				1.11	0.55–2.21	0.77			
IIP	1.29	1.03–1.61	**0.03**	1.15	0.90–1.47	0.20	1.70	0.87–3.30	0.12			
Other DPLD	1.21	0.90–1.61	0.21				1.53	0.68–3.43	0.30			
AATD	0.65	0.36–1.18	0.16				0.77	0.15–3.96	0.75			
PPH	1.16	0.68–1.96	0.59				0.35	0.02–5.63	0.46			
Cystic fibrosis	0.70	0.45–1.07	0.10				0.13	0.01–2.14	0.15			
Recipient medical or surgical history												

(Continues)

TABLE 1 | (Continued)

	Pulmonary embolism mortality						Early pulmonary embolism mortality					
	Univariate			Multivariate[a]			Univariate			Multivariate[a]		
Factor	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Chronic steroid therapy	0.93	0.75–1.17	0.56				0.56	0.27–1.15	0.11			
Diabetes	1.29	0.96–1.72	0.09				0.68	0.22–2.05	0.49			
Recent infection[b]	1.31	0.92–1.87	0.14				0.15	0.01-2.50	0.19			
CMV infection	1.23	0.98–1.53	0.07				1.25	0.64–2.43	0.51			
EBV infection	1.23	0.97–1.56	0.10				0.81	0.41–1.59	0.55			
HBV infection	0.91	0.32–2.63	0.87				1.17	0.07–19.19	0.91			
HCV infection	1.23	0.56–2.69	0.60				2.61	0.51–13.42	0.25			
HIV infection	2.01	0.12–4.20	0.63				18.42	1.09–310.06	**0.04**	26.91	1.48–488.32	**0.03**
Malignancy	0.96	0.61–1.52	0.86				2.14	0.80–5.77	0.13			
Skin cancer	0.73	0.31–1.71	0.47				3.18	0.88–11.55	0.08			
Head and neck cancer	1.84	0.11–30.28	0.67				16.85	1.00–282.97	0.05			
Thyroid cancer	7.36	2.01–26.88	**0.003**	7.36	2.01–26.98	**0.003**	12.57	0.75–209.50	0.08			
Lung cancer	1.65	0.33–8.33	0.54				15.55	2.98–81.02	**0.001**	3.20	0.90–11.50	0.07
Breast cancer	0.70	0.14–3.50	0.66				2.12	0.13–34.74	0.60			
Gastrointestinal cancer	12.33	0.64–239.26	0.10				113.19	5.74–2232.80	**0.002**	494.43	16.38–14923.18	**< 0.001**
Genitourinary cancer	2.01	0.78–5.15	0.15				6.15	1.19–31.76	**0.03**	7.01	1.15–42.88	**0.04**
Neurologic cancer	11.50	0.70–220.09	0.12				113.19	5.74–2232.80	**0.002**	527.13	23.36–11893.53	**< 0.001**
Hematologic cancer	1.56	0.44–5.48	0.49				2.81	0.17–46.00	0.47			
Lung surgery	1.09	0.69–1.70	0.72				3.55	1.51–8.34	**0.004**	2.97	1.01–8.73	**0.05**
Pneumoreduction	1.68	0.48–5.91	0.42				3.02	0.18–49.56	0.44			
Lobectomy	1.98	0.39–10.02	0.41				18.65	0.57–97.46	0.23			
Pneumonectomy	5.08	0.29–88.16	0.27				46.61	0.64–823.47	0.09			
Sternotomy	0.77	0.53–1.10	0.15				0.71	0.24–2.15	0.55			
Thoracotomy	0.99	0.56–1.74	0.96				1.83	0.51–6.64	0.36			
Floor admission	1.17	0.79–1.74	0.43				0.55	0.11–2.80	0.47			
ICU admission	1.24	0.85–1.79	0.26				1.63	0.61–4.40	0.33			
Life support	0.92	0.61–1.39	0.70				0.80	0.22–2.91	0.74			
Mechanical ventilation	1.25	0.86–1.82	0.25				0.89	0.25–3.23	0.86			

(Continues)

TABLE 1 | (Continued)

	Pulmonary embolism mortality						Early pulmonary embolism mortality					
	Univariate			Multivariate[a]			Univariate			Multivariate[a]		
Factor	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Tracheostomy	1.17	0.57–2.43	0.67				2.14	0.42–11.03	0.36			
Blood transfusion	0.79	0.44–1.43	0.44				0.30	0.02–4.92	0.40			
Inotrope support	17.27	0.83–360.39	0.07				158.47	7.47–3361.85	**0.001**	268.59	10.25–7035.53	**0.001**
CVC placement	1.30	0.90–1.88	0.16				0.53	0.24–1.19	0.12			
IABP support	9.59	0.52–178.53	0.13				88.03	4.65–1666.50	**0.003**	59.23	2.45–1433.64	**0.01**
ECMO	0.97	0.47–2.02	0.94				0.58	0.04–9.41	0.70			
Dialysis	1.98	0.56–6.96	0.29				3.54	0.22–58.10	0.38			
Recipient organ function $FEV_1 < 80\%$	1.00	1.00–1.01	0.11				1.01	0.99–1.02	0.36			
$FVC < 80\%$	1.00	0.99–1.01	0.76				1.01	0.99–1.03	0.33			
$CO < 4.0$ L/min	1.03	0.95–1.12	0.48				1.07	0.83–1.38	0.59			
$PAP > 25$ mmHg	1.00	0.99–1.01	0.86				0.99	0.96–1.03	0.77			
$PCWP > 15$ mmHg	1.00	0.98–1.02	0.81				1.07	1.02–1.12	**0.01**	1.04	0.98–1.10	0.10
$PCO_2 > 45$ mmHg	0.99	0.98–1.00	0.22				1.00	0.96–1.04	0.91			
Creatinine ≥ 1.0 mg/dL	1.06	1.01–1.12	**0.02**	1.06	1.01–1.12	**0.03**	1.11	1.04–1.18	**0.002**	1.12	1.04–1.20	**0.002**
Total bilirubin ≥ 1.0 mg/dL	0.93	0.74–1.18	0.57				1.05	1.00–1.11	0.06			
Donor characteristics												
Age ≥ 34	1.01	1.00–1.01	0.16				1.00	0.98–1.03	0.73			
Female	0.98	0.78–1.23	0.83				0.88	0.44–1.76	0.72			
Body mass index ≥ 25	0.99	0.97–1.01	0.49				1.02	0.95–1.08	0.64			
Malignancy	1.42	0.69–2.95	0.34				4.47	1.23–16.23	**0.02**	3.10	0.90–12.00	0.07
Skin cancer	0.98	0.20–4.94	0.98				2.98	0.18–48.81	0.45			
Head and neck cancer	9.59	0.52–178.53	0.13				88.03	4.65–1666.50	**0.003**	106.18	1.55–7283.75	**0.03**
Thyroid cancer	2.33	0.14–38.78	0.56				21.40	1.26–362.24	**0.03**	10.27	0.92–200.91	0.07
Lung cancer	1.01	1.00–1.01	0.21				0.97	0.93–1.01	0.08			
Breast cancer	7.42	1.40–39.46	**0.02**	7.10	1.33–37.80	**0.02**	69.91	12.75–383.26	**< 0.001**	38.11	1.04–1396.28	**0.05**
Gastrointestinal cancer	5.08	0.29–88.16	0.27				46.60	2.64–823.22	**0.01**	20.10	1.10–400.09	0.06
Genitourinary cancer	3.64	1.24–10.68	**0.02**	3.59	1.22–10.54	**0.02**	14.27	2.74–74.28	**0.002**	7.34	1.14–55.39	0.06

(Continues)

TABLE 1 | (Continued)

	Pulmonary embolism mortality						Early pulmonary embolism mortality					
	Univariate			Multivariate[a]			Univariate			Multivariate[a]		
Factor	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Neurologic cancer	1.38	0.27–6.98	0.69				4.18	0.25–68.67	0.32			
Hematological cancer	5.75	0.33–100.97	0.23				52.81	2.96–942.85	**0.01**	28.10	1.20–620.42	0.06
Malignancy-free interval ≥ 5 years	1.02	0.97–1.08	0.39				1.05	0.96–1.13	0.28			
CO < 4.0 L/min	1.05	0.87–1.27	0.60				1.51	0.87–2.64	0.15			
PAP > 25 mmHg	0.95	0.87–1.04	0.28				1.03	1.00–1.07	0.06			
PCWP > 15 mmHg	1.06	0.96–1.17	0.22				1.07	1.00–1.14	0.06			
PCO2 > 45 mmHg	0.99	0.97–1.01	0.54				1.01	0.94–1.08	0.77			
Creatinine ≥ 1.0 mg/dL	1.02	0.95–1.09	0.55				1.04	0.79–1.37	0.78			
Total bilirubin ≥ 1.0 mg/dL	1.02	0.95–1.09	0.61				1.09	1.00–1.16	0.05			
Living donor status	2.01	0.57–7.09	0.28				11.24	0.97–58.33	0.07			
Cause of death												
Anoxia	1.04	0.76–1.43	0.79				0.67	0.22–2.01	0.47			
Cerebrovascular accident	1.15	0.91–1.45	0.24				1.24	0.63–2.44	0.54			
Head trauma	0.92	0.73–1.15	0.45				0.82	0.42–1.61	0.57			
Malignancy	0.64	0.13–3.22	0.59				1.95	0.12–31.95	0.64			
Infection	1.02	0.98–1.07	0.45				1.00	0.96–1.03	0.89			
Pulmonary embolism	0.97	0.94–1.01	0.10				1.15	0.85–1.55	0.35			
Cardiovascular disease	1.01	0.99–1.04	0.32				0.85	0.65–1.12	0.24			
Hemorrhage	1.03	0.99–1.06	0.21				1.03	0.97–1.09	0.12			
Homicide	0.99	0.98–1.01	0.09				0.95	0.80–1.15	0.52			
Suicide	1.00	0.97–1.03	0.88				0.75	0.40–1.40	0.25			
Accidental	0.99	0.95–1.04	0.62				0.98	0.70–1.37	0.84			
Transplant characteristics												
LAS > 50	1.00	0.99–1.01	0.57				1.00	0.97–1.03	0.93			
Transplant waiting time > 180 days	1.00	1.00–1.00	1.00				1.00	1.00–1.01	0.16			
Transplant after 2005	1.21	0.95–1.53	0.12				0.89	0.45–1.76	0.74			

(Continues)

TABLE 1 | (Continued)

	Pulmonary embolism mortality						Early pulmonary embolism mortality					
	Univariate			Multivariate[a]			Univariate			Multivariate[a]		
Factor	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Double lung transplant	0.88	0.71–1.10	0.27				0.71	0.36–1.37	0.31			
Ischemic time > 6 h	0.97	0.91–1.03	0.34				0.98	0.81–1.19	0.82			
Posttransplant procedures												
Mechanical ventilation ≤ 48 h	1.11	0.88–1.40	0.37				0.86	0.42–1.74	0.68			
Mechanical ventilation 48 h to 5 days	1.13	0.80–1.60	0.48				1.27	0.47–3.42	0.64			
Mechanical ventilation ≥ 5 days	1.00	0.73–1.37	1.00				1.31	0.56–3.08	0.53			
ECMO	1.18	0.63–2.19	0.61				3.79	1.25–11.45	**0.02**	2.52	0.95–8.20	0.07
Dialysis	1.05	0.70–1.57	0.81				3.11	1.39–6.99	**0.01**	2.20	1.00–6.23	0.06
Induction agents	0.84	0.66–1.07	0.16				0.69	0.35–1.39	0.30			
rATG	1.48	0.85–2.56	0.16				1.47	0.29–7.55	0.65			
Basiliximab	0.82	0.64–1.05	0.11				0.59	0.26–1.32	0.20			
Alemtuzumab	0.62	0.31–1.23	0.17				1.00	0.20–5.16	1.00			
Tacrolimus	0.99	0.96–1.03	0.58				0.98	0.73–1.32	0.84			
Cyclosporine	0.84	0.58–1.21	0.35				1.08	0.40–2.90	0.88			
Mycophenolate mofetil	1.03	0.40–2.62	0.95				1.02	0.06–16.74	0.99			
Azathioprine	1.07	0.77–1.50	0.67				1.07	0.40–2.88	0.89			
Glucocorticoid	0.82	0.66–1.03	0.09				0.79	0.40–1.53	0.48			
Sirolimus	9.59	0.52–178.53	0.13				88.03	4.65–1666.50	**0.003**	78.33	3.21–1911.53	**0.01**
Everolimus	28.78	1.17–707.82	**0.04**	25.56	1.04–630.60	**0.05**	264.13	10.57–6597.33	**0.001**	948.26	34.37–26159.27	**< 0.001**
Rituximab	1.15	0.33–4.03	0.83				6.45	1.25–33.31	**0.03**	10.64	1.87–60.50	**0.01**
Maintenance agents	0.66	0.42–1.04	0.08				0.95	0.82–1.14	0.50			
rATG	12.33	0.64–239.26	0.10				113.19	5.74–2232.80	**0.002**	312.13	11.99–8128.12	**0.001**
Basiliximab	1.63	0.10–26.76	0.73				14.94	0.89–250.09	0.06			
Alemtuzumab	0.96	0.92–1.01	0.09				1.08	0.92–1.26	0.28			
Tacrolimus	3.09	1.06–9.02	**0.04**	2.96	1.01–8.65	**0.05**	3.89	0.24–63.89	0.34			
Cyclosporine	1.06	0.83–1.36	0.64				0.89	0.41–1.04	0.78			

(Continues)

TABLE 1 | (Continued)

	Pulmonary embolism mortality						Early pulmonary embolism mortality					
	Univariate			Multivariate[a]			Univariate			Multivariate[a]		
Factor	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Myocophenolate mofetil	1.09	0.87–1.37	0.44				0.50	0.25–0.99	**0.05**	0.65	0.32–1.30	0.09
Azathioprine	0.93	0.74–1.18	0.57				0.43	0.18–1.02	0.05			
Glucocorticoid	0.71	0.49–1.03	0.07				0.10	0.05–0.20	**< 0.001**	0.16	0.07–0.40	**< 0.001**
Sirolimus	1.47	0.42–5.17	0.54				2.65	0.16–43.50	0.49			
Everolimus	12.33	0.64–239.26	0.10				113.19	5.74–2232.80	**0.002**	201.33	7.04–5754.85	**0.002**
Antirejection agents	1.15	0.84–1.57	0.40				0.51	0.14–1.83	0.30			
rATG	0.32	0.02–5.22	0.43				2.98	0.18–48.81	0.45			
Basiliximab	0.97	0.06–15.76	0.98				8.89	0.54–147.29	0.13			
Alemtuzumab	5.75	0.33–100.97	0.23				52.83	0.96–943.12	0.07			
Tacrolimus	1.04	0.97–1.12	0.11				0.88	0.63–1.23	0.45			
Cyclosporine	0.43	0.03–6.90	0.55				3.93	0.24–64.53	0.96			
Myocophenolate mofetil	2.62	0.51–13.35	0.25				7.83	0.47–129.52	0.15			
Azathioprine	1.51	0.30–7.64	0.62				4.57	0.28–75.09	0.29			
Glucocorticoid	1.15	0.83–1.58	0.39				0.53	0.15–1.93	0.34			
Sirolimus	4.11	0.24–70.29	0.33				37.73	0.17–656.62	0.43			
Everolimus	1.01	0.98–1.05	0.73				1.07	0.95–1.20	0.20			
Rituximab	2.63	0.74–9.28	0.13				4.68	0.28–76.89	0.28			

Note: Bolded values indicate statistical significance at the $p < 0.05$ level.

Abbreviations: AATD, alpha-1 antitrypsin deficiency; CI, confidence interval; CMV, cytomegalovirus; CO, cardiac output; COPD, chronic obstructive pulmonary disease; CVC; central venous catheter; DPLD, diffuse parenchymal lung diseases; EBV, Epstein–Barr virus; ECMO, extracorporeal membrane oxygenation; ECOG, Eastern Cooperative Oncology Group; FEV, forced expiratory volume; FVC, forced vital capacity; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HLA, human leukocyte antigen; IABP, intra-aortic balloon pump; ICU, intensive care unit; IIP, idiopathic interstitial pneumonia; LAS, lung allocation score; OR, odds ratio; PAP, pulmonary artery pressure; PCO_2, partial pressure of carbon dioxide; PCWP, pulmonary capillary wedge pressure; PPH, primary pulmonary hypertension; rATG, rabbit anti-thymocyte globulin.

[a]Multivariate analysis was adjusted for variables with a p-value < 0.05 in the univariate analysis.

[b]Infection requiring IV drug therapy (within 2 weeks before transplant).

The use of certain immunosuppressive agents, such as sirolimus and everolimus for induction and maintenance therapy, was significantly associated with increased early PE mortality. These agents may contribute to thrombotic risk through their effects on endothelial function and coagulation pathways [13–15]. On the other hand, steroid maintenance therapy may protect against PE mortality by offsetting prothrombotic effects with anticoagulant actions, such as inhibiting platelet aggregation and tissue factor activity [16]. Careful selection and monitoring of immunosuppressive regimens are needed to optimize both rejection prevention and thrombotic risk management.

This study has several limitations. Reliance on cause-of-death records may introduce misclassification bias, leading to under- or overestimation of PE outcomes. Excluding recipients without cause-of-death data could cause selection bias by omitting patients with incomplete records. Limited granularity restricted analysis of venous thromboembolism prophylaxis, prior PE history, imaging confirmation, and anticoagulation management, imaging confirmation. Lastly, the rarity of early PE mortality required the use of Firth logistic regression, which may inflate effect estimates for variables with small sample sizes or limited variability.

PE is a significant contributor to mortality in lung transplant recipients, particularly during the early posttransplant period when survival outcomes are notably poor. This research identifies key factors associated with PE mortality—such as elevated BMI, impaired renal function, ABO blood group mismatch, prior donor malignancy, and perioperative interventions. Optimized pretransplant evaluations, improved donor-recipient matching, vigilant perioperative monitoring, and strategic immunosuppressive regimens offer actionable opportunities to mitigate thrombotic risks and reduce associated morbidity and mortality in lung transplant recipients.

Author Contributions

Hye Sung Kim: conceptualization, data curation, formal analysis, investigation, methodology, software, validation, writing – original draft preparation, writing – review and editing. **Rohit Gupta:** conceptualization, supervision, project administration, investigation, methodology, writing – original draft preparation, writing – review and editing. **Parth Rali:** conceptualization, supervision, project administration, investigation, methodology, writing – original draft preparation, writing – review and editing.

Disclosure

The data presented in this report were provided by the United Network for Organ Sharing (UNOS) in its capacity as the contractor for the Organ Procurement and Transplantation Network (OPTN). The authors are solely responsible for the interpretation and reporting of these data, and they should not be considered as representing the official policy or interpretation of the OPTN or the U.S. Government.

Ethics Statement

Research involving human participants was authorized by the Institutional Review Board Committee (IRB#: STU00207117). The studies adhered to local laws and institutional guidelines. Written informed consent for participation was not mandated from participants or their legal guardians/next of kin, in line with national legislation and institutional protocols.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data underlying this article and access to the datasets are available from the corresponding author upon reasonable request.

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