Incidence, Etiologies, and Predictors of Seven-Day Graft Loss in Adult Lung Transplantation: A National Registry Analysis

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Abstract

Objectives: **Seven-day graft loss, defined as graft failure or recipient death within 7 days posttransplant, remains poorly characterized in adult lung transplantation. We evaluated national incidence, etiologies, and predictors of 7-day graft loss and 7-day posttransplant death.**

Materials and Methods: **We used Organ Procurement and Transplantation Network data to retrospectively analyze 25 593 adult deceased donor lung transplant recipients transplanted from 2015 to 2024. We compared recipients with 7-day graft loss or 7-day posttransplant death with recipients who had ≥1-year graft or patient survival, respectively.**

Results: **Seven-day graft loss occurred in 526 recipients (2.1%). Primary nonfunction was the leading etiology (63.5%), followed by etiologies coded as "other/unknown" (35.4%). Cardiovascular failure was the leading cause of 7-day posttransplant death (24.1%), and 72-hour extracorporeal membrane oxygenation was the strongest independent predictor of 7-day graft loss (odds ratio 9.04, *P* < .001). Other predictors were retransplant (odds ratio 1.80, *P* = .01), elevated serum bilirubin at transplant (odds ratio 1.16, *P* < .001), and higher physiologic severity score (odds ratio 1.02, *P* < .001), whereas extracorporeal membrane oxygenation at listing carried lower odds (odds ratio 0.61, *P* = .04). Predictors of 7-day posttransplant death included 72-hour extracorporeal membrane oxygenation (odds ratio 21.97, *P* < .001), elevated physiologic severity score (odds ratio 1.02, *P* < .001), and bilateral lung transplant (odds ratio 2.09, *P* = .04). Male sex (odds ratio 0.64, *P* = .045) and higher match-time lung allocation score (odds ratio 0.98, *P* = .005) carried lower odds. Donor characteristics were assessed only in unadjusted comparisons.**

Conclusions: **Seven-day outcomes were associated with recipient physiologic reserve and early post-operative instability. Frequent other/unknown etiologic coding underscores the need for improved reporting and event-level granularity. Despite registry limitations, this risk profile may inform risk stratification, postoperative surveillance, donor-recipient matching, and perioperative optimization.**

Key words: *Early graft loss, Extracorporeal membrane oxygenation, Primary graft dysfunction, Retransplant*

Introduction

Lung transplantation (LuTx) remains the definitive treatment option for selected patients with end-stage lung disease. In 2025, 3460 adult LuTx procedures were performed in the United States, representing a 72% increase over the past decade.[1] Bilateral LuTx is increasingly favored for appropriate candidates because it has been associated with better long-term survival, improved functional outcomes, and lower rates of chronic graft dysfunction compared with single LuTx.[2,3]

Pulmonary fibrosis is the leading indication for LuTx in the United States, accounting for more than 40% of transplants.[4] Chronic obstructive pulmonary disease is the second most common indication.[4,5] In 2023, the United States adopted the Composite Allocation Score (CAS), a continuous distribution framework that prioritizes medical urgency while incorporating biological compatibility, patient access, and placement efficiency. This shift toward urgency-based prioritization has progressively increased the acuity and medical complexity of transplant recipients.[6] In 2023, adult waitlist mortality was 13.3

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deaths per 100 patient-years, the lowest recorded rate.[7] Among listed adult candidates, 81.2% underwent deceased donor LuTx within 1 year of listing.[7] Early reports and predictive modeling have suggested that CAS may further reduce waitlist mortality, improve allocation equity, and expand transplant access without compromising early posttransplant outcomes.[6,8]

Early graft failure after LuTx reflects a range of perioperative complications, including vascular anastomotic events, airway dehiscence, infection, and primary graft dysfunction (PGD). Among these, PGD remains the leading cause of early morbidity and mortality after LuTx, with a reported incidence of 10% to 25%.[4,9] Primary graft dysfunction arises from ischemia-reperfusion injury during transplant and is characterized by pulmonary vascular injury, increased vascular permeability, and diffuse alveolar damage.[9] Despite the importance of this immediate perioperative period, early graft loss after LuTx has traditionally been evaluated using broader 30- to 90-day windows. This lack of temporal granularity has left graft loss within the first postoperative week comparatively underexplored at the national level. Consequently, 2 discrete early endpoints remain poorly characterized: 7-day graft loss (7DGL), defined as graft failure or recipient death within 7 days posttransplant, and 7-day posttransplant death (7DD), defined as recipient death within 7 days.

Registry-based evaluations of these endpoints are further complicated by nonspecific etiologic categories, including "other/unknown" coding among early graft failure events. Accordingly, in the present analysis, we aimed to examine reported etiologies and identify independent predictors of 7DGL and 7DD among adult deceased donor LuTx recipients. By isolating 7DGL as a discrete early endpoint, this analysis may support preoperative risk stratification, informed consent, and donor-recipient matching during this critical postoperative interval.

Materials and Methods

Data source

This retrospective cohort analysis was based on Organ Procurement and Transplantation Network (OPTN) Standard Transplant Analysis and Research files provided by the United Network for Organ Sharing (UNOS). The study period extended from January 1, 2015, through December 31, 2024. Adult (≥18 years) recipients who underwent single or bilateral LuTx from deceased organ donors were identified. Individuals who underwent multiorgan transplantation, received living-donor LuTx, or experienced graft loss between postoperative days 8 and 364 were excluded from the primary analysis.

Outcomes

The primary outcome was 7DGL, defined as graft failure or recipient death within 7 days posttransplant, with death included regardless of graft function. The comparison cohort comprised recipients with at least 1 year of graft survival.

We evaluated 7DD, defined as recipient death within 7 days posttransplant regardless of graft function, as a secondary outcome. We compared recipients with 7DD with recipients with at least 1 year of patient survival. Primary causes of graft failure were abstracted from OPTN center-reported fields and categorized as primary nonfunction (PNF), acute rejection, or "other/unknown" etiologies. All cases coded as PNF were classified as 7DGL. Mechanisms of death were classified according to a hierarchical, person-level collapsed framework based on registry-reported fields (COD1-COD3).

Variables

Recipient-level variables included age, sex, race or ethnicity (White, Black, Hispanic, Asian, or Other), body mass index (BMI) at transplant, and primary diagnosis at listing. Clinical history variables included diabetes mellitus, retransplant, dialysis dependence at registration, prior malignancy, history of cigarette use, and prior lung surgery. Laboratory values included serum creatinine and total serum bilirubin at transplant. Pretransplant acuity was captured through initial, last, and match-time Lung Allocation Score (LAS) values, CAS-era designation (2023-2024), and the physiologic severity marker. Mechanical support variables included extracorporeal membrane oxygenation (ECMO) at listing, ECMO use at 72 hours posttransplant, and extracorporeal life support.

Donor-level variables included age, sex, race or ethnicity, BMI at time of death, history of cigarette use, hypertension, diabetes mellitus, and donation after circulatory death (DCD). Donor mechanisms of death were categorized as anoxia, cerebrovascular/stroke, head trauma, central nervous system tumor, or other.

Transplant-level variables included transplant type (single vs bilateral), HLA mismatch level, cold

ischemia time (CIT) modeled as both continuous and categorical variables, donor-recipient sex matching, organ sharing geography, and donor hospital to transplant center distance.

Statistical analyses

We summarized baseline recipient, donor, and transplant characteristics descriptively. We reported categorical variables as frequencies and percentages, which we compared using Pearson χ^2 or Fisher exact tests, as appropriate. We expressed continuous variables as means ± SD or medians with interquartile ranges, which we compared using *t* tests or Wilcoxon rank-sum tests, respectively.

We used the Firth penalized likelihood method for multivariable logistic regression to address separation and small-sample bias. We also performed standard logistic regression to assess model stability. We selected covariates a priori based on clinical relevance. Models evaluating 7DGL predictors included retransplant status, total serum bilirubin, ECMO use at 72 hours, ECMO at listing, and the physiologic severity marker, which are standard variables in the OPTN registry. The physiologic severity marker denotes measurement of acute respiratory distress syndrome severity with specific parameters that are classified into 4 groups: oxygenation, ventilation, ventilation energy and lung compliance, and right heart dysfunction.[10] We constructed a separate model to evaluate 7DD that included male sex, ECMO use at 72 hours, the physiologic severity marker, LAS at match time, and transplant type (bilateral vs single). Stratified subgroup analysis by transplant type was precluded by small event counts among single lung recipients. Transplant type was therefore incorporated as a binary covariate.

We reported estimated outcomes as odds ratios (ORs) with 95% CIs. Statistical significance was defined as a 2-sided $P < .05$. We performed all analyses using Stata software version 18E (StataCorp LLC, College Station, Texas, USA). This cohort analysis was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Ethical considerations

This analysis relied on deidentified, publicly accessible data and did not involve direct interaction with human subjects or animal experimentation. Accordingly, our analysis was exempt from institutional review board approval under federal regulations applicable to secondary research involving existing deidentified data (45 CFR §46.104). All organs were procured in accordance with United States regulations, with informed consent obtained from donors or their next of kin. No organs were sourced from executed prisoners or prisoners of conscience. This work was conducted in accordance with the 2013 Declaration of Helsinki and the 2018 Declaration of Istanbul.

Results

From 2015 through 2024, 25 593 adult deceased donor LuTx procedures were performed in the United States. Overall, 7DGL occurred in 2.1% of eligible recipients. After exclusion of 6876 recipients with graft loss between postoperative days 8 and 364, the 7DGL analytic cohort included 18 717 recipients. Of these, 526 had 7DGL and 18 191 had at least 1-year graft survival (Table 1). For the secondary 7DD analysis, 7094 recipients who died between postoperative days 8 and 364 were excluded. The 7DD analytic cohort included 18 499 recipients: 216 had 7DD and 18 283 had at least 1-year patient survival (Table 2).

Recipient, donor, and transplant factors

Recipients experiencing 7DGL were more frequently aged 18 to 39 years and more commonly of Black or Asian race/ethnicity. Recipients in the 7DGL cohort also had higher-acuity clinical features, including retransplant status, dialysis dependence at registration, prior lung surgery, elevated total serum bilirubin, and shorter height. Pulmonary hypertension, obliterative bronchiolitis, and combined pulmonary fibrosis and emphysema (CPFE) were overrepresented as primary diagnoses. Donor-level differences included older age, higher DCD use, underweight BMI, and prolonged CIT. The 7DGL cohort had higher rates of ECMO at 72 hours, ECMO at listing, and life support, as well as higher physiologic severity marker scores and initial, last, and match-time LAS (Table 1).

The 7DD cohort shared a similar recipient severity profile, with a greater mechanical support burden and higher physiologic severity marker scores. Retransplant, bilateral LuTx, dialysis dependence, younger age, Black or Asian race/ethnicity, elevated bilirubin, and prior lung surgery were more common among recipients with 7DD. Underweight donor

BMI, DCD, prolonged CIT, and anoxia as a donor mechanism of death were also more common in the 7DD cohort than in the reference cohort. Pulmonary hypertension, obliterative bronchiolitis, and CPFE were overrepresented among 7DD recipients (Table 2).

Table 1. Recipient, Donor, and Transplant Characteristics and Etiologies of 7-Day Graft Loss Among Adult Deceased Donor Lung Transplant Recipients (2015-2024)

Characteristic	Graft Survival ≥1 Year After LuTx (n = 18 191)	Graft Loss ≤7 Days After LuTx (n = 526)	*P* Value
Primary cause of lung graft failure, No. (%)			
PNF	0	334 (63.5%)	<.001
Acute rejection	0	6 (1.1%)	<.001
Other/unknown[a]	18 191 (100.0%)	186 (35.4%)	<.001
Reason for recipient death within 7 days (n = 216),[b] No. (%)			
Graft failure	0	18 (8.3%)	
Infection	0	6 (2.8%)	
Cardiovascular	0	52 (24.1%)	
Cerebrovascular	0	42 (19.4%)	
Hemorrhagic	0	30 (13.9%)	
Malignancy	0	0	
Respiratory failure	0	16 (7.4%)	
Multisystem failure	0	35 (16.2%)	
Other/unknown[c]	0	17 (7.9%)	
	Recipient characteristics		
Sex, No. (%)			
Male	10 950 (60.2%)	290 (55.1%)	.02
Female	7241 (39.8%)	236 (44.9%)	.02
Age group, No. (%)			
18-39 y	1904 (10.5%)	82 (15.6%)	<.001
40-59 y	5815 (32.0%)	168 (31.9%)	.99
≥60 y	10 472 (57.6%)	276 (52.5%)	.02
Race or ethnicity, No. (%)			
White	13 881 (76.3%)	378 (71.9%)	.02
Black	1695 (9.3%)	68 (12.9%)	.005
Hispanic	1967 (10.8%)	49 (9.3%)	.28
Asian	492 (2.7%)	28 (5.3%)	<.001
Other[d]	156 (0.9%)	3 (0.6%)	.63
Health profile			
Days on wait list, median (IQR)	42 (116.0)	36 (109.8)	.19
Diabetes mellitus at time of listing, No. (%)	3577 (19.7%)	114 (21.8%)	.24
Retransplant, No. (%)	505 (2.8%)	39 (7.4%)	<.001
Dialysis at registration, No. (%)	55 (5.8%)	16 (44.4%)	<.001
Lung surgery between listing and transplant (nontransplant), No. (%)	751 (4.1%)	33 (6.3%)	.02
History of cigarette use, No. (%)	10 273 (56.5%)	259 (49.3%)	.001
Previous malignancy, No. (%)	1875 (10.3%)	51 (9.7%)	.67
Serum creatinine at transplant, mean ± SD, mg/dL	1 ± 0.3	1 ± 0.5	.08
Total bilirubin at transplant, mean ± SD, mg/dL	1 ± 0.7	1 ± 2.1	<.001
cPRA, mean ± SD, %	10 ± 21.9	11 ± 23.3	.56
Height, mean ± SD, cm	170 ± 10.4	169 ± 10.2	.03
ABO blood type, No. (%)			
Type O	8279 (45.5%)	250 (47.5%)	.36
Type A	7122 (39.2%)	198 (37.6%)	.49
Type B	2070 (11.4%)	58 (11.0%)	.80
Type AB	720 (4.0%)	20 (3.8%)	.86
Transplant type, No. (%)			
Single lung	4274 (23.5%)	105 (20.0%)	.06
Bilateral lung	13 917 (76.5%)	421 (80.0%)	.06

Table 1 (Cont). Recipient, Donor, and Transplant Characteristics and Etiologies of 7-Day Graft Loss Among Adult Deceased Donor Lung Transplant Recipients (2015-2024)

Characteristic	Graft Survival ≥1 Year After LuTx (n = 18 191)	Graft Loss ≤7 Days After LuTx (n = 526)	*P* Value
BMI at transplant, mean ± SD	26 ± 4.4	26 ± 4.6	.14
BMI category at transplant, No. (%)			
Underweight (<18.5)	937 (5.2%)	35 (6.7%)	.12
Normal weight (18.5-24.9)	6485 (35.7%)	166 (31.6%)	.06
Overweight (25-29.9)	7247 (39.9%)	215 (41.0%)	.62
Obesity class I (30-34.9)	3334 (18.3%)	102 (19.4%)	.53
Obesity class II (≥35)	176 (1.0%)	7 (1.3%)	.40
Pretransplant clinical severity			
Total minutes lungs on perfusion, median (IQR)	325 (205.1)	378 (230.9)	.32
Physiologic severity marker, mean ± SD	37 ± 15.3	52 ± 24.3	<.001
ECMO status, No. (%)			
Use at 72 hours	1159 (6.4%)	219 (42.9%)	<.001
At listing	589 (3.2%)	42 (8.0%)	<.001
Life support	1156 (6.4%)	88 (16.7%)	<.001
Primary diagnosis at time of listing, No. (%)			
Fibrosis various	8989 (49.4%)	250 (47.5%)	.39
COPD/emphysema	3518 (19.3%)	61 (11.6%)	<.001
Hypersensitivity pneumonitis	742 (4.1%)	28 (5.3%)	.16
Idiopathic nonspecific interstitial pneumonia	625 (3.4%)	14 (2.7%)	.34
Pulmonary hypertension	601 (3.3%)	36 (6.8%)	<.001
Sarcoidosis	433 (2.4%)	15 (2.9%)	.49
COVID-19-related pulmonary fibrosis and ARDS	439 (2.4%)	8 (1.5%)	.19
Lung ReTx/GF: obliterative bronchiolitis	350 (1.9%)	19 (3.6%)	.006
Scleroderma, restrictive and pulmonary hypertension	327 (1.8%)	10 (1.9%)	.86
Alpha-1 antitrypsin deficiency	392 (2.2%)	12 (2.3%)	.84
Bronchiectasis	321 (1.8%)	6 (1.1%)	.28
Mixed connective tissue disease	163 (0.9%)	9 (1.7%)	.06
Rheumatoid disease	170 (0.9%)	3 (0.6%)	.64
Obliterative bronchiolitis (non-ReTx)	147 (0.8%)	2 (0.4%)	.45
Combined pulmonary fibrosis and emphysema	0	3 (0.6%)	<.001
Other diagnoses[e]	974 (5.4%)	50 (9.5%)	<.001
	Donor characteristics		
Sex, No. (%)			
Male	11 135 (61.2%)	299 (56.8%)	.04
Female	7056 (38.8%)	227 (43.2%)	.04
Age group, No. (%)			
<10 y	13 (0.1%)	0	>.99
10-19 y	2208 (12.1%)	59 (11.2%)	.52
20-39 y	9308 (51.2%)	229 (43.5%)	<.001
40-59 y	5812 (31.9%)	203 (38.6%)	.001
≥60 y	850 (4.7%)	35 (6.7%)	.04
Race or ethnicity, No. (%)			
White	11 001 (60.5%)	305 (58.0%)	.25
Black	3207 (17.6%)	108 (20.5%)	.09
Hispanic	3220 (17.7%)	89 (16.9%)	.64
Asian	563 (3.1%)	19 (3.6%)	.50
Other[d]	200 (1.1%)	5 (1.0%)	.75
History of diabetes mellitus, No. (%)	1456 (8.1%)	51 (9.8%)	.15
History of hypertension, No. (%)	4402 (24.4%)	135 (26.0%)	.41
History of cigarette use, No. (%)	1319 (7.4%)	48 (9.4%)	.09
Serum creatinine, mean ± SD, mg/dL	2 ± 1.7	2 ± 2.0	.65
BMI at time of death, mean ± SD	27 ± 5.7	26 ± 5.9	.01
BMI category at time of death, No. (%)			
Underweight (<18.5)	563 (3.1%)	30 (5.7%)	<.001
Normal weight (18.5-24.9)	7398 (40.7%)	223 (42.5%)	.41

Table 1 (Cont). Recipient, Donor, and Transplant Characteristics and Etiologies of 7-Day Graft Loss Among Adult Deceased Donor Lung Transplant Recipients (2015-2024)

Characteristic	Graft Survival ≥1 Year After LuTx (n = 18 191)	Graft Loss ≤7 Days After LuTx (n = 526)	*P* Value
Overweight (25-29.9)	5996 (33.0%)	158 (30.1%)	.17
Obesity class I (30-34.9)	2708 (14.9%)	85 (16.2%)	.41
Obesity class II (≥35)	1513 (8.3%)	29 (5.5%)	.02
Donation type, No. (%)			
DCD	1048 (5.8%)	47 (8.9%)	.002
DBD	17 143 (94.2%)	479 (91.1%)	.002
Donor mechanism of death, No. (%)			
Anoxia	6015 (33.1%)	193 (36.7%)	.08
Cerebrovascular/stroke	4810 (26.4%)	148 (28.1%)	.39
Head trauma	6909 (38.0%)	176 (33.5%)	.04
CNS tumor	85 (0.5%)	2 (0.4%)	>.99
Other[f]	0	0	
	Transplant characteristics		
HLA mismatch level (0-6), mean ± SD	5 ± 1.1	5 ± 1.0	.04
Lung CIT, mean ± SD, h	6 ± 2.4	7 ± 3.0	<.001
Lung CIT category, No. (%)			
≤6 h	11 479 (63.3%)	267 (51.1%)	<.001
>6-8 h	4633 (25.6%)	147 (28.2%)	.18
>8-10 h	1088 (6.0%)	54 (10.3%)	<.001
>10 h	928 (5.1%)	54 (10.3%)	<.001
Donor-recipient sex matching, No. (%)			
Male to female	2854 (15.7%)	90 (17.1%)	.38
Female to male	2669 (14.7%)	81 (15.4%)	.64
Male to male	8281 (45.5%)	209 (39.7%)	.009
Female to female	4387 (24.1%)	146 (27.8%)	.06
Lung allocation score, mean ± SD			
Initial	43 ± 16.0	47 ± 17.7	<.001
Last	44 ± 15.6	48 ± 17.6	<.001
At match	49 ± 18.4	55 ± 20.9	<.001
Composite allocation score			
Era, No. (%)	1091 (6.0%)	93 (17.7%)	<.001
Mean ± SD	8 ± 1.0	8 ± 1.0	.50
Organ sharing geography, No. (%)			
Local	6693 (36.8%)	183 (34.8%)	.35
Regional	4721 (26.0%)	132 (25.1%)	.66
National	6771 (37.2%)	211 (40.1%)	.18
Donor hospital to transplant center distance, mean ± SD, nautical miles	241 ± 275.0	270 ± 291.3	.047

Abbreviations: 7DD, 7-day posttransplant death; 7DGL, 7-day graft loss; ARDS, acute respiratory distress syndrome; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CIT, cold ischemia time; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; cPRA, calculated panel reactive antibody; DBD, donation after brain death; DCD, donation after circulatory death; ECMO, extracorporeal membrane oxygenation; GF, graft failure; IQR, interquartile range; LuTx, lung transplant; PNF, primary nonfunction; ReTx, retransplant

Continuous variables were compared with Wilcoxon rank-sum tests and categorical variables with Pearson χ^2 or Fisher exact tests. $P < .05$ indicated significance.

[a]Primary causes of lung graft failure reflect registry-reported graft failure categories. In the 7DGL cohort, the "Other/unknown" category encompasses graft failure attributed to other specified causes or unknown and unreported etiologies as coded in the OPTN registry. In the ≥1-year graft survival cohort, all recipients are classified as "Other/unknown" because no graft failure events occurred.

[b]The 7DD set represents a subset of the 7DGL cohort (n = 526), not an additive category. Cause of death percentages used the number of recipients who died within 7 days (n = 216) as the denominator. Because graft function status at death was not consistently recorded, deaths without documented graft failure could not always be classified as death with a functioning graft versus graft failure.

[c]"Other/unknown" under recipient cause of death encompasses deaths for which registry-reported cause of death fields (COD1-COD3) mapped to other specified or unknown etiologies after application of the collapsed classification framework.

[d]"Other" race includes American Indian/Alaska Native, Native Hawaiian/Other Pacific Islander, and multiracial recipients (combined because of small subgroup counts).

[e]"Other" primary diagnosis represents most primary causes contributing to lung transplant not otherwise specified.

[f]"Other" donor mechanism of death includes all deaths not otherwise specified (eg, infection, sudden cardiac arrest, multiorgan failure); subgroups with low frequency were combined to ensure an adequate sample size.

Etiologies of graft failure and early death

Among 7DGL events, PNF was the leading reported etiology (63.5%), followed by etiologies coded in the registry as "other/unknown" (35.4%) and acute rejection (1.1%) (Table 1). Among the 216 recipients who died within 7 days, the leading causes of death were cardiovascular events (24.1%), cerebrovascular events (19.4%), multisystem organ failure (16.2%), and hemorrhagic causes (13.9%) (Table 1). In the 7DD cohort, most registry-coded graft failure entries were classified as "other/unknown" (80.5%), with PNF recorded in 17.6% of entries and acute rejection in 1.9% (Table 2).

Table 2. Recipient, Donor, and Transplant Characteristics and Etiologies of 7-Day Posttransplant Death Among Adult Deceased Donor Lung Transplant Recipients (2015-2024)

Characteristic	Patient Survival ≥1 Year After LuTx (n = 18 283)	Posttransplant Death ≤7 Days After LuTx (n = 216)	*P* Value
Primary cause of lung graft failure, No. (%)			
PNF	81 (0.4%)	38 (17.6%)	<.001
Acute rejection	0	4 (1.9%)	<.001
Other/unknown[a]	18 202 (99.6%)	174 (80.5%)	<.001
	Recipient characteristics		
Sex, No. (%)			
Male	11 001 (60.2%)	109 (50.5%)	.004
Female	7282 (39.8%)	107 (49.5%)	.004
Age group, No. (%)			
18-39 y	1917 (10.5%)	34 (15.7%)	.01
40-59 y	5840 (31.9%)	61 (28.2%)	.25
≥60 y	10 526 (57.6%)	121 (56.0%)	.65
Race or ethnicity, No. (%)			
White	13 955 (76.3%)	157 (72.7%)	.21
Black	1704 (9.3%)	29 (13.4%)	.04
Hispanic	1973 (10.8%)	17 (7.9%)	.17
Asian	495 (2.7%)	11 (5.1%)	.03
Other[b]	156 (0.9%)	2 (0.9%)	.71
Days on wait list, median (IQR)	42 (116.0)	42 (114.5)	.93
Diabetes mellitus at time of listing, No. (%)	3595 (19.7%)	52 (24.2%)	.10
Retransplant, No. (%)	508 (2.8%)	19 (8.8%)	<.001
Dialysis at registration, No. (%)	56 (5.8%)	10 (55.6%)	<.001
History of cigarette use, No. (%)	10 322 (56.5%)	111 (51.6%)	.16
Lung surgery between listing and transplant (nontransplant), No. (%)	756 (4.1%)	16 (7.4%)	.02
Previous malignancy, No. (%)	1883 (10.3%)	21 (9.8%)	.80
cPRA, mean ± SD, %	10 ± 22.0	12 ± 23.4	.34
Serum creatinine at transplant, mean ± SD, mg/dL	1 ± 0.3	1 ± 0.6	.06
Total bilirubin at transplant, mean ± SD, mg/dL	1 ± 0.7	1 ± 0.9	<.001
Height, mean ± SD, cm	170 ± 10.4	169 ± 10.1	.05
ABO blood type, No. (%)			
Type O	8317 (45.5%)	109 (50.5%)	.15
Type A	7159 (39.2%)	82 (38.0%)	.72
Type B	2080 (11.4%)	19 (8.8%)	.24
Type AB	727 (4.0%)	6 (2.8%)	.37
Transplant type, No. (%)			
Single lung	4303 (23.5%)	27 (12.5%)	<.001
Bilateral lung	13 980 (76.5%)	189 (87.5%)	<.001
BMI at transplant, mean ± SD	26 ± 4.4	26 ± 4.5	.13

Table 2 (Cont). Recipient, Donor, and Transplant Characteristics and Etiologies of 7-Day Posttransplant Death Among Adult Deceased Donor Lung Transplant Recipients (2015-2024)

Characteristic	Patient Survival ≥1 Year After LuTx (n = 18 283)	Posttransplant Death ≤7 Days After LuTx (n = 216)	*P* Value
BMI category at transplant, No. (%)			
Underweight (<18.5)	942 (5.2%)	14 (6.5%)	.38
Normal weight (18.5-24.9)	6519 (35.7%)	65 (30.1%)	.09
Overweight (25-29.9)	7283 (39.9%)	90 (41.7%)	.59
Obesity class I (30-34.9)	3351 (18.3%)	45 (20.8%)	.35
Obesity class II (≥35)	176 (1.0%)	2 (0.9%)	>.99
Total minutes lungs on perfusion, median (IQR)	325 (205.0)	350 (148.4)	.36
Physiologic severity marker, mean ± SD	37 ± 15.3	57 ± 26.8	<.001
ECMO status, No. (%)			
Use at 72 hours	1170 (6.5%)	91 (44.4%)	<.001
At listing	592 (3.2%)	23 (10.6%)	<.001
Life support	1162 (6.4%)	43 (19.9%)	<.001
Primary diagnosis at time of listing, No. (%)			
Fibrosis various	9041 (49.5%)	95 (44.0%)	.11
COPD/emphysema	3536 (19.3%)	27 (12.5%)	.01
Hypersensitivity pneumonitis	747 (4.1%)	9 (4.2%)	.95
Idiopathic nonspecific interstitial pneumonia	627 (3.4%)	6 (2.8%)	.60
Pulmonary hypertension	603 (3.3%)	20 (9.3%)	<.001
Sarcoidosis	433 (2.4%)	7 (3.2%)	.40
COVID-19-related pulmonary fibrosis and ARDS	439 (2.4%)	3 (1.4%)	.33
Lung ReTx/GF: obliterative bronchiolitis	351 (1.9%)	12 (5.6%)	.001
Scleroderma, restrictive and pulmonary hypertension	328 (1.8%)	3 (1.4%)	>.99
Alpha-1 antitrypsin deficiency	395 (2.2%)	6 (2.8%)	.48
Bronchiectasis	324 (1.8%)	2 (0.9%)	.60
Mixed connective tissue disease	163 (0.9%)	1 (0.5%)	>.99
Rheumatoid disease	171 (0.9%)	1 (0.5%)	.73
Obliterative bronchiolitis (non-ReTx)	147 (0.8%)	1 (0.5%)	>.99
Combined pulmonary fibrosis and emphysema	0	2 (0.9%)	<.001
Other diagnoses[c]	978 (5.3%)	21 (9.7%)	.005
	Donor characteristics		
Sex, No. (%)			
Male	11 191 (61.2%)	124 (57.4%)	.25
Female	7092 (38.8%)	92 (42.6%)	.25
Age group, No. (%)			
<10 y	13 (0.1%)	0	>.99
10-19 y	2222 (12.2%)	20 (9.3%)	.20
20-39 y	9352 (51.2%)	99 (45.8%)	.12
40-59 y	5841 (31.9%)	82 (38.0%)	.06
≥60 y	855 (4.7%)	15 (6.9%)	.12
Race or ethnicity, No. (%)			
White	11 052 (60.4%)	129 (59.7%)	.83
Black	3226 (17.6%)	46 (21.3%)	.16
Hispanic	3235 (17.7%)	36 (16.7%)	.69
Asian	568 (3.1%)	4 (1.9%)	.29
Other[b]	202 (1.1%)	1 (0.5%)	.74
History of diabetes mellitus, No. (%)	1459 (8.1%)	23 (10.8%)	.14
History of hypertension, No. (%)	4422 (24.4%)	60 (28.2%)	.21
History of cigarette use, No. (%)	1330 (7.4%)	17 (8.1%)	.71
Serum creatinine, mean ± SD, mg/dL	2 ± 1.7	2 ± 1.8	.80
BMI at time of death, mean ± SD	27 ± 5.7	26 ± 5.8	.14
BMI category at time of death, No. (%)			
Underweight (<18.5)	568 (3.1%)	14 (6.5%)	.005
Normal weight (18.5-24.9)	7434 (40.7%)	91 (42.1%)	.67
Overweight (25-29.9)	6024 (33.0%)	66 (30.6%)	.45
Obesity class I (30-34.9)	2729 (14.9%)	32 (14.8%)	.96
Obesity class II (≥35)	1515 (8.3%)	13 (6.0%)	.23
Donation type, No. (%)			
DCD	1051 (5.7%)	20 (9.3%)	.03
DBD	17 232 (94.3%)	196 (90.7%)	.03
Donor mechanism of death, No. (%)			
Anoxia	6053 (33.1%)	87 (40.3%)	.03
Cerebrovascular/stroke	4831 (26.4%)	58 (26.9%)	.89
Head trauma	6942 (38.0%)	66 (30.6%)	.03
CNS tumor	85 (0.5%)	1 (0.5%)	>.99
Other[d]	0	0	
	Transplant characteristics		
HLA mismatch level (0-6), mean ± SD	5 ± 1.1	5 ± 1.1	.82
Lung CIT, mean ± SD, h	6 ± 2.4	7 ± 3.0	<.001
Lung CIT category, No. (%)			
≤6 h	11 542 (63.3%)	98 (46.0%)	<.001
>6-8 h	4654 (25.5%)	56 (26.3%)	.80
>8-10 h	1090 (6.0%)	32 (15.0%)	<.001
>10 h	934 (5.1%)	27 (12.7%)	<.001
Donor-recipient sex matching, No. (%)			
Male to female	2873 (15.7%)	41 (19.0%)	.19
Female to male	2683 (14.7%)	26 (12.0%)	.28
Male to male	8318 (45.5%)	83 (38.4%)	.04
Female to female	4409 (24.1%)	66 (30.6%)	.03
Lung allocation score, mean ± SD			
Initial	43 ± 16.0	48 ± 18.3	<.001
Last	44 ± 15.6	49 ± 18.6	<.001
At match	49 ± 18.5	55 ± 21.3	<.001
Composite allocation score			
Era, No. (%)	1095 (6.0%)	39 (18.1%)	<.001
Mean ± SD	8 ± 1.0	8 ± 1.0	.79
Organ sharing geography, No. (%)			
Local	6728 (36.8%)	73 (33.8%)	.36
Regional	4745 (26.0%)	57 (26.4%)	.89
National	6804 (37.2%)	86 (39.8%)	.43
Donor hospital to transplant center distance, mean ± SD, nautical miles	241 ± 274.7	266 ± 292.3	.39

Abbreviations: ARDS, acute respiratory distress syndrome; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CIT, cold ischemia time; CNS, central nervous system; COPD, chronic obstructive pulmonary disease; cPRA, calculated panel reactive antibody; DBD, donation after brain death; DCD, donation after circulatory death; ECMO, extracorporeal membrane oxygenation; GF, graft failure; IQR, interquartile range; LuTx, lung transplant; PNF, primary nonfunction; ReTx, retransplant

Continuous variables were compared with Wilcoxon rank-sum tests and categorical variables with Pearson χ^2 or Fisher exact tests. $P < .05$ indicated significance. The ≥1-year patient survival reference group here (n = 18 283) exceeds the ≥1-year graft survival reference group in Table 1 (n = 18 191) because 92 recipients experienced graft failure within the first year but survived as patients beyond 1 year.

[a]Primary causes of lung graft failure reflect registry-reported graft failure categories among recipients who died within 7 days posttransplant. The "Other/unknown" category encompasses deaths without documented graft failure, other specified causes, unknown etiologies, and unreported values as coded in the OPTN registry.

[b]"Other" race includes American Indian/Alaska Native, Native Hawaiian/Other Pacific Islander, and multiracial recipients (combined because of small subgroup counts).

[c]"Other" primary diagnosis represents most primary causes contributing to lung transplant not otherwise specified.

[d]"Other" donor mechanism of death includes all deaths not otherwise specified (eg, infection, sudden cardiac arrest, multiorgan failure); subgroups with low frequency were combined to ensure an adequate sample size.

Multivariable predictors of 7-day graft loss and 7-day posttransplant death

On multivariable analysis, ECMO support at 72 hours had the strongest association with 7DGL. Retransplant, total serum bilirubin at transplant, and physiologic severity marker scores were also significantly associated with 7DGL, with ECMO at listing inversely associated with 7DGL (Table 3). For 7DD, ECMO at 72 hours had the strongest association, followed by physiologic severity marker scores and bilateral LuTx. Male sex and higher match-time LAS were inversely associated with 7DD (Table 4).

Table 3. Firth Penalized Likelihood Multivariable Logistic Regression Model of 7-Day Graft Loss in Lung Transplant Recipients (2015-2024) (n = 12 602)

Predictor	OR (95% CI)	*P* Value
Recipient characteristic		
Retransplant	1.80 (1.15-2.83)	.01
Serum total bilirubin at transplant	1.16 (1.09-1.23)	<.001
ECMO status		
Use at 72 hours	9.04 (7.17-11.40)	<.001
At listing	0.61 (0.39-0.97)	.04
Physiologic severity marker	1.02 (1.02-1.03)	<.001

Abbreviations: ECMO, extracorporeal membrane oxygenation; OR, odds ratio

P < .05 indicated significance. Multivariable logistic regression was performed using the Firth penalized likelihood method to address separation and small-sample bias. A parallel standard logistic regression produced concordant estimates across all covariates, confirming the stability of the penalized model. Covariates were selected a priori on the basis of clinical relevance. The difference between the analytic sample (n = 12 602) and the full cohort (N = 18 717) reflects listwise deletion of records with missing covariate data.

Table 4. Firth Penalized Likelihood Multivariable Logistic Regression Model of 7-Day Posttransplant Death in Lung Transplant Recipients (2015-2024) (n = 11 644)

Predictor	OR (95% CI)	*P* Value
Male recipient	0.64 (0.41-0.99)	.045
ECMO status		
Use at 72 hours	21.97 (13.22-36.51)	<.001
Physiologic severity marker	1.02 (1.01-1.03)	<.001
Lung allocation score		
At match	0.984 (0.973-0.995)	.005
Bilateral vs single lung transplant	2.09 (1.02-4.29)	.04

Abbreviations: ECMO, extracorporeal membrane oxygenation; OR, odds ratio

P < .05 indicated significance. Multivariable logistic regression was performed using the Firth penalized likelihood method to address separation and small-sample bias. A parallel standard logistic regression produced concordant estimates across all covariates, confirming the stability of the penalized model. Covariates were selected a priori on the basis of clinical relevance. The difference between the analytic sample (n = 11 644) and the full cohort (N = 18 499) reflects listwise deletion of records with missing covariate data.

Discussion

Summary of principal findings

The Global Observatory on Donation and Transplantation report documented 8236 LuTx procedures across 48 countries in 2024.[11] In the United States, a record 3049 adult LuTx procedures were performed in 2023. Despite increases in the number of LuTx, first-week outcomes remain poorly characterized at the national level. Prior LuTx investigations have largely evaluated early graft loss and mortality across broader 30-day, 90-day, or 1-year intervals.[12,13] Accordingly, we evaluated 7DGL and 7DD as discrete first-week outcomes among adult deceased donor LuTx recipients. Although 7DGL occurred in only 2.1% of eligible recipients, 7DGL represents a clinically severe phenotype marked by frequent PNF attribution, substantial early mortality, and a risk profile centered on recipient vulnerability and postoperative instability. Our analyses of 7DD reinforced this pattern and identified bilateral LuTx as an additional signal of early mortality. Male sex and higher match-time LAS were inversely associated with 7DD, suggesting a partially distinct risk profile for early death compared with 7DGL. Entries coded as "other/unknown" in the registry accounted for 80.5% of graft failure entries among recipients with 7DD. These findings suggest that national registry fields incompletely capture the clinical context of early LuTx events, limiting differentiation among graft-specific dysfunction, systemic collapse, and nonspecific first-week reporting.

Mechanistic framework of 7-day graft loss

Seven-day graft loss may represent the most severe phenotype within the PGD spectrum. Primary graft dysfunction is an acute lung injury syndrome evaluated within the first 72 hours after transplant.[14] The International Society for Heart and Lung Transplantation consensus framework grades PGD severity using hypoxemia and radiographic criteria at standardized early time points.[14] This classification system provides a structured approach for assessment of early allograft injury. Within contemporary multicenter cohorts, severe PGD is strongly associated with early and 1-year mortality.[15-17] Together, these data support interpreting 7DGL not as a distinct or isolated complication but as a catastrophic failure of early graft recovery within the PGD spectrum.

Ischemia-reperfusion injury remains central to early allograft injury, initiating endothelial activation, increased permeability, and diffuse alveolar damage, which can impair gas exchange and contribute to early graft dysfunction.[18,19] In recipients with limited

physiologic reserve or sustained perioperative instability, these mechanisms may overwhelm early recovery. Clinically, this can manifest as refractory hypoxemia, persistent need for mechanical support, and graft collapse.[18,20] This framework is consistent with the observed risk profile. We noted that 7DGL was associated with clinical markers of recipient vulnerability and unresolved postoperative instability, including retransplant, elevated bilirubin, higher physiologic severity marker scores, and ECMO requirement at 72 hours.

The first postoperative week appears to capture a dynamic injury state marked by physiologic instability and the need for mechanical support. This pattern reinforces the interpretation of 7DGL as a severity-dependent failure of graft recovery. Severe early allograft injury has been linked to adverse long-term outcomes, including bronchiolitis obliterans syndrome, impaired baseline graft function, and long-term mortality.[4,21,22] However, recovery trajectories are not deterministic and remain heterogeneous even among recipients with severe initial dysfunction.[23] Accordingly, 7DGL is best interpreted as the extreme manifestation of failed early recovery from severe perioperative graft injury and systemic instability.

The predictors identified in this analysis suggest that 7DGL reflects a multidimensional risk state shaped by recipient physiologic reserve and perioperative instability. Recent validation of a pretransplant biomarker panel for mortality after liver transplant supports the feasibility of objective prognostic tools.[24] At present, no validated instrument exists for 7DGL prediction in LuTx. This biomarker model nevertheless shows that pretransplant biological vulnerability can be quantified and incorporated into posttransplant outcome prediction. These registry-derived predictors define the clinical context for integrating future biomarker, intraoperative, and early postoperative data into individualized donor-recipient matching and perioperative optimization.

Etiologic divergence between graft failure and mortality

Among recipients with 7DGL, PNF was the most reported graft failure etiology (63.5%), followed by registry-coded "other/unknown" events (35.4%); acute rejection, typically manifesting within the first posttransplant year,[25] represented a negligible proportion (1.1%). A substantial number of cases were recorded as early death within the graft failure field rather than assigned discrete etiologic diagnoses. Together, these patterns suggest that 7DGL is centered on severe early allograft dysfunction, whereas the high burden of nonspecific coding limits more precise attribution during the first postoperative week.

The high proportion of etiologies coded in the registry as "other/unknown" represented a major interpretive limitation rather than a biologically specific mechanism. This issue was especially pronounced among recipients with 7DD, in whom 80.5% of registry-coded graft failure entries were classified as "other/unknown." This pattern is consistent with broader concerns with OPTN/UNOS data integrity, including incomplete coding, variable reporting practices, and limited reliability of registry-derived classifications.[26] Cause of death attribution in transplant registries is also imperfect. Prior work demonstrated discordance between registry-recorded causes of death and systematically adjudicated classifications.[27] In LuTx specifically, prior UNOS-based analyses have relied on registry-defined primary graft failure outcomes, underscoring the dependence of national LuTx literature on center-reported classifications.[28] Accordingly, "other/unknown" coding in the present analysis likely reflected a heterogeneous mixture of PNF, PGD, technical or vascular complications, systemic postoperative collapse, and death with incompletely documented graft function. The etiologic distribution of 7DGL and 7DD should therefore be interpreted as registry-reported attribution rather than definitive mechanistic classification.

Despite these registry constraints, the overall pattern suggests that 7DGL and 7DD represented related but distinct first-week endpoints. Although 7DGL appeared more closely linked to graft dysfunction and persistent postoperative instability, 7DD captured broader systemic and non-graft-specific pathways. Prior registry analyses similarly demonstrated that early death after LuTx reflected a wider spectrum of perioperative and systemic causes,[29] consistent with observations in our present cohort. This divergence supports separate evaluation of 7DGL and 7DD when developing perioperative risk stratification and early postoperative management strategies.

Recipient severity profile associated with 7-day graft loss and 7-day posttransplant death

Independent of etiologic classification, unadjusted comparisons showed that 7DGL was associated with greater recipient physiologic severity and

perioperative instability. Compared with recipients with ≥1-year graft survival, recipients with 7DGL demonstrated elevated LAS, greater ECMO use, longer ischemic times, and higher rates of dialysis and retransplant. After multivariable adjustment, a more focused risk profile emerged. Retransplant, higher total serum bilirubin at transplant, ECMO requirement at 72 hours posttransplant, and higher physiologic severity marker scores remained independently associated with 7DGL.

Extracorporeal membrane oxygenation at listing was inversely associated with 7DGL, suggesting that pretransplant mechanical support and persistent postoperative dependence represent distinct risk states. LAS variables, dialysis at listing, and prior nontransplant lung surgery between listing and transplant were not included in the a priori 7DGL model. Within this model, retransplant, biochemical dysfunction, and physiologic vulnerability were each associated with 7DGL.[30,31] This interpretation aligns with prior reports that identified lung retransplant as a higher-risk setting that may involve greater perioperative complexity.[30] Overall, these findings suggest that first-week graft failure is shaped by recipient physiologic reserve and early postoperative instability.

Unadjusted comparisons demonstrated higher proportions of younger, female, Black, and Asian recipients among those with 7DGL. These demographic variables were not entered in the a priori 7DGL model, and their independent contribution was not assessed.

When we evaluated 7DD separately, a partially distinct recipient severity profile emerged. Independent predictors included ECMO requirement at 72 hours posttransplant, elevated physiologic severity marker scores, and bilateral LuTx. Male recipient sex and higher match-time LAS were inversely associated with 7DD. Greater technical complexity, longer cumulative ischemic exposure, and higher recipient acuity inherent to bilateral procedures may underlie the elevated early mortality risk associated with bilateral LuTx despite its superior long-term outcomes.[2,3] This association should be interpreted cautiously, as transplant type may reflect procedural complexity, selection factors, and recipient acuity rather than a direct causal effect of bilateral transplantation itself.

Collectively, these results indicate that 7DD represents broader systemic physiologic compromise and disease-specific vulnerability, distinct from the graft-centric instability that characterizes 7DGL. Prior analyses in high-risk LuTx populations have similarly identified advanced life support at transplant, elevated bilirubin, and prolonged ischemic exposure as independent predictors of early posttransplant mortality.[32] These results support the interpretation that severe physiologic derangement is central to early posttransplant mortality after LuTx.

Donor and allograft characteristics

Donor and allograft characteristics were evaluated in relation to 7DGL and 7DD. In unadjusted comparisons, recipients experiencing 7DGL had older donors, higher DCD allograft use, and longer CIT compared with recipients with ≥1-year graft survival. Prolonged CIT contributes to lung ischemia-reperfusion injury, a key mechanistic driver of PGD following LuTx.[33] Ischemic time, donor age, DCD status, and HLA mismatch level were not entered in the a priori multivariable models, so their independent associations with 7DGL and 7DD were not tested. Match-time LAS was evaluated within the recipient severity framework and was inversely associated with 7DD.

Prior LuTx meta-analyses have demonstrated comparable PGD rates between DCD transplants and donation after brain death transplants.[34,35] However, recent policy-focused work has emphasized that DCD LuTx procedures are underutilized in the United States despite evidence of similar posttransplant outcomes.[36] The donor differences in the present cohort were unadjusted and do not establish independent donor effects.

Donor biology and ischemic exposure remain mechanistically important in PGD pathogenesis, and models that enter donor, allograft, and recipient variables together are needed to define their relative contributions to first-week outcomes.

Perioperative and early postoperative determinants

In contrast to baseline recipient and donor characteristics, perioperative and early postoperative factors emerged as key determinants of both 7DGL and 7DD. Extracorporeal membrane oxygenation provides temporary mechanical support for severe cardiac or respiratory failure.[37] In LuTx, ECMO may be used before, during, or after transplant. Across these phases, it may provide intraoperative cardiopulmonary support, facilitate postoperative

management of PGD or cardiopulmonary instability, and serve as a bridge to transplant.[38]

Unadjusted comparisons showed higher rates of ECMO support at listing and greater overall perioperative mechanical support requirements among recipients with 7DGL. However, after multivariable adjustment, posttransplant ECMO requirement remained positively associated with 7DGL. This pattern suggests that 7-day graft loss is centered on unresolved graft dysfunction or systemic compromise in the immediate postoperative period, rather than pretransplant mechanical support alone. Prior cohort and registry analyses similarly demonstrated that postoperative ECMO use is associated with reduced survival after LuTx.[39,40] This survival signal appears most relevant when ECMO persists beyond intraoperative use.

As a bridge to transplant, ECMO is linked to higher pretransplant complication rates and suboptimal posttransplant outcomes.[41] Conversely, retrospective analysis has suggested that ECMO support for <14 days before transplant may be associated with favorable posttransplant outcomes.[42] The present investigation distinguishes pretransplant support from postoperative dependence. In this context, continued ECMO requirement in the immediate postoperative period may signal unresolved graft dysfunction or ongoing physiologic instability that is not fully captured by baseline listing severity.

Physiologic severity marker scores were independently associated with both 7DGL and 7DD. Higher severity indices corresponded to increased odds of both endpoints, reinforcing the central role of early physiologic instability in modulating short-term outcomes. Together, physiologic severity and postoperative ECMO dependence identified the first postoperative week as a key inflection point. Persistent hemodynamic compromise and graft dysfunction during this interval may amplify vulnerability and shape the early posttransplant trajectory.

The present analysis did not specifically evaluate intraoperative ECMO in relation to 7DGL or 7DD. Prior literature has shown a higher prevalence of grade 3 PGD during postoperative days 1 to 3 following LuTx.[43] Conflicting results on routine intraoperative ECMO use likely reflect confounding by indication, recipient risk profiles, and evolving ECMO technology and management strategies, with no clear evidence that the variation reflects intrinsic differences in graft protection.[44] Recent multicenter registry data have suggested that intraoperative venoarterial ECMO cannulation strategy may not independently determine grade 3 PGD risk or overall survival.[45] Broader perioperative context and recipient severity may therefore be more influential determinants. Overall, these data indicated that persistent postoperative instability is a strong marker of early graft failure and mortality.

Limitations

This analysis was inherently constrained by the structure of registry-based observational data. Residual confounding cannot be excluded, and causal inference cannot be established despite multivariable adjustment. Variables related to socioeconomic factors, center-level practices, intraoperative ventilator and perfusion strategies, and postoperative management were not captured in the OPTN dataset. These omissions represent potential sources of unmeasured confounding. Incomplete data for certain race and cause of death variables necessitated exclusion of some recipients and donors from category-specific analyses. Rare early-event counts also limited model precision despite the large overall cohort size. The multivariable models were restricted to covariates selected a priori, so donor and allograft variables were compared only without adjustment.

Misclassification of graft failure etiology is a central limitation of registry-based etiologic analysis. Distinguishing PNF from PGD or early acute rejection is complicated by overlapping clinical features, evolving PGD grading criteria, and variable PNF definitions across centers.[4,46] The registry's predefined coding framework consolidates distinct processes into fixed categories, limiting granular differentiation among PGD, PNF, rejection, and systemic postoperative causes. Differences between graft failure etiology and cause of death attribution likely reflect structural reporting constraints rather than true biologic equivalence. Cause of death attribution is further subject to intercenter variability in practice. Additional factors associated with early graft loss, including fat emboli, donor pulmonary emboli, cardiopulmonary bypass utilization, donor imaging, and biomarker data, were not captured in the registry.[47] Standardized definitions of early lung graft failure and uniform coding of PNF, PGD, rejection, and death with graft failure are needed to improve comparability across registry-based studies.

The transplant landscape is transitioning toward broader adoption of machine perfusion technologies, a development not fully captured during the present observation period. These data therefore serve as a baseline before routine machine perfusion, against which future 7-day outcomes can be evaluated as these technologies become increasingly incorporated into LuTx. As a retrospective registry analysis, the intraoperative and preservation-related mechanisms underlying early graft failure cannot be fully elucidated.

Conclusions

Seven-day graft loss after adult LuTx is uncommon but clinically consequential. In this national registry-based analysis, 7DGL and 7DD were associated with recipient physiologic vulnerability and persistent early postoperative instability. Requirement for ECMO at 72 hours emerged as the dominant predictor of both endpoints.

Frequent use of "other/unknown" etiologies in the registry and limited event-level granularity emphasized the reporting constraints inherent to national LuTx registry analyses. These findings underscore the need for improved etiologic reporting, standardized definitions, and greater temporal precision. Greater specificity in reporting may help refine preoperative risk assessment, early postoperative surveillance, donor-recipient matching, and perioperative optimization in adult LuTx.

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