Exploring Blood Transfusions and Outcomes of Lung Transplant Patients

BTC1877H- Data Science in Health II

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1.0 Introduction

1.1 Lung Transplantation in End-Stage Lung Disease

Lung transplantation represents the final therapeutic option for patients with end-stage lung disease when medical and surgical strategies have been exhausted.[1] While survival rates and surgical techniques have improved over time, perioperative bleeding remains a persistent and significant complication that impacts both immediate surgical outcomes and long-term patient survival.[1] The resulting requirement for blood product transfusion introduces additional risks that extend well beyond the operating room, affecting intensive care unit length of stay, duration of mechanical ventilation, and overall mortality.[2,3]

Perioperative hemorrhage during lung transplantation can significantly alter patient trajectory. Significant blood loss requires transfusion of red blood cells, fresh frozen plasma, platelets, and cryoprecipitate, each carrying distinct risks including coagulopathy, hypothermia, and metabolic derangements.[1] The downstream consequences of transfusion are also concerning. Patients receiving perioperative blood products demonstrate significantly higher rates of primary graft dysfunction (PGD) (a severe form of acute lung injury occurring within 72 hours of transplantation) with rates of 25.3% in transfused patients compared to only 6.8% in those not requiring transfusion.[2] Additionally, transfused patients experience prolonged ICU stays (median 7 days versus 4 days), extended mechanical ventilation (median 1.1 days versus 1.0 days), and increased need for postoperative extracorporeal membrane oxygenation support (ECMO).[2] Most critically, perioperative transfusion is associated with increased mortality, with some studies reporting 30-day mortality rates of 7% in transfused patients compared to 0% in non-transfused patients.[2]

1.2 Understanding Perioperative Bleeding and Transfusion in Lung Transplantation

The pathophysiology underlying bleeding during lung transplantation differs from other surgical procedures due to unique hemostatic challenges that are inherent to the operation. Extensive surgical dissection creates large surfaces prone to diffuse oozing, while the presence of dense pleural adhesions, particularly common in patients with cystic fibrosis (CF) or prior thoracic procedures, substantially increases operative complexity and bleeding risk.[4,5] These vascularized adhesions result from long-lasting inflammatory processes and contribute significantly to blood loss by complicating surgical techniques and prolonging operations.[1]

Transfusion needs in lung transplantation are usually divided into two meaningful groups because they don't carry the same clinical weight. Needing any perioperative transfusion is important on its own, since it affects patient safety and resource use. But massive transfusion (defined by the Universal Definition of Perioperative Bleeding as more than 10 units of red blood cells within 24 hours) is a very different situation.[3] Patients who experience massive bleeding have much worse outcomes across the board. They show higher rates of grade 3 PGD at 72 hours (32.7% vs 5.9%), stay in hospital much longer (median 40 days vs 20 days), have markedly higher one-year mortality (22.2% vs 7.3%), and are far less likely to achieve "textbook outcomes" (2.9% vs 35.6%).[3] They also need more reinterventions (62.6% vs 8.7%), dialysis (26.9% vs 4.5%), and tracheostomies (30.4% vs 9.5%).[3]

The mechanisms linking transfusion to adverse outcomes involve both the volume of blood

products administered and the inflammatory response they trigger. Transfusion-related complications contribute to the development of PGD through mechanisms similar to transfusion-related acute lung injury, characterized by pulmonary inflammation and coagulopathy.[2] This relationship demonstrates a pattern, with increasing volumes of transfused products correlating with progressively worse outcomes.[6]

1.3 Risk Factors for Perioperative Transfusion Requirement

Demographic factors have been shown to contribute to bleeding risk during lung transplantation. Younger age has been identified as a predictor of severe-to-massive bleeding, with the median age of severe-to-massive bleeders (55 years) significantly lower than insignificant-to-moderate bleeders (63 years).[3] Body mass index demonstrates an inverse relationship with bleeding risk, as each 1-unit increase in BMI decreases the odds of severe bleeding (odds ratio 0.89).[3] Lower BMI likely reflects nutritional deficiencies common in patients with end-stage lung disease, which impair hemostatic function and wound healing while increasing surgical difficulty due to poor tissue quality.

1.4 Disease Severity and Underlying Diagnosis

The Lung Allocation Score (LAS), an integrated measure combining disease severity and predicted transplant benefit, serves as an important predictor of bleeding risk. Patients with severe-to-massive bleeding demonstrate significantly higher mean LAS (54.14 versus 46.72), reflecting greater disease acuity and physiologic derangement.[3] This correlation likely captures the increased complexity and hemodynamic instability associated with more severely ill patients, who more frequently require preoperative mechanical ventilation or ECMO.[3]

Certain underlying diagnoses contribute to unique bleeding risks that extend beyond simple disease severity. Patients with CF in particular present challenges due to multiple converging factors that increase both surgical complexity and hemorrhagic risk. Cystic fibrosis recipients are especially prone to serious perioperative and postoperative bleeding complications due to dense pleural adhesions resulting from recurrent infections and prior thoracic procedures.[4] When chest surgeries or pleural adhesions have been performed prior to lung transplantation, surgical risk is greatly increased, and it is not unusual for patients to require return to the operating room for bleeding control even after successful transplantation.[4] Beyond adhesive complications, CF patients often experience malabsorption of fat-soluble vitamins, particularly vitamin K, leading to coagulopathy that may not be fully apparent on routine preoperative testing.[4] The combination of these factors, dense adhesions, prior procedures, and vitamin K deficiency, creates a particularly high-risk profile for bleeding in this patient population.

Pulmonary hypertension (PH) introduces additional challenges that frequently necessitate cardiopulmonary bypass (CPB) or ECMO for hemodynamic support during transplantation.[1,7] This requirement for ECMO, discussed in detail below, fundamentally alters the hemostatic environment and significantly increases bleeding risk. Additionally, each 1-unit increase in mean pulmonary artery pressure is associated with increased odds of severe bleeding (odds

ratio 1.04), suggesting that the severity of PH itself, independent of the need for bypass, contributes to hemorrhagic risk.[3]

1.5 Baseline Hematologic and Hemostatic Status

Preoperative laboratory values provide crucial prognostic information regarding bleeding risk. Patients who develop severe-to-massive bleeding have significantly lower preoperative hemoglobin levels (median 11.8 g/dL versus 12.6 g/dL), indicating that baseline anemia reduces the margin for tolerable blood loss and lowers the threshold at which transfusion becomes necessary.[3,8] This finding underscores the importance of optimizing hemoglobin levels preoperatively when safely achievable.

Thrombocytopenia, defined as platelet counts below 150 × 10^9^/L, represents an established risk factor for perioperative bleeding complications. Low platelet counts impair primary hemostasis and have been consistently associated with increased transfusion requirements.[2,8] The mechanisms underlying thrombocytopenia in lung transplant candidates are diverse and may include bone marrow suppression from chronic illness, nutritional deficiencies, or immune-mediated destruction.[2,8]

Coagulopathy, evidenced by an International Normalized Ratio (INR) exceeding 1.5, reflects reduced synthesis of vitamin K-dependent clotting factors and predicts increased bleeding risk.[9,10] In a large cohort study, low postoperative fibrinogen levels and coagulation abnormalities were independently associated with severe postoperative bleeding requiring surgical revision.[10] Specifically, each mg/dL increase in postoperative fibrinogen was associated with decreased odds of severe bleeding (odds ratio 0.99), highlighting the critical importance of maintaining adequate fibrinogen concentrations throughout the perioperative period.[10] Interestingly, preoperative fibrinogen levels were not predictive of bleeding, suggesting that intraoperative consumption and dilution play more important roles than baseline status.[10]

1.6 Surgical and Procedural Complexity

The type of transplant procedure plays a major role in bleeding risk because it directly affects how complex and how long the surgery is. Bilateral lung transplants consistently use more blood products than single-lung procedures, mainly due to longer operative times and the overall increased complexity of the surgery.[1] Studies comparing the two approaches show that bilateral procedures require more dissection, take longer, and often rely more heavily on ECMO, all of which contribute to higher blood loss.[11] Because bilateral transplantation is done sequentially, the first implanted lung receives the entire cardiac output while the second lung is being implanted, which can put the new graft at risk of uncontrolled reperfusion and sometimes forces the team to use ECMO.[4]

Redo lung transplantation adds another layer of difficulty and is one of the highest-risk scenarios for intraoperative bleeding. Prior lung transplantation was linked to roughly a 50% relative increase in blood loss, although this only just reached statistical significance.[7] Scar tissue, distorted anatomy, and dense adhesions from previous surgeries make the operation

much longer and create many opportunities for vascular injury.[5] Patients with any history of cardiothoracic surgery had significantly longer operative times (509 minutes vs 391 minutes) and far higher transfusion needs (7.2 units vs 2.1 units) compared to those without prior surgery.[5] Among previous procedures, chemical pleurodesis stood out as an independent predictor of mortality and was associated with the highest rate of moderate or severe pleural adhesions (52%) at the time of transplant.[5] Prior cardiac and thoracic surgery were also tied to higher rates of reexploration for bleeding (9.0% and 8.0%, vs 4.7% in patients without prior surgery).[5]

Using ECMO during lung transplantation has major effects on hemostasis through several different mechanisms. Both prior lung transplantation and pre- or intraoperative ECMO were independent predictors of increased blood loss, with intraoperative support raising blood loss by 107% and preoperative support by 59%.[7] Another large study found that pre- and postoperative ECMO were each independently associated with severe postoperative bleeding that required surgical revision.[10] Preoperative ECMO use carried a 14-fold increase in bleeding risk (OR 14.41), while postoperative use increased risk fourfold (OR 4.25).[10] Interestingly, intraoperative ECMO was not associated with increased bleeding in that series, likely reflecting differences in anticoagulation protocols and the shorter duration of exposure.[10]

The reasons extracorporeal support increases bleeding are multifactorial. Systemic anticoagulation is required to keep the circuit from clotting, and cardiopulmonary bypass usually requires even higher levels of anticoagulation than ECMO.[1] Blood contact with the artificial circuit surface triggers platelet activation and consumption, disturbances in the coagulation cascade, and platelet dysfunction.[7] Patients can also develop acquired von Willebrand syndrome within 24 hours of starting ECMO, which further impairs hemostasis and isn't detected by standard coagulation tests.[10] Hemodilution from the priming volume lowers fibrinogen and clotting factor levels, while the inflammatory response to circuit exposure activates multiple coagulation pathways.[10] Overall, the longer a patient remains on extracorporeal support, the more pronounced these bleeding-related changes become.[10]

1.7 Impact of Transfusion on Clinical Outcomes

The link between perioperative transfusion and worse outcomes has been shown repeatedly across multiple studies. PGD (defined as diffuse pulmonary infiltrates within 72 hours of transplant without another identifiable cause) occurs much more often in patients who receive transfusions.[2] This severe form of acute lung injury is the leading cause of early mortality after lung transplantation, and there is a clear dose-response relationship: the more blood a patient receives, the higher the risk.[2] Proposed mechanisms include the pro-inflammatory effects of stored blood products and transfusion-related lung injury, though it can be difficult to distinguish these injuries from PGD because the clinical presentations overlap.[2]

Transfusion also has major downstream effects on resource use and morbidity. Patients who receive blood products spend significantly longer in the ICU and require longer periods of mechanical ventilation, increasing their risk of complications such as ventilator-associated

pneumonia and critical illness myopathy.[3] Median ICU stay rises from 4 days in non-transfused patients to 7 days in those who receive blood, which represents both added clinical burden and notable resource use.[2] Mechanical ventilation duration also increases in transfused patients, with all the associated risks, including barotrauma and ventilator-induced lung injury.[2]

The effect on mortality is most obvious in the early postoperative period. In one study, every patient who died within 30 days of transplant (all seven) had received a transfusion, although the sample size limited statistical power.[2] Patients who require massive transfusion have particularly poor outcomes, with a 30-day mortality of 7.0% compared to 0.6% in patients with insignificant-to-moderate bleeding, and one-year mortality rates of 22.2% versus 7.3%.[3] Even after adjusting for other risk factors, this mortality gap persists, suggesting that bleeding itself, the transfusion, or both, fundamentally shift the patient's postoperative trajectory.[3]

There is also evidence that intraoperative transfusion affects longer-term graft function. Higher volumes of all blood products were associated with worse lung function up to one year after transplant, as shown by predicted FEV1 at 3, 6, and 12 months.[6] While transfusion did not increase the risk of acute rejection or overall mortality in that study, the prolonged hospital stays, longer ICU duration, and slower recovery of lung function highlight the importance of minimizing transfusion when possible.[6]

1.8 Knowledge Gap and Study Rationale

Even though perioperative bleeding is known to affect outcomes and many individual risk factors have been identified, there are still relatively few comprehensive, multifactorial analyses that compare the relative importance of different risk domains. Most studies isolate one risk factor at a time or focus on narrow patient subgroups, which makes it hard to understand how patient demographics, disease-specific features, baseline hematologic status, and surgical complexity interact to influence bleeding risk. And while the negative effects of transfusion on outcomes are increasingly clear, we still lack detailed insight into how specific risk-factor combinations translate into different patterns of clinical outcomes, which is information that is essential for preoperative risk stratification, resource planning, and informed consent.

Knowing which patients are most likely to experience significant perioperative bleeding supports several key clinical goals. First, good preoperative risk assessment allows clinicians to optimize issues, such as untreated anemia, thrombocytopenia, or reversible coagulopathies. Second, risk stratification guides procedural planning, including decisions about extracorporeal support, choice of surgical approach, and required blood bank resources. Third, identifying high-risk patients improves informed consent by grounding discussions in individualized risk rather than population-level estimates. Finally, understanding how specific risk factors relate to bleeding severity and postoperative outcomes highlights opportunities for quality improvement and strategies to reduce transfusion-related morbidity and mortality.

1.9 Study Objectives

The primary aim of this study is to identify patient demographic characteristics, disease-specific factors, baseline hematologic parameters, and procedural variables associated with perioperative transfusion requirements in lung transplantation. Specifically, we seek to determine which factors independently predict both any perioperative transfusion and massive transfusion, recognizing these as distinct outcomes with different clinical implications and prognostic significance. Our secondary aim is to evaluate the impact of perioperative transfusion on clinically meaningful outcomes, specifically 12-month mortality and intensive care unit length of stay, to quantitatively assess the downstream consequences of bleeding and transfusion and thereby inform the clinical importance of our predictive model. Through comprehensive analysis incorporating the full spectrum of established risk factors, we aim to develop a framework for preoperative risk assessment that can guide clinical decision-making, optimize perioperative management, and potentially improve outcomes for this high-risk patient population.

2.0 Methods

2.1 Data Cleanup and Selection

This study included 192 adult patients who underwent lung transplantation. The dataset contained 117 variables including patient demographics, preoperative laboratory values, operative details, and postoperative outcomes. Predictor variables were selected based on literature review identifying established risk factors for perioperative bleeding in lung transplantation. Individual predictors included age, BMI, gender, lung allocation score, preoperative hemoglobin, platelet count, INR, underlying diagnosis (CF, PH), transplant type (single versus bilateral), redo transplantation status, and intraoperative extracorporeal life support use (ECMO versus CBP). Four composite variables were constructed from the dataset. The "any transfusion" variable identified patients receiving any red blood cell transfusion (total 24-hour RBC > 0). "Massive transfusion" was defined as more than 10 units of packed red blood cells within 24 hours. The "high risk patient" variable flagged patients with redo transplantation, intraoperative extracorporeal support, cardiopulmonary bypass use, CF, or PH, characteristics that increase surgical complexity and bleeding risk. "Baseline coagulopathy" identified patients with preoperative INR greater than 1.5 or platelet count less than 150 × 10^9/L. Primary outcomes were any perioperative transfusion and massive transfusion. Secondary outcomes included 12-month all-cause mortality and intensive care unit length of stay in days.

2.2 Multivariable logistic regression: the screening model for who needs transfusions

Multivariable logistic regression was selected as the appropriate approach because the outcome (any transfusion requirement) is binary and the primary objective was inference. We are identifying risk factors and estimating their independent associations with transfusion needs, rather than prediction. This approach allows us to estimate the independent association between each clinical variable and transfusion requirement, so testing all predictors together while simultaneously adjusting for other covariates. By accounting for potential confounding, the model provides interpretable odds ratios that reflect the unique contribution of each predictor.

The multivariable logistic regression model was used to identify factors associated with any transfusion requirement (this was defined as ≥1 RBC unit within 24 hours post-operatively). Predictor variables were selected a priori, based on clinical relevance and literature review, including patient demographics (age, gender, BMI), surgical factors (transplant type: single vs bilateral), clinical risk markers (high-risk patient composite, baseline coagulopathy), disease severity (Lung Allocation Score), and hematologic status (pre-operative hemoglobin). Complete case analysis was performed, excluding patients with missing data. Model assumptions were checked using events-per-variable ratio (EPV ≥10), to make sure we had sufficient outcome events relative to the number of predictors to avoid overfitting. Variance inflation factors (VIF <5) was also used, which assess whether predictor variables are too highly correlated with each other. Model discrimination was assessed using the area under the curve (AUC). Odds ratios (OR) with 95% confidence intervals (CI) were calculated, with statistical significance set at $p < 0.05$.

2.3 Multiple logistic regression for massive transfusion

We developed a logistic regression model to identify factors associated with *massive transfusion*. Predictors were chosen based on clinical relevance and prior literature, and included: age, gender, BMI, transplant type, high-risk patient indicator, pre-operative hemoglobin, baseline coagulopathy, and Lung Allocation Score (LAS). The model was fit using complete-case data; patients with missing values in any predictor or the outcome were automatically excluded, resulting in 171 complete observations. The sample contained only 9 massive transfusion events, which was substantially lower than the recommended minimum number of predictors (predictors < smallest class size /15), indicating that the model was likely at risk for unstable coefficient estimates. Multicollinearity among predictors was assessed using Variance Inflation Factors (VIF). Odds ratios with 95% confidence intervals were calculated. The statistical significance threshold was set as 0.05.

2.4 Multiple linear regression for transfusion volume

To investigate the predictors of transfusion volume, we fit a multiple linear regression model using total 24-hour RBC units transfused as the continuous outcome. The initial model included all clinically relevant predictors: age, gender, transplant type, BMI, high-risk status, pre-operative hemoglobin, baseline coagulopathy, and LAS score. After fitting the model using ordinary least squares, we examined the estimated coefficients, corresponding p-values, and 95% confidence intervals to summarize associations between predictors and transfusion volume.

However, since linear regression relies on several assumptions, we systematically assessed linearity, homoscedasticity, normality, independence, and multicollinearity. The histogram of residuals was examined to assess whether the residuals appear symmetric, as substantial skewness may indicate violation of distributional assumptions. Linearity and homoscedasticity were assessed using a residuals versus fitted values plot, which is expected to show residuals randomly scattered around zero with no visible fanning pattern if both assumptions are met. Normality of residuals was evaluated using a Q–Q plot, where points falling along the reference line indicate that the residuals follow a Normal distribution. To assess potential multicollinearity among predictors, variance inflation factors (VIF) were computed; values below the commonly used thresholds (e.g., <5) suggest that predictors are not excessively correlated.

Inspection of diagnostic plots revealed that residuals from the untransformed model were right-skewed, suggesting violation of the normality assumption. To address this, we applied a square-root transformation to the outcome variable, which is commonly used for continuous, right-skewed data. We refit the model using the transformed outcome and re-evaluated all diagnostic checks, including residual histograms, residuals-versus-fitted plots, Q–Q plots, and VIF. The transformation improved the symmetry and distributional properties of residuals, resulting in a model that better satisfied linear regression hypothesis testing assumptions.

2.5 Survival Analysis

A survival analysis with 12-month mortality as the primary outcome was conducted to determine whether RBC transfusion volume independently influences patient survival. Survival time was calculated as the number of days between transplant surgery (OR date) and death. Patients who were alive at the 12-month time point were censored at 365 days.

2.6 Kaplan-Meier Analysis

Kaplan-Meier survival curves were stratified by RBC transfusion level and estimated for the overall cohort. For visualization, transfusion was divided into four groups: none (0 units), low (1-5 units), moderate (6-10 units), and high (>10 units). One year survival probabilities with 95% confidence intervals were calculated for each group. The survival distributions between transfusion groups were compared using the log-rank test. The proportional hazards assumption was assessed visually using complementary log-log plots prior to running the log-rank test.

2.7 Cox Proportional Hazards Model

A Cox proportional hazards model was fitted to assess the relationship between RBC transfusion volume (continuous) and 12-month mortality, while adjusting for potential confounders. Covariates included: age (continuous, per year), LAS score (continuous, per point), high-risk patient status (binary), and gender (binary). Patients with missing LAS scores were excluded from the multivariable analysis, resulting in complete case analysis. For each predictor, hazard ratios (HR) with 95% confidence intervals were calculated. The concordance index (C-index) was used to evaluate model discrimination. Schoenfeld residual plots were used to test the proportional hazards assumption using both formal statistical testing (cox.zph) and graphical assessment. For the global test, a pre-determined alpha of less than 0.05 was considered indicative of a violation. The survival and survminer packages in R (version 4.5) were additionally used for statistical analysis.

2.8 Multiple Linear Regression: Impact of RBC Units on Length of ICU Stay

A multiple linear regression was done to assess the impact of transfusion on patient outcomes, using duration of ICU stay in days as a surrogate endpoint for patient outcome. The variable of interest is the number of RBC units transfused in 24 hours and covariates (age, gender, BMI, transplant type, high-risk patient indicator, pre-operative hemoglobin, baseline coagulopathy, and LAS) were chosen through literature review. The model aimed to discern, on average, how many days are added to a patient's ICU stay with each additional unit of RBCs transfused. The model was fit using complete case analysis, where out of 192 observations, 179 cases were analyzed. Multicollinearity was assessed through VIFs where scores greater than 5, indicate concerning collinearity. 95% CIs were calculated and the statistical significance threshold was set to $p < 0.05$.

3.0 Results

3.1 Multivariable logistic regression: the screening model for who needs transfusions

A summary of the characteristics of the population within the study is included in Figure 1. Of the 192 patients in the dataset, 180 had complete data and were included in the analysis, with 12 patients excluded due to missing Lung Allocation Score values. Among the 180 patients analyzed, 107 (59.4%) received at least one unit of RBCs within 24 hours post-operatively. The events-per-variable ratio was 13.4, indicating an adequate sample size to avoid overfitting. All variance inflation factors were below 2.0, confirming no multicollinearity concerns. The multivariable logistic regression model demonstrated excellent discrimination (AUC = 0.885).

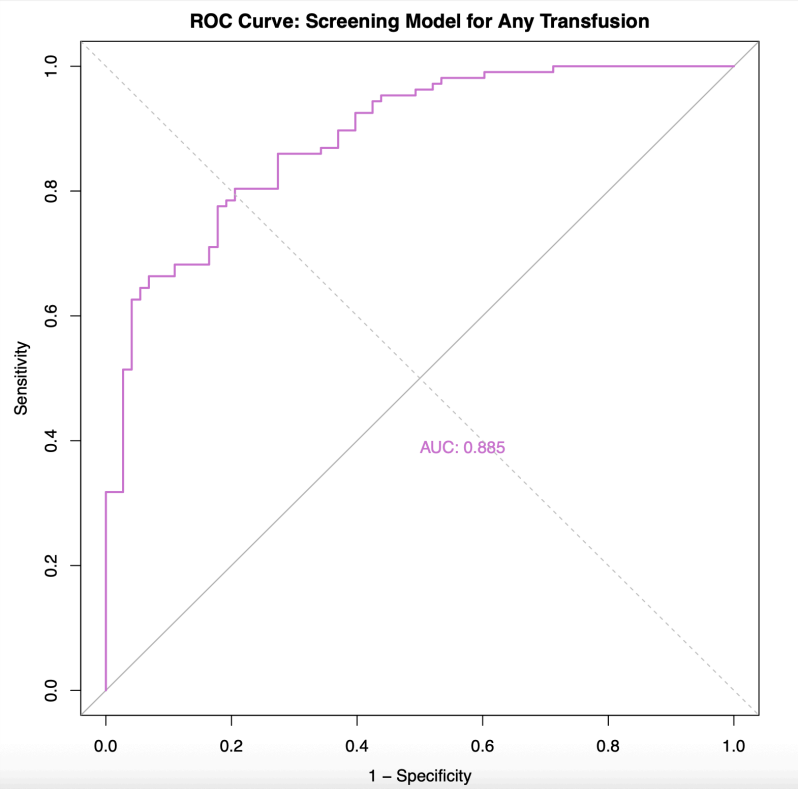

Figure 1. Receiver Operating Characteristics (ROC) Curve for the Transfusion Screening Model

Table 1. Multivariable Logistic Regression analysis for Any RBC Transfusion within 24 Hours Post-Transplant

Variable	Coefficient	Odds Ratio	CI lower	CI upper	P value
Age	0.041	1.042	1.006	1.082	0.027
Gender*	-0.224	0.799	0.335	1.935	0.614
BMI	-0.109	0.896	0.801	0.997	0.049
High Risk Patient	2.164	8.705	3.56	23.275	<0.001

Preop Hb	-0.08	0.924	0.891	0.952	<0.001
Baseline Coagulopathy	-0.543	0.581	0.178	1.897	0.363
Bilateral Type	2.323	10.206	3.122	38.998	<0.001
LAS score	0.039	1.04	0.986	1.111	0.173

* Males serve as the predictor which represents the comparison of males vs females. Female was coded as the reference category in the logistic regression

Five factors were independently associated with transfusion requirement after adjusting for all covariates (Table 1).Bilateral transplant was the strongest predictor (OR = **10.21**, 95% CI: 3.12–39.00, p < **0.001**), with bilateral transplants having over 10-fold higher odds of requiring transfusion compared to single lung transplants. High-risk patient status was also strongly associated with transfusion (OR = 8.71, 95% CI: 3.56–23.28, p < 0.001). Pre-operative hemoglobin was inversely associated with transfusion need (OR = 0.92 per g/L, 95% CI: 0.89–0.95, p < 0.001); each 10 g/L decrease in hemoglobin was associated with approximately 2-fold higher odds of transfusion. Age showed a modest positive association (OR = 1.04 per year, 95% CI: 1.01–1.08, p = 0.027), with each 10-year increase associated with 48% higher odds. BMI showed a weak protective effect (OR = 0.90 per kg/m², 95% CI: 0.80–1.00, p = 0.049). Gender (OR = 0.80, 95% CI: 0.34–1.94, p = 0.614), baseline coagulopathy (OR = 0.58, 95% CI: 0.18–1.90, p = 0.363), and Lung Allocation Score (OR = 1.04, 95% CI: 0.99–1.11, p = 0.173) were not independently associated with transfusion requirement.

3.2 Multivariable logistic regression for massive transfusion

Table 2. Logistic Regression Results For Massive Transfusion

Variable	**Coefficient**	**Odds Ratio**	**CI lower**	**CI upper**	**P value**
Age	-0.0415	0.9594	0.8914	1.0326	2.693×10^{-1}
Gender (Male)	-1.1769	0.3082	0.0261	3.6365	3.500×10^{-1}
Type (Bilateral)	16.1157	9,976,463.7095	0.0000	Inf	9.967×10^{-1}
BMI	0.0061	1.0062	0.7899	1.2817	9.603×10^{-1}
High Risk Status	16.3075	12,085,819.0753	0.0000	Inf	9.958×10^{-1}
Pre Hb	-0.0684	0.9339	0.8891	0.9809	6.378×10^{-3}

Baseline Coargulopathy (TRUE)	-0.5836	0.5579	0.0574	5.4254	6.151×10^{-1}
LAS score	0.0548	1.0563	0.9832	1.1349	1.344×10^{-1}

In the logistic regression analysis evaluating predictors of massive transfusion, most variables did not show statistically significant associations. The estimated intercept coefficient is $\beta = -27.2174$ with a p-value of 0.9957. Age did not show significance with massive transfusion (OR = 0.9594, 95% CI: 0.8914–1.0326, p = 0.2693). Sex similarly showed no meaningful effect (OR = 0.3082, 95% CI: 0.0261–3.6365, p = 0.3500). Transplant type demonstrated an extremely large odds ratio (OR = 9,976,463.71), with a confidence interval ranging from 0 to infinity (p = 0.9967). High-risk patient status produced a similar pattern (OR = 12,085,819.08; 95% CI: 0–∞; p = 0.9958). BMI was not associated with the outcome (OR = 1.0062, 95% CI: 0.7899–1.2817, p = 0.9603). Baseline coagulopathy also showed a wide interval (OR = 0.5579, 95% CI: 0.0574–5.4254, p = 0.6151), indicating no reliable effect. LAS score demonstrated a small, non-significant positive association (OR = 1.0563, 95% CI: 0.9832–1.1349, p = 0.1344).

The only statistically significant predictor in the model was pre-operative hemoglobin, where higher pre-operative hemoglobin levels were associated with lower odds of massive transfusion (OR = 0.9339, 95% CI: 0.8891–0.9809, p = 0.0064).

All VIF values are between ~1.0 and 1.75, which is well below the common threshold of 5. Therefore, there is no evidence of concerning multicollinearity among predictors in this logistic regression model.

3.3 Multiple linear regression for transfusion volume

Non-transformed approach:

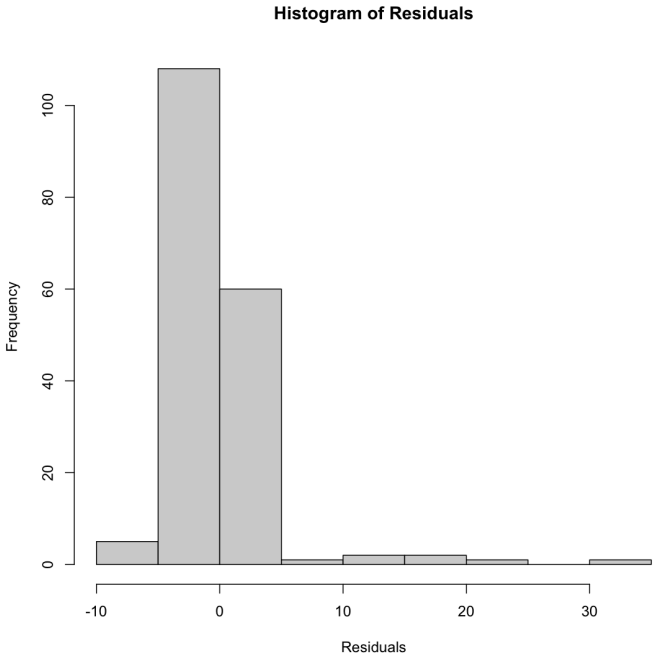

Figure 2. Histogram of Residuals For Transfusion Volume Model (Non-transformed)

The histogram shows a strong right skew, with most residuals clustered near zero but a long tail extending to very large positive values. This indicates that the residuals are not normally distributed, violating the normality assumption of linear regression.

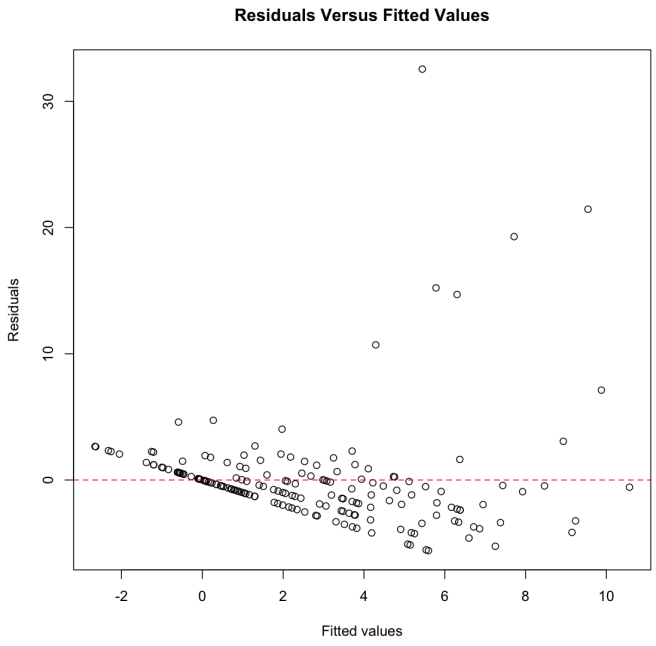

Figure 3. Residuals Versus Fitted Values For Transfusion Volume Model (Non-transformed)

The residual–fitted plot shows a funnel-shaped pattern, where residuals spread out more as fitted values increase. This indicates heteroscedasticity (non-constant variance), violating another key linear regression assumption.

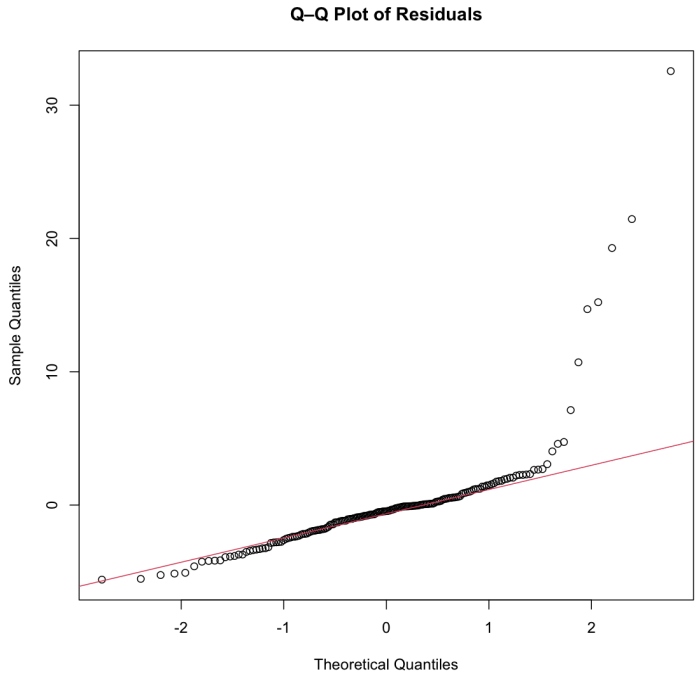

Figure 4. Q-Q Plot For Transfusion Volume Model (Non-transformed)

The Q–Q plot shows heavy deviation from the straight line in the upper right tail. The extreme positive residuals pull the points far above the line, confirming that the residual distribution is right-skewed with heavy tails and is not normally distributed.

After sqrt transformation:

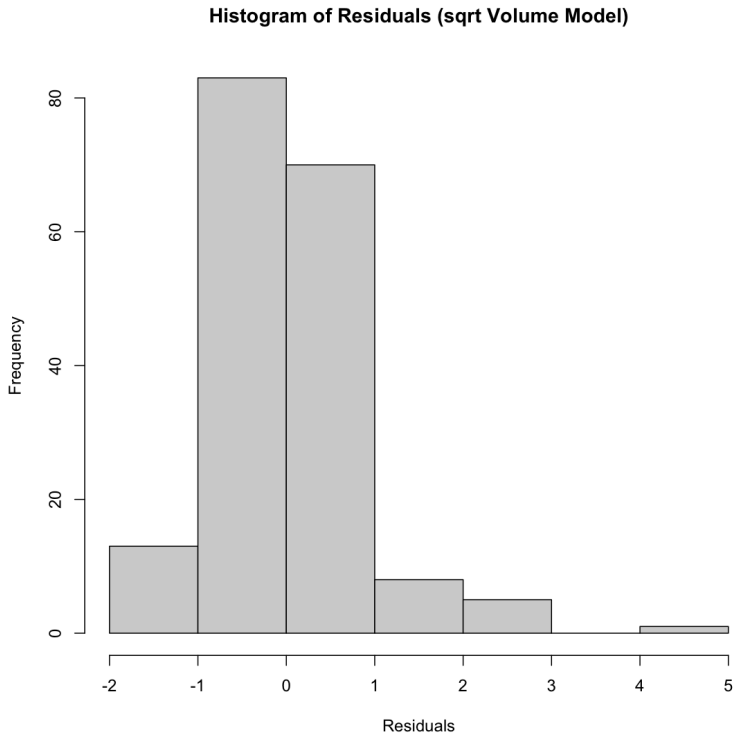

Figure 5. Histogram of Residuals For Transfusion Volume Model (Sqrt-transformed)

The histogram still shows some right skew, but the distribution is much more centered around zero compared with the untransformed model.

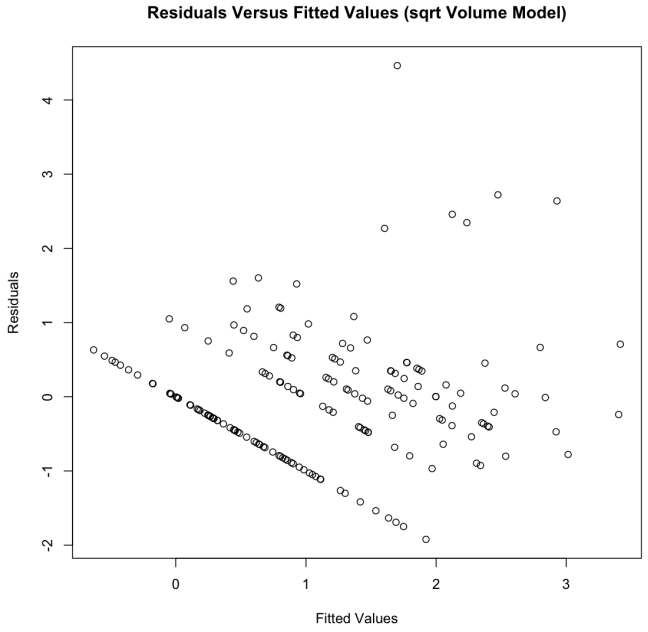

Figure 6. Residuals Versus Fitted Values For Transfusion Volume Model (Sqrt-transformed)

The residual–fitted plot shows a more even spread of residuals across the range of fitted values compared with the untransformed model. The untransformed approach that showed a strong funnel shape has been reduced in the sqrt-transformed figure, suggesting improved homoscedasticity.

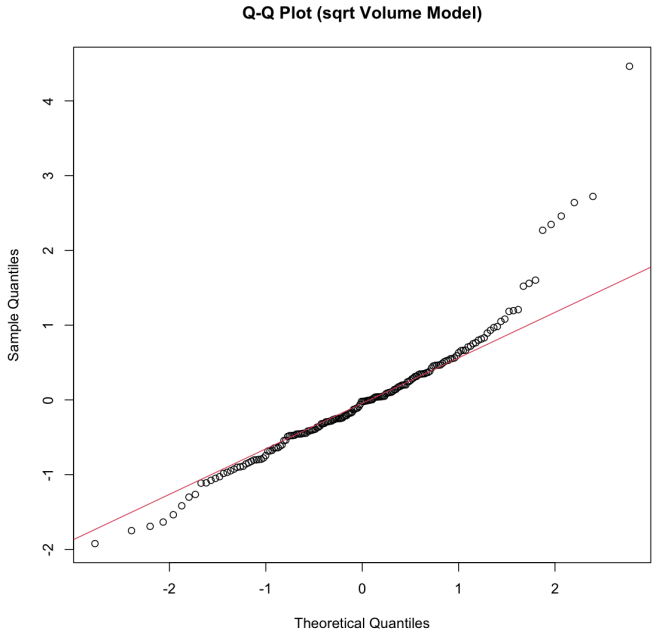

Figure 7. Q-Q Plot For Transfusion Volume Model (Sqrt-transformed)

The Q–Q plot shows that residuals align much more closely with the theoretical normal line. This indicates that the sqrt-transformation substantially improved normality.

Table 3. Linear Regression for Transfusion Volume Model (sqrt-transformed)

Variable	Coefficient	P-value	CI lower	CI upper
(Intercept)	3.8221	1.364×10^{-7}	2.4504	5.1939
Age	0.0041	4.510×10^{-1}	−0.0067	0.0150
Gender (Male)	−0.1192	4.006×10^{-1}	−0.3985	0.1601
Type (Bilateral)	0.4366	1.582×10^{-2}	0.0830	0.7902
BMI	−0.0258	1.407×10^{-1}	−0.0603	0.0086
High Risk Status	0.7971	1.877×10^{-7}	0.5075	1.0866
Pre Hb	−0.0287	8.093×10^{-12}	−0.0364	−0.0210

Baseline Coargulopathy (TRUE)	−0.1182	5.123×10^{-1}	−0.4735	0.2371
LAS score	0.0161	3.331×10^{-2}	0.0013	0.0310

The intercept had an estimated coefficient of $\beta_0 = 3.822$ with a p-value of 1.36e-07. Age had an estimated coefficient of $\beta = 0.0041$ with a p-value of 0.4510. Gender (reference = Female) had an estimated coefficient of $\beta = –0.1192$ with a p-value of 0.4006. For transplant type (reference = Single), there was an estimated coefficient of $\beta = 0.4366$ with a p-value of 0.0158. BMI had an estimated coefficient of $\beta = –0.0258$ with a p-value of 0.1407. High-risk patient status (reference = Not high-risk) had an estimated coefficient of $\beta = 0.7971$ with a p-value of 1.88e-07. Pre-operative hemoglobin had an estimated coefficient of $\beta = –0.0287$ with a p-value of 8.09e-12. Baseline coagulopathy (reference = No coagulopathy) had an estimated coefficient of $\beta = –0.1182$ with a p-value of 0.5123. LAS score had an estimated coefficient of $\beta = 0.0161$ with a p-value of 0.0333.

Variance inflation factors (VIFs) for all predictors were low: age (1.52), gender (1.21), transplant type (1.19), BMI (1.20), high-risk status (1.22), pre-operative hemoglobin (1.34), baseline coagulopathy (1.09), and LAS score (1.14). Because all VIF values are well below the commonly accepted threshold of 5, there is no evidence of problematic multicollinearity among the predictors, indicating that the estimated coefficients are stable and not inflated due to correlations among covariates.

3.4 Survival Analysis: Impact of RBC Transfusion on 12-Month Mortality

Overall Survival

Of the 192 lung transplant patients, 23 (12.0%) died within 12 months of transplant. Overall, 1-year survival probability was 88% (95% CI: 83.5%–92.7%). Due to missing LAS scores, 12 patients were excluded from analysis, resulting in an analytic sample of 180 patients and 21 observed deaths.

Descriptive Characteristics by Survival Status

Patients who died within 12 months were slightly older (mean age 60.9 vs 56.0 years), had higher LAS scores (38.0, 36.8), and were more likely to be categorized as high-risk (66.7% vs 62.3%). However, patients who died received fewer RBC transfusions on average (mean 1.9 vs 2.78 units, and median 2 vs 1 unit). The gender distribution was similar between groups (52.4% vs 52.8% male) (Table 4).

Table 4. Characteristics by 12-Month Survival Status

Characteristic	Survived % (n=159)	Died % (n=21)
Mean RBC Units	2.78	1.90
Median RBC Units	1	2

Mean Age (years)	56.0	60.9
Mean LAS Score	36.8	38.0
High Risk Patient (%)	62.3	66.7
Male (%)	52.8	52.4

Kaplan-Meier Analysis

The Kaplan-Meier survival curves were stratified by RBC transfusion level and showed no significant difference in survival between groups (log-rank p = 0.6) (Figure 8). One-year survival probabilities were 89.7% for no transfusion (n=78), 86.3% for low transfusion (n=95), 81.8% for moderate transfusion (n=11), and 100% for high transfusion(n=8). The high transfusion group did not have any deaths, limiting interpretation of the subgroup. Log-Log plot displayed 3 approximately parallel curves, supporting the proportional hazards assumption (Figure S1).

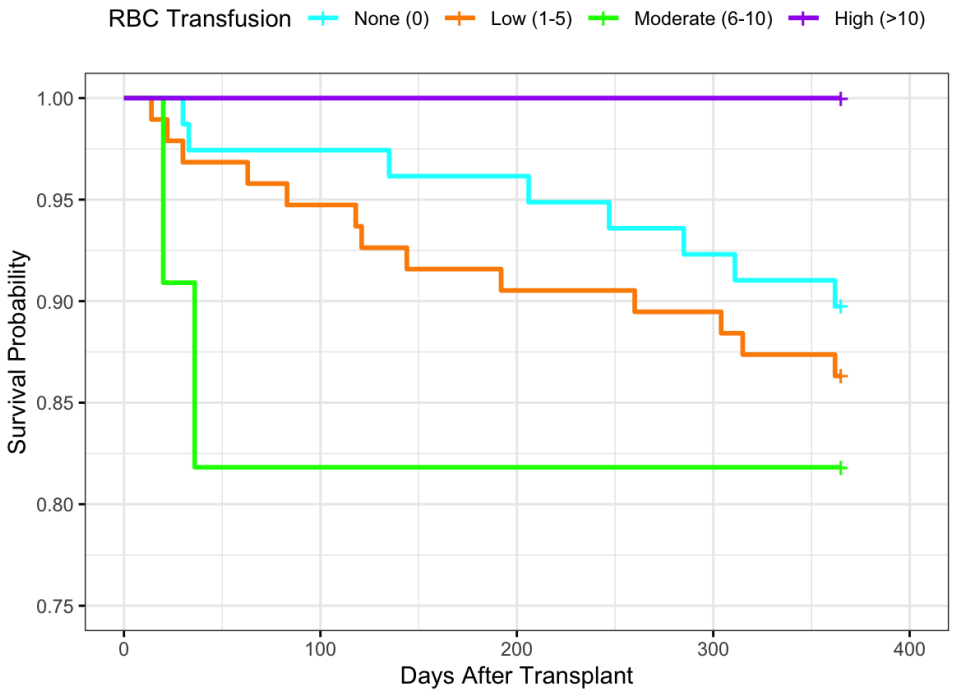

Figure 8. Kaplan-Meier curves stratified by RBC transfusion level

Cox Proportional Hazards Model

A cox proportional hazards model was fitted to assess the association between RBC transfusion volume and 12-month mortality, while adjusting for age, LAS score, high-risk patient status, and gender (Table 5).

Table 5. Cox Proportional Hazards Model for 12-Month Mortality

Variable	HR	95% CI	p-value
RBC Transfusion (per unit)	0.93	0.79–1.10	0.415
Age (per year)	1.03	0.99–1.07	0.122
LAS Score (per point)	1.02	0.98–1.06	0.432

High Risk Patient	1.59	0.59–4.31	0.360
Gender (Male vs Female)	0.76	0.31–1.86	0.549

Every 1 additional unit of RBC transfusion the risk of death decreased by 7% (HR= 0.93, 95% CI: 0.79–1.10, p = 0.415). For every additional 1 year of age, the risk of death increased by 3% (HR = 1.03, 95% CI: 0.99–1.07, p = 0.122). For every 1 additional point in LAS score, there was a 2% increase in the risk of death (HR = 1.02, 95% CI: 0.98–1.06, p = 0.432). Patients who were categorized as high-risk had a 59% higher risk of death (HR = 1.59, 95% CI: 0.59–4.31, p = 0.360). Males had a 24% lower risk of death compared to females (HR = 0.76, 95% CI: 0.31–1.86, p = 0.549) (Figure 9). None of these associations were less than our predetermined alpha of 0.05, therefore we fail to reject the null hypothesis that RBC transfusion volume has no effect on 12-month mortality.

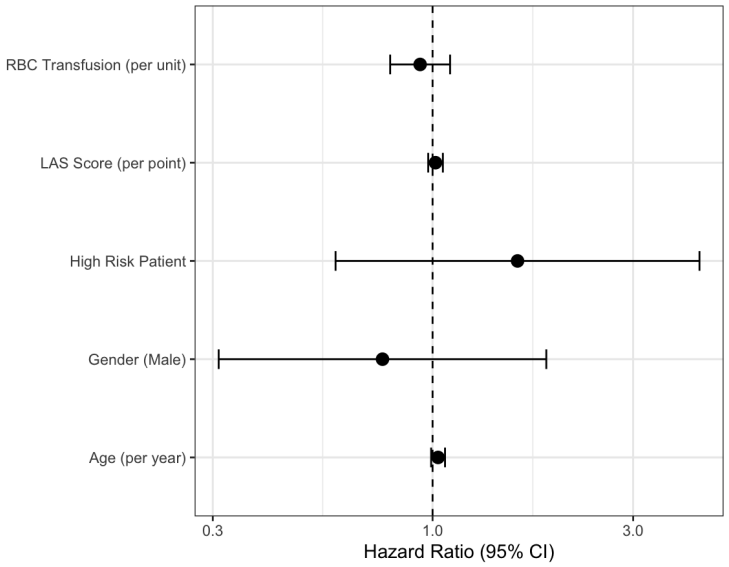

Figure 9: Hazard Ratios for 12-Month Mortality

The proportional hazards assumptions were tested using Schoenfeld residuals with no significant violations detected (global test p=0.93) (Figure S2). The model had a concordance index (C-index) of 0.635, which indicates acceptable discrimination ability.

3.5 Multiple linear regression: Impact of RBC Units on Length of ICU Stay

A multiple linear regression model was used to evaluate the number of RBC units transfused on ICU length of stay. The model was statistically significant ($F(9, 169) = 3.93$, $p = 0.00015$) and explained approximately 17.3% of the variance in ICU stay (adjusted $R^2 = 0.13$).
Total 24 hour units of RBCs was the only significant predictor of ICU stay, where each additional unit of RBC transfused within 24 hours was associated with an increase of 0.81 days in ICU length of stay ($\beta = 0.81$, $SE = 0.19$, $p < 0.001$). Higher BMI also showed association with longer ICU stay ($\beta = 0.37$, $SE = 0.22$, $p = 0.099$), however this relationship was not significant. All remaining variables including age, sex, high-risk status, preoperative hemoglobin, baseline coagulopathy, surgical laterality, and LAS score were not significantly

associated with ICU length of stay ($p > 0.15$ for all). Overall, increased RBC units in 24 hours was associated with prolonged ICU stay in this cohort.

Table 6: Table outlining results of predictors for multiple linear regression for ICU LOS as patient outcome with 24hr RBC units being the variable of interest.

Variable	**Estimate**	**95% CI**	**p-value**
24hr RBCs (units)	0.806	[0.429, 1.18]	0.0000387
Age	-0.00168	[-0.139, 0.136]	0.981
Gender: male	0.376	[-3.16, 3.92]	0.834
BMI	0.365	[-0.0699, 0.800]	0.0994
High Risk: true	2.01	[-1.74, 5.75]	0.292
Baseline Anemia	-0.0196	[-0.123, 0.0842]	0.710
Baseline Coagulopathy: true	2.90	[-1.59, 7.39]	0.204
Transplant Type: bilateral	1.66	[-2.82, 6.13]	0.466
LAS Score	-0.137	[-0.326, 0.0517]	0.154

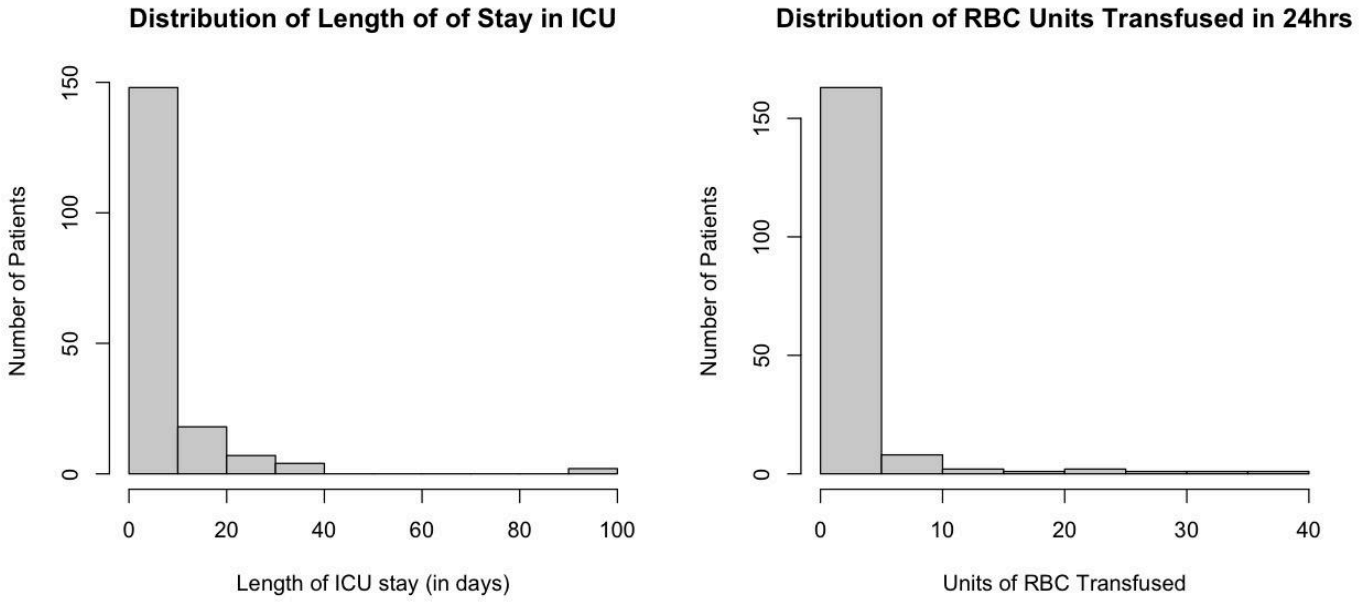

Figure 9: Histograms visualizing the right-skewed distribution of ICU LOS and 24hr RBC Units, where most patients have low values in both variables.

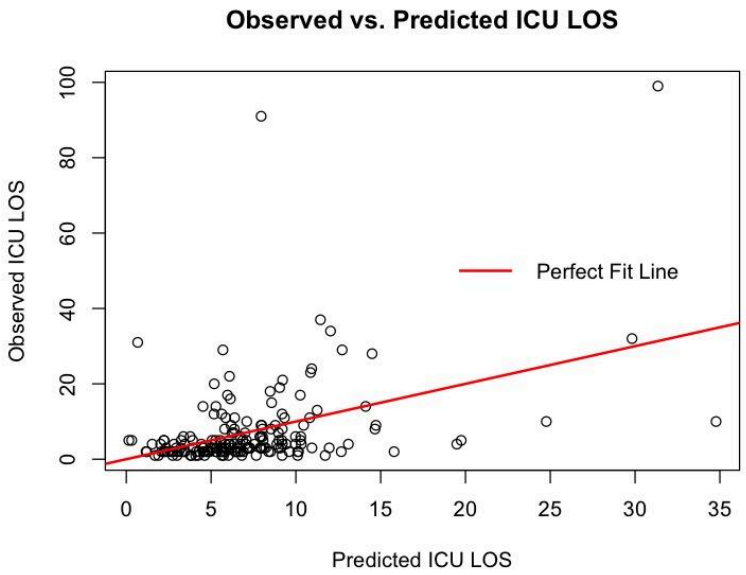

Figure 10: Observed vs. Predicted ICU LOS using fitted multiple linear regression model, where red line indicates perfect prediction. Right-skewed distribution seen as most patients have low ICU LOS

4.0 Discussion

4.1 Patient Characteristics Analysis

This study of 192 lung transplant recipients identified several key risk factors associated with perioperative transfusion requirements. Patients receiving transfusions demonstrated significantly higher disease acuity, as evidenced by elevated lung allocation scores (38.4 versus 34.7), and lower body mass index (23.5 versus 25.0 kg/m²), suggesting more advanced illness and nutritional depletion. The transfusion group also had markedly higher rates of surgical complexity markers, including bilateral transplantation (92.1% versus 66.7%), redo transplantation (8.8% versus 0%), and intraoperative extracorporeal life support use (69.3% versus 20.8%).

Our composite "high-risk patient" variable, encompassing cystic fibrosis, idiopathic pulmonary hypertension, redo transplantation, and extracorporeal support requirement, effectively stratified bleeding risk, with 81.6% of transfused patients classified as high-risk compared to only 37.2% of non-transfused patients. This finding validates our approach of framing these disease-specific and procedural factors as proxies for surgical complexity.

The clinical consequences of transfusion were substantial. Transfused patients experienced prolonged intensive care unit stays (median 4.0 versus 3.0 days) and higher rates of massive transfusion (7.9% versus 0%). Notably, baseline coagulopathy prevalence was similar between groups (17.5% versus 12.8%), suggesting that procedural factors may be more influential than preoperative hemostatic status in determining transfusion requirements. These findings underscore the importance of preoperative risk stratification and optimization strategies to minimize bleeding and transfusion-related morbidity in this high-risk population.

4.2 Screening model for transfusion

The screening model identified bilateral transplant type and high-risk patient status as the dominant predictors of any transfusion requirement, both showing odds ratios exceeding 8. The strong association with bilateral transplantation reflects both the greater surgical complexity and larger bleeding surface area inherent to the procedure. Importantly, preoperative hemoglobin emerged as a potentially modifiable risk factor, with each 10 g/L decrease approximately doubling transfusion odds - this supports the clinical value of preoperative anemia optimization when safely achievable. The lack of association between baseline coagulopathy and transfusion requirement was unexpected given existing literature, and may reflect either the relatively low prevalence of severe coagulopathy in our cohort or that procedural factors overwhelm baseline hemostatic status in determining bleeding risk

There are some limitations to be acknowledged. First, 12 patients (6.3%) were excluded for missing LAS scores, which may introduce selection bias if the reason for missingness was not at random. Second, the composite high-risk patient variable combines heterogeneous conditions, limiting assessment of individual risk factors. Third, wide confidence intervals for bilateral transplant and high-risk status reflect few events in some subgroups. This first model addresses only the binary outcome of any transfusion and does not capture volume or massive transfusion risk, which are examined in subsequent analyses. Fifth, the AUC represents

apparent performance without train-test splitting. The model's performance metrics (AUC = 0.885) reflect performance on the same dataset used for model development, without train-test splitting or cross-validation. However, our analysis prioritizes risk factor identification and effect estimation rather than predictive model development. The multivariable regression provides odds ratios with confidence intervals representing associations in our study population. While we report AUC as a measure of overall model fit and discrimination, external validation would only be necessary if this model were to be implemented as a clinical prediction tool for prospective patient risk stratification, which is beyond the scope of this exploratory analysis focused on understanding transfusion determinants.

This model identifies preoperative risk factors for any transfusion requirement in the first 24 hours post-transplant. The three strongest predictors are bilateral transplant, high-risk status, and preoperative hemoglobin. This could inform blood bank preparation and patient optimization strategies.

4.3 Massive Transfusion

A key limitation of this analysis is the small size of the massive transfusion group, with only 9 patients experiencing the outcome while the model included 8 predictors. According to the common rule of $p < m/10$, which recommends at least 10 outcome events per predictor, the current model increases the risk of unstable or inflated beta coefficients, wide confidence intervals, and poorer model reliability.

Because of the size of the massive transfusion group (n= 9) and complete separation in several key predictors, multivariable logistic regression yielded unstable estimates. Transplant type and risk-risk status both exhibited separation patterns that prevented meaningful effect estimation, as evidenced by the infinite odds ratios and undefined CIs. Since every patient who experienced a massive transfusion belonged to the bilateral transplant group, the predictor “transplant type” perfectly separates the outcome: the model never observes a massive transfusion in the “single lung” group. As a result, the model drives the effect estimate for bilateral transplant toward positive infinity, which produces an enormously large odds ratio and a confidence interval that extends from 0.0000 to infinity. This behavior reflects a mathematical limitation of standard logistic regression when a predictor perfectly classifies the outcome, and explains why transplant type appears with infinite or undefined confidence interval limits in the results.Additionally, since all patients who required a massive transfusion were classified as high-risk patients, this predictor perfectly separated the outcome. With no massive transfusion events in the low-risk group, the logistic model produces a confidence interval that is mathematically undefined (0 to infinity). This separation reflects a limitation of standard logistic regression when a predictor completely classifies the outcome. Overall, due to these limitations we couldn't draw significant conclusions from this model.

4.4 Volume Model

The transfusion volume model identified several clinically meaningful predictors of perioperative blood requirements in lung transplant recipients. Bilateral transplant type, high-risk patient status, lower pre-operative hemoglobin, and higher LAS scores were independently associated with greater transfusion volume. These findings align with established clinical expectations: bilateral procedures are more surgically extensive, high-risk patients typically present with more complex pathology, and low hemoglobin naturally predisposes patients to higher transfusion needs. The positive association with LAS score further suggests that patients with greater disease severity enter surgery physiologically disadvantaged, increasing the likelihood of bleeding and transfusion. In contrast, age, gender, BMI, and baseline coagulopathy did not show meaningful relationships with transfusion volume in this cohort. The absence of association with coagulopathy was notable and may reflect the small number of affected patients or perioperative correction strategies that mitigated bleeding risk. Overall, the model highlights that transfusion volume is primarily driven by surgical complexity, baseline physiologic reserve, and patient severity rather than demographic factors. Clinically, this reinforces the importance of preoperative anemia optimization and enhanced preparation for patients undergoing bilateral procedures or classified as high-risk. Additionally, the improved model fit after applying a sqrt transformation supports that transfusion volume is inherently right-skewed, and transformation yields more stable and interpretable estimates.

4.5 Survival Analysis

Contrary to our initial hypothesis and findings from some prior literature, RBC transfusion volume was not independently associated with increased 12-month mortality in this cohort. The observed paradox, where patients who died received fewer transfusions on average, warrants careful interpretation. Several mechanisms could account for this counterintuitive finding. First, patients who died early in the postoperative period may not have survived long enough to accumulate higher transfusion volumes, creating survival bias in the high-transfusion group. Second, patients receiving more blood products may have also received more aggressive overall supportive care, potentially masking any negative transfusion effects through superior critical care management. Third, it is possible that in modern lung transplantation with contemporary blood banking practices and transfusion protocols, perioperative RBC transfusion genuinely has minimal independent impact on mortality when appropriately indicated.

The absence of deaths in the high transfusion group (>10 units), while challenging traditional assumptions about massive transfusion risk, is heavily constrained by the small subgroup size (n=8) and should not be over-interpreted. Several important limitations temper these findings. The small number of death events (21 deaths) limited statistical power to detect modest but clinically meaningful mortality increases and produced wide confidence intervals that cannot exclude small to moderate effects. Confounding by indication remains a fundamental concern in observational transfusion research, patients who receive more blood differ systematically from those who do not in ways that may independently affect survival. Additionally, this

single-center analysis from 2018 may not generalize to other institutions with different transfusion thresholds, blood management protocols, or patient populations.
Despite these limitations, the findings have practical clinical implications. There is no evidence from this analysis suggesting that appropriately indicated blood transfusion independently increases mortality risk, supporting the principle that transfusion should neither be withheld when clinically necessary nor reflexively avoided based solely on mortality concerns. However, the demonstrated association between transfusion volume and prolonged ICU stay (see section 4.6) indicates that minimizing perioperative bleeding through optimization strategies remains clinically valuable. Validation of these findings through larger multi-center studies with adequate power for subgroup analyses is needed to definitively characterize the transfusion-mortality relationship in contemporary lung transplantation.

4.6 Transfusion volume on ICU length of stay
In this analysis, we examined the impact of RBC transfusion volume associated with ICU length of stay. The model adjusted for demographic differences such as age and gender, in addition to baseline clinical characteristics such as BMI, coagulopathy, anemia, and high risk flags. Procedure-related factors were also adjusted for such as laterality of transplant and LAS score. These covariates were included to isolate the effect of transtransfusion volume within the first 24 hours on duration of ICU stay. The results show that transfusion volume emerged as the only statistically significant predictor of prolonged ICU stay, where each additional unit of RBCs was associated with an estimated 0.81 day increase in ICU LOS. This finding aligns with previous literature linking transfusion exposure to worse short-term postoperative outcomes, including increased morbidity, organ dysfunction, and prolonged critical care needs.

This analysis primarily focused on the impact of 24hr transfusion volume, however all other covariates including age, sex, BMI, preoperative hemoglobin, baseline coagulopathy, and type of transplant, LAS, and high risk flags were all not significantly associated with ICU length of stay. BMI showed a trend toward significance, suggesting that higher body mass may contribute to longer postoperative recovery, however the effect did not meet significance thresholds. This may indicate that transfusion volume is a stronger indicator of early postoperative instability than these baseline factors, or that this model was underpowered to detect additional associations.

Although the model was statistically significant, the explained variance was modest as merely 13% of the variance was captured by this regression. Additionally, we used ICU LOS as a measure of patient outcome, in place of a direct measure due to the availability of the data. Although ICU LOS may be correlated with patient outcomes, where a longer stay in the ICU could reflect worse conditions or the presence of complications, a direct clinical outcome would have been the best choice for the outcome variable. A measure of post-operative quality of life or post-operative lung function would be a superior measure of patient outcome as opposed to ICU LOS as there may be several confounders that affect duration of stay, independent of patient outcomes. This model should be interpreted such that

increased transfusion volume is correlated with increased ICU LOS, as a surrogate end-point of patient outcome.

Finally, this regression model was built on n = 179 patients with 9 predictors, both continuous and categorical. The inclusion of several predictors reduces the effective sample size within each subgroup, limiting statistical power to detect smaller associations. As a result, some clinically relevant predictors may not have reached statistical significance due to insufficient power, rather than absence of effect. The modest sample size also increases the risk of overfitting and may contribute to the wide confidence intervals observed for several variables.

5.0 Conclusion

In conclusion, this analysis identified key perioperative risk factors for transfusion requirements in lung transplantation and examined their impact on clinical outcomes. The screening model demonstrated that bilateral transplant type, high-risk patient status, and lower preoperative hemoglobin were the strongest independent predictors of any transfusion requirement, with excellent discrimination. These findings support targeted preoperative optimization strategies, particularly correction of anemia and enhanced blood bank preparation for bilateral transplants and high-risk patients.[13-16] While the analysis of massive transfusion was limited by sample size and separation issues, the volume model confirmed that bilateral transplant type, high-risk status, lower preoperative hemoglobin, and higher LAS scores independently predicted greater transfusion volumes.[13,16] Contrary to our initial hypothesis, RBC transfusion volume was not independently associated with 12-month mortality in this cohort (HR = 0.93, $p = 0.415$).[17] However, this finding should be interpreted cautiously, given the limited number of death events (n = 21) and potential unmeasured confounding. However, transfusion volume significantly predicted prolonged ICU length of stay, with each additional RBC unit associated with 0.81 additional ICU days ($p < 0.001$), highlighting the substantial resource utilization burden of perioperative bleeding.[13,18] These results emphasize that while transfusion should not be withheld when clinically indicated, strategies to minimize bleeding through careful patient selection, preoperative optimization, and meticulous surgical technique remain important for reducing postoperative morbidity and healthcare costs.[19,20] Future studies with larger sample sizes are needed to validate these findings and further elucidate the complex relationship between transfusion, including amount, and outcomes in lung transplantation.

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(Often shows transfusion as an association of severity rather than an independent driver of mortality, especially when adjusting for confounders).

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Appendix

Table 1. Baseline Characteristics of the Study Cohort

	No Transfusion (N=78)	Recieved Transfusion (N=114)	Overall (N=192)
Age (years)			
Mean (SD)	59.9 (13.9)	53.7 (14.9)	56.3 (14.8)
Median [Min, Max]	63.0 [19.0, 76.0]	58.0 [21.0, 76.0]	61.0 [19.0, 76.0]
BMI (kg/m²)			
Mean (SD)	25.0 (3.54)	23.5 (4.16)	24.1 (3.98)
Median [Min, Max]	25.2 [18.5, 31.3]	23.8 [15.5, 31.8]	24.4 [15.5, 31.8]
Transplant type			
Single	26 (33.3%)	9 (7.9%)	35 (18.2%)
Bilateral	52 (66.7%)	105 (92.1%)	157 (81.8%)
Redo lung transplant			
Yes	0 (0%)	10 (8.8%)	10 (5.2%)
No	78 (100%)	104 (91.2%)	182 (94.8%)
Intraoperative ECLS			
Yes	24 (30.8%)	79 (69.3%)	103 (53.6%)
No	54 (69.2%)	35 (30.7%)	89 (46.4%)
CPB/ECLS use			
Yes	0 (0%)	2 (1.8%)	2 (1.0%)
No	78 (100%)	112 (98.2%)	190 (99.0%)
Cystic fibrosis			
Yes	5 (6.4%)	25 (21.9%)	30 (15.6%)
No	73 (93.6%)	89 (78.1%)	162 (84.4%)
Idiopathic pulmonary HTN			
Yes	2 (2.6%)	4 (3.5%)	6 (3.1%)
No	76 (97.4%)	110 (96.5%)	186 (96.9%)
LAS score			
Mean (SD)	34.7 (7.57)	38.4 (9.84)	36.9 (9.15)
Median [Min, Max]	33.0 [24.0, 88.0]	35.0 [24.0, 90.0]	34.0 [24.0, 90.0]
Missing	5 (6.4%)	7 (6.1%)	12 (6.3%)
RBC transfusion 0–24h (units)			
Mean (SD)	0 (0)	4.50 (5.79)	2.67 (4.98)
Median [Min, Max]	0 [0, 0]	3.00 [1.00, 38.0]	1.00 [0, 38.0]
ICU LOS (days)			
Mean (SD)	5.95 (11.5)	8.22 (11.4)	7.29 (11.5)
Median [Min, Max]	3.00 [1.00, 91.0]	4.00 [1.00, 99.0]	4.00 [1.00, 99.0]
Missing	0 (0%)	1 (0.9%)	1 (0.5%)
Massive transfusion			
Yes	0 (0%)	9 (7.9%)	9 (4.7%)
No	78 (100%)	105 (92.1%)	183 (95.3%)
High-risk patient			
Yes	29 (37.2%)	93 (81.6%)	122 (63.5%)
No	49 (62.8%)	21 (18.4%)	70 (36.5%)
Baseline coagulopathy			
Yes	10 (12.8%)	20 (17.5%)	30 (15.6%)
No	68 (87.2%)	94 (82.5%)	162 (84.4%)

Table S1. Baseline Characteristics and Outcomes Stratified by Transfusion Status

Comparison of demographic variables, preoperative parameters, procedural characteristics, and clinical outcomes between patients who received no perioperative transfusion (n=78), those who received any red blood cell transfusion (n=114), and all patients combined (n=192). Continuous variables are presented as mean (standard deviation) and median [minimum, maximum]. Categorical variables are presented as count (percentage). BMI, body mass index; ECLS, extracorporeal life support; CPB, cardiopulmonary bypass; HTN, hypertension; LAS, lung allocation score; RBC, red blood cell; ICU LOS, intensive care unit length of stay.

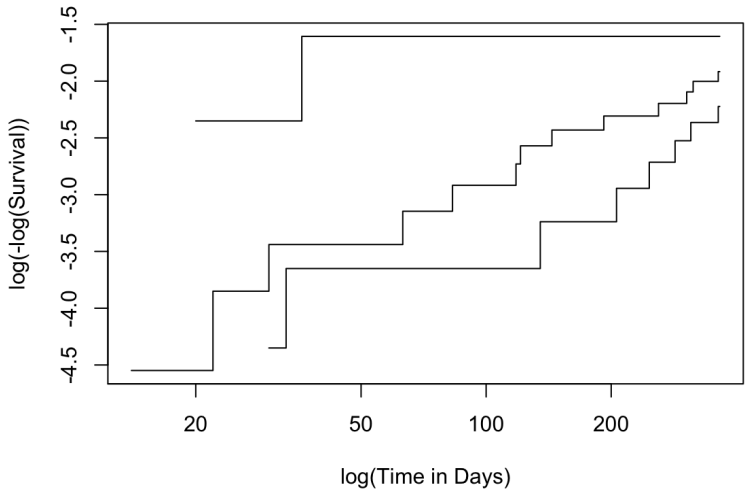

Figure S1: Complementary log-log plot for assessment of proportional hazards assumption

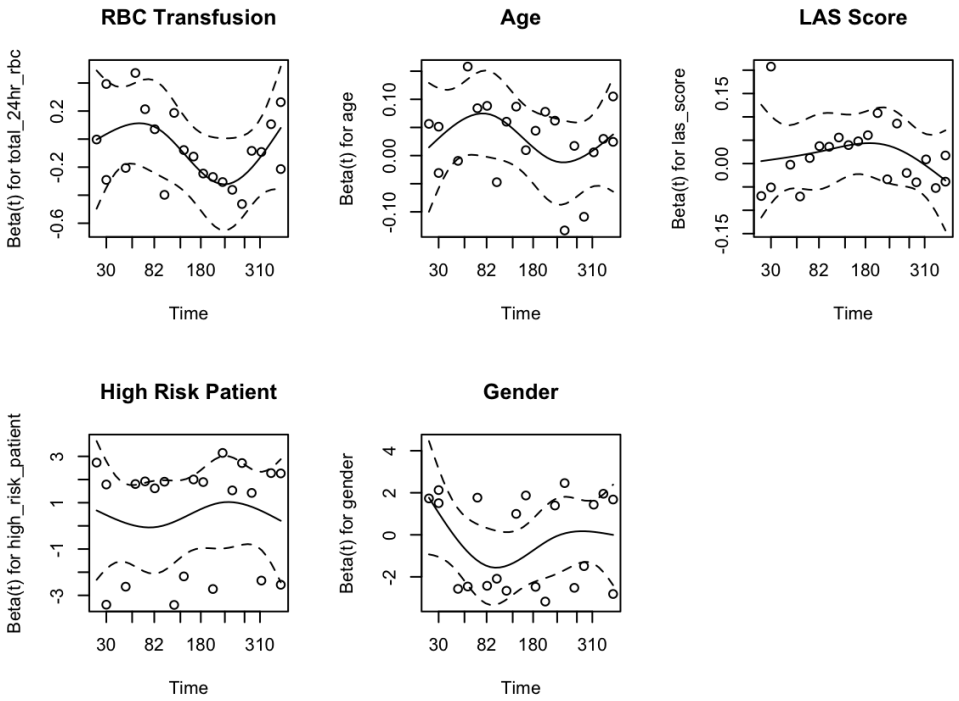

Figure S2. Schoenfeld residual plots for proportional hazards assumption testing.