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An Acute Change in Lung Allocation Score and Survival After Lung Transplantation A Cohort Study

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Abstract

Background—Lung transplantation is an effective treatment for patients with advanced lung disease. In the United States, lungs are allocated on the basis of the lung allocation score (LAS), a composite measure of transplantation urgency and utility. Clinical deteriorations result in increases to the LAS; however, whether the trajectory of the LAS has prognostic significance is uncertain.

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Objective—To determine whether an acute increase in the LAS before lung transplantation is associated with reduced posttransplant survival.

Design—Retrospective cohort study of adult lung transplant recipients listed for at least 30 days between 4 May 2005 (LAS implementation) and 31 December 2010 in the United Network for Organ Sharing registry. An acute increase in the LAS was defined as an LAS change (LAS) greater than 5 units between the 30 days before and the time of transplantation. Multivariable Cox proportional hazards models were used to examine the relationship between an LAS >5 and posttransplant graft survival.

Setting—All U.S. lung transplantation centers.

Patients—5749 lung transplant recipients.

Measurements—Survival time after lung transplantation.

Results—702 (12.2%) patients experienced an LAS >5. These patients had significantly worse posttransplant survival (hazard ratio, 1.31 [95% CI, 1.11 to 1.54]; $P=0.001$) after adjustment for the LAS at transplantation and other clinical covariates. The effect of an LAS >5 was independent of the LAS at transplantation, underlying diagnosis, center volume, or donor characteristics.

Limitation—Analysis was based on center-reported data.

Conclusion—An acute increase in LAS before transplantation is associated with posttransplant survival after adjustment for LAS at transplantation. Further emphasis on serial assessment of the LAS could improve prognostication after transplantation.

Lung transplantation is an effective treatment for selected patients with advanced lung diseases (1, 2). In the United States, the United Network for Organ Sharing (UNOS) uses the lung allocation score (LAS) to prioritize organ allocation to patients in greatest need, a system implemented in May 2005 (3). This score, ranging from 0 to 100, is assigned to potential recipients on the basis of their clinical characteristics and reflects the expected survival if on the waiting list for 1 year and that after transplantation. Higher scores indicate a greater priority for transplantation. In practice, patients are listed and then must wait before transplantation. During this time, the LAS is updated in response to changes in clinical status or at least every 6 months.

Since implementation of the LAS, the absolute number of waiting-list deaths has decreased, consistent with a primary goal of the LAS to address clinical urgency for lung transplantation (4–8). However, transplant recipients with higher LASs also have increased posttransplant mortality (9–12), an important consideration when weighing the net benefit of lung transplantation. In contrast to studies focused on the LAS at transplantation (LAS-T), evidence also shows that many patients experience changes in the LAS between listing and transplantation (13). However, the clinical implications of such changes, particularly acute increases in the LAS before transplantation, are unknown.

In our analysis, we hypothesized that acute increases in the LAS before transplantation would be associated with worse survival after transplantation. To test this hypothesis, we leveraged UNOS registry data collected since implementation of the LAS and modeled the effect of an acute increase in LAS on posttransplant survival time with adjustment for the LAS-T.

Methods

Study Cohort

We performed a retrospective cohort study of adult patients who had single or bilateral lung transplantation after 4 May 2005 (LAS implementation) until 31 December 2010 by using the UNOS registry. Of 8933 recipients, 6310 had been listed for at least 30 days before transplantation (Figure 1). Multiorgan recipients ($n = 201$; 2.3%), patients who had transplantation between 4 May and 3 June 2005 (thus listed for <30 days in the LAS era [$n = 128$; 1.4%]), those younger than 12 years ($n = 120$; 1.4%), those with an LAS of 0 (thus suspended from the wait list [$n = 107$; 1.2%]), or those with missing LAS data ($n = 5$; <0.1%) were excluded from analysis. The final study cohort comprised 5749 patients who were listed for 30 days or more before transplantation and met all other inclusion criteria.

LAS Change Groups

The measure of exposure was defined as an LAS change (LAS) greater than 5 units at transplantation compared with the LAS 30 days before transplantation. We reasoned that an acute worsening of 5 or more points represents a clinically important deterioration in a patient's status after consultation among the authors and transplant clinicians who manage patients with the LAS. We considered alternative definitions of an acute increase in LAS (2.5, 5.0, 10.0, and 15.0 points) and the period over which the change was calculated (7, 14, 30, and 60 days), and we also considered LAS as a continuous rather than dichotomous covariate (Appendix, available at www.annals.org).

UNOS Data

This study was declared exempt by the Duke University Institutional Review Board (Pro00032532) (Durham, North Carolina). Data use was in accordance with the UNOS data-use agreement. The data reported here have been supplied by UNOS as the contractor for the Organ Procurement and Transplantation Network. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by UNOS.

Native diseases were grouped according to UNOS-defined categories: restrictive (primarily idiopathic pulmonary fibrosis), obstructive (primarily chronic obstructive pulmonary disease), cystic or bronchiectasis (primarily cystic fibrosis), and vascular (primarily pulmonary hypertension). Complete data were available for all of the recipient factors included in the analysis because we restricted our analysis to variables necessary for transplantation listing and calculation of the LAS-T. The only covariates considered in our analysis with missing values were donor PO₂ (1.3%) and donor lung ischemic time (7.0%). Given the limited missingness, the median covariate value was imputed for missing values.

Statistical Analysis

Posttransplant survival was defined as freedom from death or retransplantation, that is, graft survival, by using all available transplantation and follow-up data captured in the UNOS registry. Kaplan–Meier survival estimates were used to compare patients in the LAS >5 and LAS ≤5 groups and within 4 strata of the LAS-T. Relatively similar numbers of participants had an LAS >5 in each group (1 to 49, 50 to 59, 60 to 79, and 80 to 100). A mixed-effect Cox proportional hazards model was used to examine the association between an acute increase in LAS and posttransplant survival; LAS was considered dichotomously as LAS >5 or ≤5.

The following recipient, donor, and transplantation characteristics were chosen a priori for inclusion in the model on the basis of their previous association with survival: recipient sex,

recipient native disease, LAS stratum at transplantation, recipient and donor ages, donor PO₂, donor cigarette smoking history, donor lung ischemic time, use of expanded donor criteria, transplantation procedure, and average annual volume of adult lung transplantation centers. There was little evidence that center confounds the effect of acute change (Appendix). On the basis of Thabut and colleagues' analysis (14), we included a random effect for transplantation center. Plots of Schoenfeld residuals and log(−log[survival]) were examined and indicated that the proportional hazards assumption was reasonable.

We further considered whether an acute LAS was associated with residual wait-list survival. Patients active on the lung wait list for at least 30 days between 4 May 2005 and 31 December 2010, were not listed for simultaneous transplantation, and were U.S. citizens (to ascertain Social Security Administration Death Master File death dates) were included in the analysis. To analyze the effect of an acute LAS on wait-list mortality, we considered a sequential stratification or sequential Cox approach (15–20). The wait-list mortality model adjusted for all factors considered in the posttransplant model except for donor characteristics.

Follow-up in each sequential Cox model was censored at the time of transplantation. This censoring mechanism is informative, because patients who deteriorate more quickly are more likely to undergo the transplantation and therefore be censored. To correct for this informative censoring, we considered the inverse probability of censoring weighted estimators (21). The Appendix includes this and other modeling details.

A multivariable logistic model was used to evaluate demographic and pretransplant clinical factors associated with an acute increase in LAS. Two-sided *P* values of 0.05 or less were considered significant. All data were analyzed with SAS, version 9.2 (SAS Institute, Cary, North Carolina), and R, version 2.14.1 (R Core Team, Vienna, Austria). The mixed-effect Cox models were estimated using the *coxme* function (*coxme* package) in R (22).

Role of the Funding Source

Drs. Palmer and Tsuang's efforts were partly supported through National Heart, Lung, and Blood Institute awards. No other funding sources were involved. This work was supported in part by Health Resources and Services Administration. The authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. The funding source had no role in the study design, implementation, or data analysis.

Results

Demographic and Clinical Characteristics of the Study Cohort

Among the 5749 participants, 702 (12.2%) had an LAS >5 and the remaining 5047 (87.8%) had an LAS ≤5. Table 1 shows baseline participant characteristics. The groups had similar racial and sex compositions. Slightly more patients with an LAS >5 were younger than 60 years and had bilateral transplantation.

For participants with an LAS >5, the most common indication for lung transplantation was restrictive lung disease (*n* = 427; 60.8%), whereas obstructive lung disease was the most common indication in the LAS ≤5 group (*n* = 2150; 42.6%). Participants with an LAS >5 had a higher LAS-T than those with smaller changes in LAS (Appendix Table 1, available at www.annals.org). Donor characteristics were generally similar across the 2 groups. Among the entire cohort, the median LAS-T was 37.9 (25th to 75th percentile 34.0 to 42.4) with a median posttransplant follow-up of 2.7 years. Recipients included in the study were on the wait list for a median of 145 days (25th to 75th percentile, 68 to 342 days) and a mean 318 days.

Association of an LAS Δ >5 With Posttransplant Survival

Figure 2 shows Kaplan–Meier estimates of survival by LAS groups and LAS-T strata. The LAS >5 group had consistently worse survival rates than the LAS ≤ 5 group across each stratum tested, suggesting that the effect of an LAS >5 is not simply explained by an association with higher LAS-T.

We then considered the effect of an LAS >5 on posttransplant survival in a multivariable mixed-effects Cox proportional hazards model of time to graft failure, which adjusted for the factors described in the Methods section. An LAS >5 was independently associated with a significant increase in the hazard of posttransplant death (hazard ratio, 1.31 [95% CI, 1.11 to 1.54]; $P = 0.001$) compared with patients with an LAS ≤ 5 (Table 2). As expected, factors previously associated with posttransplant survival, including older age (>60 years), single lung transplantation, expanded donor criteria, longer ischemic time (>6.0 hours), smaller center volume, and stratification within the highest LAS-T stratum (80 to 100), were associated with a significantly increased hazard for death after lung transplantation.

A test for interaction between an LAS >5 and LAS-T strata in the multivariable proportional hazards model found no significant difference in the effect of LAS >5 by LAS-T strata ($P = 0.59$), consistent with the previous results in Figure 2. In addition, the effect of an LAS >5 was not modified by native disease group ($P = 0.74$), center volume ($P = 0.61$), or transplantation center effects ($P = 0.34$). However, given the limited number of patients who experience an acute change, we may be underpowered to detect such interactions. Appendix Figure 1 (available at www.annals.org) shows adjusted survival curves for prototypical patients.

Clinical Factors Associated With an LAS Δ >5

We sought to identify characteristics present 30 days before transplantation that were associated with an LAS >5 . With use of multivariable logistic regression, we found that patients aged 60 years or younger at transplantation (odds ratio [OR], 1.21; $P = 0.05$) with nonobstructive lung disease (restrictive OR, 3.13; cystic or bronchiectasis OR, 2.75; and vascular OR, 2.99; $P < 0.001$) or with an LAS greater than 40 at 30 days before transplantation (compared with an LAS ≤ 35) ($P < 0.001$) were more likely to have an acute increase in LAS. The Appendix shows the full results.

Alternative Approaches to Define Acute Increase in LAS

To determine whether our results were specific to acute LAS as defined in our analysis, we considered the multivariable Cox model but with alternative definitions of acute change by using times of 7, 14, and 60 days before transplantation and acute increases in LAS of 2.5, 10, and 15 points (Appendix). Analysis of these alternative definitions of change consistently reflected the trend that after adjustment for LAS-T and other relevant recipient and donor covariates, patients experiencing an acute increase in LAS have an increased hazard of death (Appendix Table 2, available at www.annals.org). In summary, our selection of an increase of 5 points in the LAS within 30 days of transplantation compared with these alternative approaches reflected a clinically meaningful acute change that was observed in a reasonable number of participants.

LAS Δ as a Continuous Covariate

To further understand the effect of an acute increase in the LAS on posttransplant survival, we next considered the LAS as a continuous covariate with a restricted cubic spline transformation to allow for a nonlinear relationship (Appendix Figure 2, available at www.annals.org). In the multivariable proportional hazards model, an LAS greater than 2.5

was significantly associated with an increase in the hazard of posttransplant death (Appendix Table 3, available at www.annals.org).

Frequency of LAS Updates

Patients who have no component scores updated during the 30 days before transplantation presumably show no changes in clinical status and may clinically differ from those who are monitored more closely. To show that our conclusions about the frequency with which the LAS is updated are robust, we restricted the analysis to patients who had at least 1 LAS component updated during the 30 days before transplantation. The estimated hazard ratio associated with an acute LAS relative to no acute LAS in multivariable Cox proportional hazards model 1.47 (CI, 1.04 to 2.07; $P = 0.026$) when restricted to the smaller cohort, which is close to the estimate in the larger cohort.

LASA and Wait-List Survival

Appendix Table 10 (available at www.annals.org) shows results from the wait-list analysis. A total of 3094 patients with a current LAS greater than 40 at the time of each landmark or sequential analysis were included in this analysis. The hazard ratio associated with an acute change should be interpreted as the relative increase in the hazard of death while on the wait list, assuming that no one underwent transplantation, for a patient with compared with one without an acute change. The estimated hazard ratio associated with an acute change over the first 30 days is substantial (3.23 [CI, 2.65 to 3.94]). However, the effects of an acute change attenuate over time as the hazard ratio declines to 2.07 (CI, 1.59 to 2.71) over the next 30 days and to 1.50 (CI, 1.21 to 1.85) over the rest of the first year. In fact, over 1 year acute change and non-acute change groups did not statistically significantly differ (hazard ratio, 1.37 [CI, 0.83 to 2.25]). This finding contrasts with the analysis of posttransplant data, where the effect of acute change was sustained over the follow-up.

Discussion

We have shown that an LAS >5 is associated with a 31% increased hazard of death after lung transplantation, adjusting for LAS-T, transplantation center, and other important donor or recipient covariates. We found that such changes occur in an appreciable number of patients, specifically 12% of all patients listed for lung transplantation for 30 or more days. Furthermore, the magnitude of the effect of an LAS >5 is similar to that of having an LAS-T of 80 to 100 in our study, emphasizing the clinical importance of this observation. Thus, we show, for the first time to our knowledge, that the trajectory of pretransplant LAS offers important prognostic information about posttransplant survival beyond that captured by the LAS-T.

Our results extend previous efforts to refine prediction of posttransplant survival by using the LAS-T. Several studies have shown an increased risk for death after lung transplantation in patients with a higher LAS-T compared with those with lower scores (23, 24). Merlo and colleagues (23) reported that patients with an LAS greater than 46 had significantly worse 1-year survival than those with an LAS of 46 or less ($P < 0.001$). Liu and associates (24) also found that the hazard for posttransplant death was 1.5-fold higher for those with an LAS-T of 60 to 79 and 2-fold higher for those with an LAS-T of 80 to 100 than for those with an LAS-T of 46 or less (24). As a complement to these studies, we make the novel observation that an LAS >5 is associated with significantly worse survival regardless of the LAS-T, an effect observed consistently across all of the LAS strata considered.

The incorporation of serial clinical measures to assess prognosis in a large population of solid-organ transplant recipients is a relatively new idea. Adult liver transplantation in the

United States utilizes the model for end-stage liver disease score to prioritize patients for hepatic transplant, a score that combines a recipient's bilirubin level, international normalized ratio, and creatinine level (25). Two previous single-center reports have evaluated the prognostic value of acute changes in the model for end-stage liver disease score on pretransplant wait-list mortality but have produced conflicting results and did not consider the effect of these changes on posttransplant survival (26, 27).

In the case of the LAS, the only major change since its inception was that the PCO₂ was added as a static variable at the time of listing and as a dynamic variable in 2008. A higher priority is assigned to patients with an acute increase in the PCO₂ of 15% or more, primarily because of concern for increased risk for death before transplantation (28).

Our approach differs from these studies in that we considered dynamic changes in the composite LAS rather than individual components, and we focused on the effect of LAS on posttransplant survival. We favored the use of the LAS as a composite measure to assess changes in a patient's clinical trajectory because this approach increases power and avoids multiple comparisons associated with analysis of individual components. Furthermore, an advantage of the LAS system is that, because the score weighs each component, the LAS allows us to appropriately pool changes in the component scores. In fact, although we did not examine the effects of changes in each individual LAS component on survival, we did consider the factors driving acute changes.

As the Appendix shows, we found that no 1 component dominated the development of an acute LAS among patients with an acute change. As such, our results have substantial public policy implications and suggest that future updates to the allocation algorithm should focus on composite score dynamics rather than individual component dynamics (as was done with the addition of PCO₂) to better improve prediction of posttransplant mortality.

Our finding of increased mortality associated with acute increases in the LAS raises questions about the optimal approach to organ allocation. A critical consideration for UNOS policy and current U.S. allocation is utility, weighing consideration of posttransplant mortality with wait-list mortality. As we show in the Results section and Appendix, acute changes in the LAS are also associated with significantly worse wait-list mortality, an effect that attenuates over time. Thus, despite the increased posttransplant mortality associated with an acute LAS, transplantation in such patients could provide a net survival benefit. However, we did not attempt a formal calculation of net benefit given the statistical and analytic challenges imposed by attempting to do so within the context of the LAS, which several recent articles address (29–31).

Although further analysis of net benefit is beyond the scope of this paper, approaches that consider residual survival (Appendix) could provide a basis from which to begin to ascertain the effect of a change in LAS on an individual patient's net benefit from lung transplantation. Until such comprehensive analyses are performed, we refrain from making specific recommendations on the allocation of organs regarding patients experiencing an acute change. However, our current analyses highlight for the first time that changes in score dynamics are associated with posttransplant and wait-list survival, an important consideration in a broader discussion of net benefit as public policy.

Despite the large registry cohort and adjusted models, our analysis has several limitations. First, updates to the LAS depend on center-specific reporting. Although we expect that, in patients with clinical deterioration, most centers would promptly update LAS information, center-specific practices may have varied. Center-specific patterns of updating patient information could be confounded with posttransplant outcomes, but the Appendix shows that there is little evidence of confounding by center. Furthermore, 33.7% of patients who do

not experience an acute change had at least 1 component of the LAS updated in the 30 days before transplantation. This finding indicates that, even among those who are not deteriorating, this patient population is closely managed. When we limit our analysis to patients with an LAS updated in the 30 days before transplantation, our conclusions remain unchanged (Appendix).

Second, we chose to dichotomize LAS at 5 or more units over the 30 days before transplantation after consultation among the authors and transplant clinicians who manage patients by using the LAS to identify a clinically meaningful level of acute change. However, other approaches to define the LAS trajectory could be used. Our sensitivity analysis considered alternative cut points for LAS (>5 or <5 units) and alternative time periods (> or <30 days) from which to assess the effect of change in LAS. These alternative analyses reinforced our decision that dichotomization of the LAS is a useful approach to capture clinically meaningful changes in a sizable number of patients awaiting lung transplantation.

Finally, certain limitations are inherent in the UNOS data, including their self-reported nature and potential for missingness. However, regarding the variables used to compute the LAS, missing or expired components are given a default value, generally the least beneficial value for that variable. As such, data are nearly complete for all variables used in this analysis with the exception of PCO₂, reflecting its addition several years after implementation of the LAS. Because using default values for missing LAS components reflects the practice used to generate a patient's actual LAS and would bias against an acute change, we reasoned that this approach was the most appropriate for our analysis.

The LAS has proven to be a clinically useful means to allocate organs within the United States and has reduced wait-list deaths without adversely affecting posttransplant survival (32). Further analysis of the patterns of change in LAS and its effect on posttransplant survival could help refine estimations of net benefit of lung transplantation and improve organ allocation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Context

The lung allocation score (LAS) incorporates clinical variables to balance expected survival with and without transplantation to prioritize patients awaiting transplant. Whether acute changes in the LAS are associated with altered survival after transplantation is unknown.

Contribution

In this study of lung transplant recipients in the United States, an acute change in the LAS during the 30 days before transplantation was associated with worse survival.

Caution

Whether an acute change in LAS alters the net benefit balancing survival with and without transplantation was not studied.

Implication

Further study of changes in LAS may help refine the most beneficial approaches to lung transplantation.

—The Editors

Figure 1. Study flow diagram. LAS = lung allocation score; UNOS = United Network for Organ Sharing.

Figure 2. Survival between LAS >5 and LAS ≤ 5 cohorts by LAS at Transplant strata. The number of patients still at risk in each cohort is located above the horizontal axis.

Table 1

Clinical Characteristics of LAS >5 and LAS ≤5 Cohorts

Variable	LAS >5 (n = 702), n (%)	LAS ≤5 (n = 5047), n (%)
Men	373 (53.1)	2695 (53.4)
Age >60 y	197 (28.2)	1735 (34.3)
Race		
White	563 (80.2)	4291 (85.0)
African American	69 (9.8)	419 (8.3)
Other	70 (10.0)	337 (6.7)
Single transplantation	184 (26.2)	1845 (36.6)
Native disease		
Obstructive	111 (15.8)	2150 (42.6)
Restrictive	427 (60.8)	2004 (39.7)
Cystic/bronchiectasis	125 (17.8)	699 (13.8)
Vascular	39 (5.6)	194 (3.8)
LAS-T		
0–49	240 (34.1)	4552 (90.2)
50–59	143 (20.4)	251 (5.0)
60–79	166 (23.6)	179 (3.5)
80–100	153 (21.8)	65 (1.3)
Donor age		
20 y	168 (23.9)	1282 (25.4)
21–30 y	160 (22.8)	1302 (25.8)
31–45 y	187 (26.6)	1235 (24.5)
46 y	187 (26.6)	1228 (24.3)
Donor PO₂		
235 mm Hg	195 (27.8)	1240 (24.6)
236–425 mm Hg	167 (23.8)	1373 (27.2)
426–500 mm Hg	163 (23.2)	1308 (25.9)
501 mm Hg	177 (25.2)	1126 (22.3)
Donor cigarette smoking history >20 pack-years and recent use	85 (12.1)	631 (12.5)
Donor ischemic time		
3.9 h	132 (18.8)	1297 (25.7)
4.0–4.9 h	164 (23.3)	1378 (27.3)
5.0–5.9 h	195 (27.8)	1249 (24.7)
6.0 h	211 (30.1)	1123 (22.3)
	79 (11.3)	495 (9.8)
Annual transplantation center volume		
0–10 transplantations	42 (6.0)	405 (8.0)

Variable	LAS >5 (n = 702),n (%)	LAS 5 (n = 5047),n (%)
11–25 transplantations	160 (22.8)	1203 (23.8)
26–49 transplantations	242 (34.5)	1939 (38.4)
50 transplantations	258 (36.8)	1500 (29.7)

LAS = lung allocation score; LAS-T = LAS at transplantation.

Table 2

Effect of LAS >5 in Adjusted Multivariable Cox Proportional Hazards Model on Posttransplant Survival

Variable	Hazard Ratio (95% CI)	P Value
LAS group		
LAS ≤5	Reference	
LAS >5	1.31 (1.11–1.54)	0.001
Sex		
Women	Reference	
Men	1.08 (0.98–1.19)	0.125
Age		
≤60 y	Reference	
>60 y	1.23 (1.10–1.37)	<0.001
Transplantation		
Bilateral	Reference	
Single	1.17 (1.04–1.32)	0.011
Native disease		
Obstructive	Reference	
Restrictive	1.11 (0.99–1.24)	0.065
Cystic/bronchiectasis	1.09 (0.93–1.29)	0.27
Vascular	1.31 (1.01–1.69)	0.041
LAS-T		
0–49	Reference	
50–59	0.99 (0.81–1.22)	0.93
60–79	1.08 (0.86–1.34)	0.53
80–100	1.33 (1.02–1.73)	0.035
Donor age		
<21 y	Reference	
21–30 y	1.00 (0.87–1.14)	0.94
31–45 y	0.97 (0.85–1.12)	0.70
46 y	0.96 (0.82–1.13)	0.60
Donor PO₂		
<236 mm Hg	Reference	
236–425 mm Hg	1.02 (0.89–1.17)	0.77
426–500 mm Hg	1.08 (0.94–1.24)	0.27
501 mm Hg	1.09 (0.95–1.26)	0.22
Donor cigarette history		
Nonsmoker or <20 pack-years	Reference	
>20 pack-years and recent use	1.02 (0.89–1.18)	0.77
Donor ischemic time, h		
<4.0 h	Reference	
4.0–4.9 h	1.00 (0.88–1.15)	0.96

Variable	Hazard Ratio (95% CI)	P Value
5.0–5.9 h	0.96 (0.83–1.11)	0.55
6.0 h	1.19 (1.02–1.39)	0.027
Donor expanded criteria		
No	Reference	
Yes	1.26 (1.04–1.53)	0.017
Annual transplantation center volume		
<11	Reference	
11–25	1.00 (0.82–1.24)	0.97
26–49	0.76 (0.62–0.94)	0.010
50	0.68 (0.54–0.85)	0.001

LAS = lung allocation score; LAS-T = LAS at transplantation.