



Lung Allocation Score for Lung Transplantation*

Impact on Disease Severity and Survival

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Background: Prior to implementation of the lung allocation score (LAS) system, allocation of donor lungs was based on accrued time on the waiting list and was potentially influenced by center-specific thresholds for listing. The impact of LAS implementation on patient characteristics and survival is unknown.

Methods: United Network of Organ Sharing data were obtained on all lung transplant candidates listed and all patients undergoing transplantation in region 6 between May 4, 2003, and May 4, 2006. Each data set was divided into two cohorts: 2 years before LAS implementation, and 1 year after LAS implementation. LAS was calculated and compared by cohort. Pre-LAS and post-LAS differences in patient characteristics were examined. Waiting list and posttransplant survival rates for each cohort were examined using Kaplan-Meier estimates and Cox regression.

Results: After LAS implementation, the distribution of diagnoses in patients undergoing transplantation significantly changed ($p = 0.02$), while the distribution of diagnoses in those listed did not ($p = 0.17$). Characteristics of patients on the waiting list were similar, except that a higher proportion of nonwhite patients were listed ($p = 0.04$) and lower FVC ($p < 0.001$) was observed after LAS implementation. Similarly, characteristics of patients undergoing transplantation did not change, except that posttransplant hospital length of stay was shorter ($p = 0.01$) after LAS implementation. Calculated LAS was higher after LAS implementation ($p = 0.006$). After controlling for age and diagnosis, neither waiting list nor transplant survival was significantly different ($p = 0.93$ and $p = 0.81$, respectively).

Conclusions: After LAS implementation, the distribution of diagnoses in lung transplant recipients was significantly changed, while that of candidates was not. Posttransplant and waiting list survival were not affected by the LAS system, but power was limited. Larger and long-term survival studies are needed to determine if the LAS system improves overall allocation and survival for patients interested in lung transplantation.

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Key words: lung allocation score; lung transplantation; organ allocation; resource allocation

Abbreviations: CI = confidence interval; CF = cystic fibrosis; HR = hazard ratio; IPAH = idiopathic pulmonary artery hypertension; IQR = interquartile range; LAS = lung allocation score; NYHA = New York Heart Association; OPTN = Organ Procurement and Transplantation Network; PA = pulmonary artery; PCWP = pulmonary capillary wedge pressure; UNOS = United Network of Organ Sharing; 6MWT = 6-min walk test

With advancements in immunosuppressive and surgical techniques, lung transplantation has become one of the treatments of choice for advanced lung disease.¹ Before May 2005, priority for lung allocation was primarily based on accumulated time on a waiting list.² However, due to the relative scarcity of organs, the growing number of patients on the waiting list, and the increasing number of deaths,

the necessity of a new lung allocation system became apparent.³ In May 2005, the Organ Procurement and Transplantation Network (OPTN) implemented a composite score, the lung allocation score (LAS), which prioritized candidates by expected posttransplant survival and predicted waiting list urgency.³ Prior to the LAS system, time on the waiting list varied greatly because of differences in center-

specific thresholds and practices for active listing. ~~Region 6 includes only one lung transplant center (University of Washington Medical Center), for which criteria has not changed since LAS implementation.~~ Therefore, the regional impact of the LAS on listing diagnosis and severity of disease can be uniquely assessed in this region without the confounding of changes in center-specific thresholds for listing.

~~Diagnosis has been shown to be an important predictor of both waiting list and posttransplant survival.^{5,6} Therefore, understanding how the LAS system affects recipient diagnosis, posttransplant survival, and rates of death on the list for each diagnostic grouping is essential for future improvements of the LAS. In addition, the underlying premise of the LAS is to improve waiting list survival by performing transplantation in patients with the highest mortality risk before transplantation and by improving posttransplant survival by avoiding lung transplantation in patients who are unlikely to survive after transplantation.⁴ However, it is unknown if the LAS has indeed established this balance.~~

In addition, the LAS algorithm was modeled from data that were collected during the pre-LAS period. If the LAS system affects the characteristics and survival of patients who are listed and receive transplantation, data from the pre-LAS period may not be the best predictor of post-LAS survival.⁶ Identifying these changes may be useful for refining the LAS system and counseling patients and their families confronted with lung transplantation.

In this study, we evaluated the effect of LAS implementation on patient diagnosis, patient demographics, and pretransplant clinical parameters such as lung function and hemodynamic values. We hypothesized that patients who underwent transplanta-

tion after implementation of the LAS system would be less likely to have a pretransplant diagnosis of COPD and more likely to have diseases such as pulmonary fibrosis and cystic fibrosis (CF). We believe that understanding the impact of the LAS is important in order to further refine the allocation system and maximize overall survival on the waiting list and after lung transplantation.

MATERIALS AND METHODS

Data Collection

Using data from the United Network of Organ Sharing (UNOS), we performed analyses on two different data sets available as of May 05, 2007: (1) 170 patients listed between May 4, 2003, and May 3, 2006, at University of Washington Medical Center; and (2) 127 lung transplant recipients who underwent transplantation in the same time period. Each data set was then divided into two cohorts: the pre-LAS cohort included patients who were listed (or underwent transplantation) 2 years prior to LAS implementation, and the post-LAS cohort included patients who were listed (or underwent transplantation) 1 year after LAS implementation (Fig 1). Listing criteria for transplantation followed national guidelines.^{7,8} Patient characteristics at the time of listing and the time of transplant were obtained from the UNOS. Human subject approval for this study was obtained from the University of Washington prior to obtaining data from UNOS.

Grouping of Lung Disease Diagnosis

Using the diagnosis codes from the UNOS database, we classified our data sets into six diagnosis groups: (1) COPD/ α_1 -antitrypsin deficiency; (2) pulmonary fibrosis, including idiopathic pulmonary fibrosis, sarcoidosis, rheumatoid lung, CREST (calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) syndrome, scleroderma, Sjogren syndrome, and other fibrosis; (3) CF; (4) idiopathic pulmonary arterial hypertension (IPAH) and secondary pulmonary arterial hypertension; (5) bronchiectasis; and (6) other, including bronchiolitis obliterans retransplant, obliterative bronchiolitis nontransplant, acute rejection after transplantation, lymphangiomyomatosis, Eisenmenger syndrome, and pulmonary hemosiderosis.

Calculation of LAS

LAS values for patients in the transplant data set were calculated in both cohorts. OPTN defaults⁹ of New York Heart Association (NYHA) class I and > 150 feet for 6-min walk test (6MWT) were entered for all subjects. Also, OPTN⁹ default hemodynamic values including systolic pulmonary artery (PA) pressures, mean PA pressures, and pulmonary capillary wedge pressure (PCWP) were entered into the LAS calculation if the value was missing.

Data Analysis

In order to determine differences in patient characteristics between the pre-LAS and post-LAS cohorts in both data sets, we performed a χ^2 analysis (or Fisher exact) test for categorical variables, two-sample mean comparison for normally distributed continuous variables, and Mann-Whitney rank-sum test for skewed continuous variables. The Kruskal-Wallis

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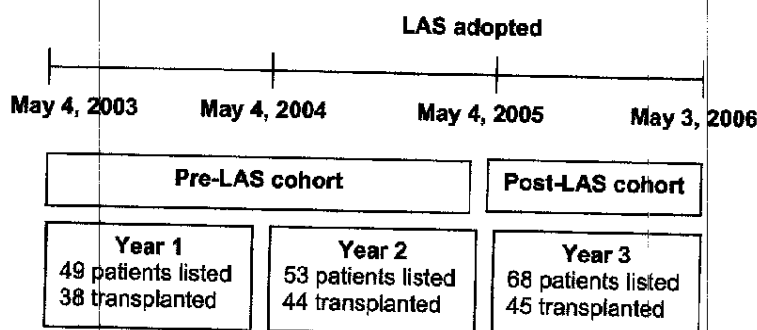


FIGURE 1. Time division of LAS cohorts for patients undergoing transplantation and listed patients.

test was used to determine differences between the distribution of median lung allocation scores between pre-LAS and post-LAS cohorts.

Survival estimates for patients listed were calculated from time of listing to time of death, transplantation, or 360 days of follow-up. Survival estimates for transplant recipients were calculated from time of transplant to time of death or 360 days of follow-up. Survival estimates were calculated with Kaplan-Meier product limit estimator. Cox proportional hazard model was used in both data sets to examine survival differences between LAS cohorts with and without adjustment for potential confounders (age and diagnosis). The proportional hazards assumption was tested with graphical inspection of log-log survival curves [$-\ln(S(t))$ vs time plots] and assessment of Schoenfeld residuals. Significance was reported at two-tailed p value < 0.05 for all statistical tests. Statistical software (STATA SE version 9.0; StataCorp; College Station, TX; copyright from 1984 to 2005) was used for all analyses.

RESULTS

Waiting List Patients

A total of 170 patients (pre-LAS cohort, $n = 102$; post-LAS cohort, $n = 68$) were listed for lung transplantation in region 6 between May 4, 2003, and May 3, 2006 (Fig 1). No differences in patient characteristics were observed between LAS cohorts, except for the following: (1) proportionately fewer white patients were listed in the post-LAS cohort in comparison to the pre-LAS cohort (pre-LAS cohort, 94%; vs post-LAS cohort, 84%; $p = 0.04$); and (2) the patients listed after LAS had a lower mean FVC percentage of predicted (pre-LAS cohort, 54.1%; vs post-LAS cohort, 45.2%; $p < 0.001$).

Table 1—Characteristics at the Time of Listing for Patients Listed 2 Years Prior to and 1 Year After Implementation of the LAS*

Characteristics	Total ($n = 170$)	Before LAS ($n = 102$)	After LAS ($n = 68$)	p Value
Age at listing, yr	50.1 \pm 14.1	50.6 \pm 14.3	49.2 \pm 14.8	0.19
Female gender	79 (46.5)	45 (44.12)	34 (50)	0.53
Race				0.04
White	153 (90)	96 (94.1)	57 (83.8)	
Nonwhite	17 (10.0)	6 (5.9)	11 (16.2)	
Body mass index	25.0 \pm 4.3	25.2 \pm 4.33	24.6 \pm 4.3	0.38
Blood type				0.053
Type A	66 (38.8)	33 (32.4)	33 (48.5)	
Type AB	5 (2.9)	5 (4.9)	0 (0)	
Type B	18 (10.6)	10 (9.8)	8 (11.8)	
Type O	81 (47.7)	54 (53.0)	27 (39.7)	
Diabetes	29 (17.3)	17 (17)	12 (17.7)	0.54
Oxygen requirement, L	2 (2-4)	2 (2-3)	3 (2-4)	0.20
FEV ₁ , % predicted	33.3 \pm 19.1	33.5 \pm 20.3	33.1 \pm 18.5	0.91
FVC, % predicted	50.5 \pm 16.9	54.1 \pm 17	45.2 \pm 15.5	0.0006
Mean PA pressure, mm Hg	25 (20-30)	25 (20-30)	24 (20-29)	0.49
Systolic PA pressure, mm Hg	36 (30-42)	36 (30-42)	36 (29-44.5)	0.90
PCWP, mm Hg	10 (7-13)	11 (8-13)	9 (7-12)	0.10
Waiting list time, d	72 (23-180)	60.5 (21-176)	76 (24-225)	0.36

*Data are presented as mean \pm SD, No. (%), or median (IQR).

[Table 1]. After stratifying by diagnosis, post-LAS COPD/ α_1 -antitrypsin deficiency patients waited longer (median, 57.5 days; interquartile range [IQR], 22 to 133 days; vs median, 137 days; IQR, 49 to 357 days; $p = 0.02$) and post-LAS CF patients had a lower FVC percentage of predicted ($48.8 \pm 13.2\%$ of predicted vs $36.3 \pm 9.9\%$ of predicted; $p = 0.007$).

There was no significant difference in recipient listing diagnosis between the pre-LAS and post-LAS cohorts ($p = 0.17$). The percentage of COPD/ α_1 -antitrypsin deficiency patients listed decreased from 45.1 to 26.5%, while the percentage of pulmonary fibrosis and CF patients listed increased from 27.5 to 41.2% and from 15.7 to 20.6%, respectively (Table 2).

The proportion of pre-LAS patients surviving on the waiting list from the time of listing to the time of death, transplant, or 360 days follow-up was 0.69 (95% confidence interval [CI], 0.47 to 0.83) in the pre-LAS cohort, compared to the post-LAS cohort of 0.84 (95% CI, 0.72 to 0.92) [Table 3, Fig 2]. Cox regression demonstrated no significant difference in waiting list survival between pre-LAS and post-LAS cohorts without adjustment (hazard ratio [HR], 0.92; 95% CI, 0.39 to 2.15; $p = 0.85$) and with adjustment for age at listing and diagnosis (HR, 0.93; 95% CI, 0.40 to 2.21; $p = 0.93$). The proportional hazards assumption was not violated.

Transplant Recipients

A total of 127 patients (pre-LAS cohort, $n = 82$; post-LAS cohort, $n = 45$) underwent lung transplantation between May 4, 2003, and May 3, 2006 (Fig 1). There were no significant differences in patient characteristics between the pre-LAS and post-LAS

Table 3—Survival of Lung Transplant Candidates Stratified by LAS Cohort on the Waiting List at 90, 180, and 360 Days*

Variables	90 Days	180 Days	360 Days
Before LAS	0.88 (0.79–0.94)	0.80 (0.67–0.89)	0.69 (0.47–0.83)
After LAS	0.84 (0.72–0.92)	0.84 (0.72–0.92)	0.84 (0.72–0.92)
Overall	0.87 (0.80–0.92)	0.82 (0.72–0.89)	0.77 (0.64–0.85)

*Data are presented as median (IQR).

cohorts, except creatinine was slightly lower in the post-LAS cohort ($p = 0.04$) and median hospital length of stay after transplant was lower in the post-LAS cohort ($p = 0.01$) [Table 4]. Excluding patients who died, median hospital length of stay after transplantation was still significantly lower after implementation of the LAS (pre-LAS cohort, 13 days [IQR, 10 to 17.5 days]; vs post-LAS cohort, 10 days [IQR, 8 to 15 days]; $p = 0.02$). Median time on the waiting list in the pre-LAS cohort was 58 days (IQR, 19 to 137 days), while waiting time for the post-LAS cohort was 72 days (IQR, 28 to 139 days). This was not significantly different. No differences in patient characteristics were observed between pre-LAS and post-LAS cohorts when stratified by diagnosis except in the pulmonary fibrosis strata. Among patients with pulmonary fibrosis, differences included a higher age (mean \pm SD) after LAS implementation (pre-LAS cohort, 53.2 ± 9.0 years; vs post-LAS cohort, 59.8 ± 5.7 years; $p = 0.01$) and lower prevalence of diabetes in the post-LAS cohort (30% vs 0%; $p = 0.02$). After implementation of the LAS, recipients differed by listing diagnosis ($p = 0.02$); the proportion of patients with COPD/ α_1 -antitrypsin deficiency decreased from 50.0 to 26.7%, and the proportion of patients with pulmonary fibrosis increased from 24.4 to 37.8% (Table 5).

Table 2—Distribution of Diagnosis on the Waiting List 2 Years Prior to and 1 Year After Implementation of the LAS*

Diagnoses	Total ($n = 170$)	Before LAS ($n = 102$)	After LAS ($n = 68$)
COPD/ α_1 -antitrypsin deficiency	64 (37.7)	46 (45.1)	18 (26.5)
All pulmonary fibrosis (IPF only: pre-LAS cohort, $n = 20$; post-LAS cohort, $n = 15$)†	56 (32.9)	28 (27.5)	28 (41.2)
CF	30 (17.7)	16 (15.7)	14 (20.6)
All pulmonary arterial hypertension (IPAH only: pre-LAS cohort, $n = 4$; post-LAS cohort, $n = 2$)‡	7 (4.1)	5 (4.9)	2 (2.9)
Bronchiectasis	8 (4.7)	4 (3.9)	4 (5.9)
Other§	5 (2.9)	3 (2.9)	2 (2.9)

*Fisher exact test for all diagnosis ($p = 0.17$). Data are presented as No. (%).

†All pulmonary fibrosis: idiopathic pulmonary fibrosis (IPF), sarcoid, CREST (calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia), rheumatoid lung, other.

‡All pulmonary hypertension: IPAH, secondary pulmonary arterial hypertension.

§Other, before LAS implementation: bronchiolitis obliterans retransplant, bronchiolitis obliterans nontransplant, acute rejection after transplantation.

||Other, after LAS implementation: lymphangioleiomyomatosis, Eisenmenger syndrome.

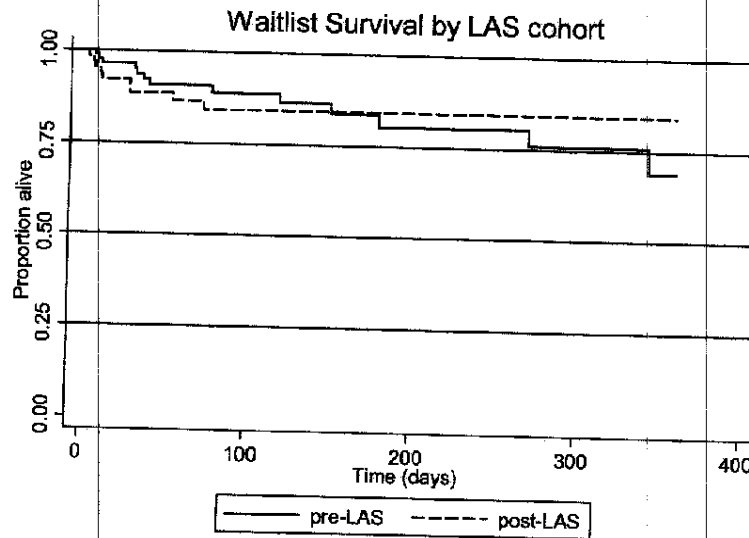


FIGURE 2. Kaplan-Meier graph of survival from time of listing to time of death, transplant, or end of follow-up (360 days) by patients undergoing transplantation 2 years prior to (pre-LAS) and 1 year after (post-LAS) implementation of the LAS.

The median LAS was significantly lower before implementation of the LAS compared to after (pre-LAS cohort, 33.1 [IQR, 32.2 to 35.2]; vs post-LAS cohort, 35.0 [IQR, 33.0 to 37.4]; $p = 0.006$). However, no significant difference was seen in LAS be-

tween patients within specific diagnostic groups (Table 6). The COPD/ α_1 -antitrypsin patients had lower median LAS values than other disease groups.

The survival estimates after transplantation were similar between LAS cohorts (Table 7, Fig 3). We

Table 4—Characteristics at the Time of Transplant for Patients Undergoing Transplantation 2 Years Prior to and 1 Year After Implementation of the LAS*

Characteristics	Total (n = 127)	Before LAS (n = 82)	After LAS (n = 45)	p Value
Age, yr	51 ± 13.7	50 ± 13.72	51.5 ± 13.74	0.76
Male gender	73 (57.5)	48 (58.5)	25 (55.6)	0.85
Race				0.61
White	124 (96.9)	80 (97.6)	43 (95.6)	
Nonwhite	4 (3.1)	2 (2.4)	2 (4.4)	
Body mass index	25 ± 4.4	25 ± 4.3	25 ± 4.7	0.93
Blood type				0.57
Type A	46 (36.2)	29 (35.4)	17 (37.8)	
Type AB	5 (3.9)	4 (4.9)	1 (3.2)	
Type B	14 (11.0)	7 (8.5)	9 (15.6)	
Type O	62 (48.8)	42 (51.2)	20 (44.4)	
Diabetes	20 (15.9)	14 (17.0)	6 (13.6)	0.80
Oxygen requirement, L	2 (2-4)	2 (2-3)	3 (2-4)	0.36
FEV ₁ , % predicted	33.9 ± 20.3	33.1 ± 21.1	35.1 ± 19.0	0.60
FVC, % predicted	51.8 ± 16.1	53.4 ± 17.0	48.7 ± 14.3	0.12
Mean PA pressure, mm Hg	25 (20-30)	25.5 (20-31)	23.5 (20-29)	0.61
Systolic PA pressure, mm Hg	36 (30-44)	36 (30-46)	35 (30-40.5)	0.57
PCWP, mm Hg	10 (8-13)	10 (7-13)	11 (8-14)	0.44
Creatinine, mg/dL	0.85 ± 0.23	0.82 ± 0.20	0.90 ± 0.27	0.04
Length of stay, d	13 (9-20)	13 (8-23)	10 (8-15)	0.01
Length of stay for survivors only, d	12 (9-16)	13 (10-17.5)	10 (8-15)	0.02
Waiting list time, d	64 (22-139)	57.5 (19-137)	72 (28-139)	0.30

*Data are presented as mean ± SD, No. (%), or median (IQR).

Table 5—Distribution of Diagnosis in Patients Undergoing Transplantation 2 Years Prior to and 1 Year After Implementation of the LAS*

Diagnoses	Total (n = 127)	Before LAS (n = 82)	After LAS (n = 45)
COPD/ α_1 -antitrypsin deficiency	53 (41.7)	41 (50)	12 (26.7)
All pulmonary fibrosis (IPF only: pre-LAS cohort, n = 14; post-LAS cohort, n = 2)†	37 (29.1)	20 (24.4)	17 (37.8)
CF	22 (17.3)	14 (17.1)	8 (17.8)
All pulmonary arterial hypertension (IPAH only: pre-LAS cohort, n = 4; post-LAS cohort, n = 2)‡	7 (5.5)	5 (6.1)	2 (4.4)
Bronchiectasis	5 (3.9)	2 (2.4)	3 (6.7)
Other§	3 (2.4)	0 (0)	3 (6.7)

*Fisher exact test for all diagnoses ($p = 0.02$). Data are presented as No. (%). See Table 2 for expansion of abbreviation.

†All pulmonary fibrosis: idiopathic pulmonary fibrosis, sarcoid, Sjogren syndrome, scleroderma, rheumatoid lung, other.

‡All pulmonary hypertension: IPAH, secondary pulmonary arterial hypertension.

§Other, post-LAS cohort: lymphangioleiomyomatosis (n = 2), pulmonary hemosiderosis.

found no significant difference in pre-LAS survival compared to post-LAS survival whether we controlled for age and diagnosis (HR, 1.10; 95% CI, 0.50 to 2.43; $p = 0.81$) or did not control for these potential confounders (HR, 1.13; 95% CI, 0.52 to 2.45; $p = 0.76$). Proportional hazards assumption was not violated.

Missing Data

Calculation of the LAS in both time periods was complicated by missing data. NYHA class was missing for all patients; therefore, the OPTN default⁹ of NYHA class I was entered for all observations. Results for the 6MWT were missing for a greater percentage of the pre-LAS cohort than the post-LAS cohort (pre-LAS cohort, 96%; post-LAS cohort, 38%). Therefore to avoid bias, we entered the OPTN default⁹ of a value > 150 feet for all patients. Of the recipients who did have a 6MWT distance recorded, only 2 of 74 patients (2.7%) were reported to have a 6MWT distance < 150 feet.

There were 14 pre-LAS recipients (17%) and 4 post-LAS recipients (9%) who had missing hemody-

amic values. Again, OPTN default⁹ values were entered into the LAS calculator for missing values. In order to evaluate for bias, we compared recipients with missing hemodynamics to those without missing hemodynamics in each LAS cohort. Patients in the pre-LAS cohort with no missing hemodynamic values had an LAS median of 33.53 (IQR, 32.25 to 35.79) and were not significantly different than patients in the pre-LAS cohort with missing hemodynamic values who had a median LAS of 32.94 (IQR, 31.95 to 33.75; $p = 0.23$). Patients in the post-LAS cohort with no missing hemodynamic values had a median LAS of 35.04 (IQR, 32.97 to 37.25), and were not significantly different than the post-LAS cohort with missing hemodynamic values who had a median LAS of 32.94 (IQR, 31.95 to 33.75) [$p = 0.19$].

In addition, we used values from the 95th percentile in our data to perform a sensitivity analysis for missing data. For missing hemodynamics, we entered 71 mm Hg, 46 mm Hg, and 18 mm Hg for the PA systolic, mean PA pressure, and the PCWP values, respectively, into the LAS calculator. Using

Table 6—LAS Before and After LAS Implementation by Pretransplant Diagnosis*

Diagnosis Group	Total	Before LAS	After LAS	p Value
COPD/ α_1 -antitrypsin deficiency	33.2 (31.7–34.4)	32.3 (31.6–32.9)	33.2 (31.8–34.4)	0.23
All pulmonary fibrosis†	37.2 (35.2–38.8)	37.3 (34.8–38.3)	36.8 (35.7–40.7)	0.74
CF	33.7 (33.0–35.2)	33.5 (32.9–34.6)	36.0 (33.1–39.6)	0.17
All pulmonary hypertension‡	34.1 (32.4–35.6)	34.1 (32.4–35.6)	34.3 (33.6–35.0)	1.0
Bronchiectasis	33.7 (32.6–36.0)	33.1 (32.6–33.7)	36.0 (31.8–38.0)	0.56
Other§	32.28 (32.2–33.6)		32.28 (32.2–33.6)	
All patients	33.7 (32.3–36.2)	33.1 (32.2–35.2)	35.0 (33.0–37.4)	0.006

*Data are presented as median (IQR).

†All pulmonary fibrosis: idiopathic pulmonary fibrosis, sarcoid, CREST (calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia), Sjogren syndrome, scleroderma, rheumatoid lung, other.

‡All pulmonary hypertension: primary pulmonary hypertension, secondary pulmonary hypertension.

§Other, pre-LAS cohort: bronchiolitis obliterans retransplant, bronchiolitis obliterans nontransplant, acute rejection after transplantation.

||Other, post-LAS cohort: lymphangioleiomyomatosis, Eisenmenger syndrome, pulmonary hemosiderosis.

Table 7—Survival of Lung Transplant Candidates Stratified by LAS Cohort on the Waiting List at 90, 180, and 360 Days*

Variables	Survival at 90 Days	Survival at 180 Days	Survival at 360 Days
Before LAS	0.91 (0.84–0.96)	0.87 (0.79–0.93)	0.85 (0.78–0.91)
After LAS	0.91 (0.78–0.97)	0.89 (0.75–0.95)	0.82 (0.68–0.91)
Overall	0.91 (0.85–0.95)	0.88 (0.81–0.93)	0.84 (0.77–0.90)

*Data are presented as HR (95% CI).

these values, the median LAS score for the pre-LAS cohort was 33.77 (IQR, 32.30 to 36.52) and for the post-LAS cohort was 35.18 (IQR, 33.01 to 37.51). With this sensitivity analysis, the difference between the LAS scores between the two cohorts remained significant (Kruskal Wallis *p* value of 0.046). Finally, in order to evaluate the potential bias of using default values overall, we compared our calculated LAS score to that recorded in UNOS. There was no significant difference between our calculated LAS and the LAS that was listed in the UNOS database (median calculated LAS, 35.04 [IQR, 33.01 to 37.37]; vs UNOS LAS median, 34.87 [IQR, 33.62 to 38.4]; *p* = 0.55).

DISCUSSION

Our findings suggest that the implementation of the LAS system led to significant differences in the

diagnoses for patients who underwent transplantation; however, there was no significant change in diagnoses listed. Few clinically significant changes between pre-LAS and post-LAS cohorts were observed in patient characteristics overall and when stratified by disease in either the transplant-recipient or candidate data set. In addition, we also observed that transplant recipients in the pre-LAS cohort had a significantly lower overall LAS median than patients in the post-LAS cohort. Finally, no difference in survival after listing or transplantation was observed between LAS cohorts, although the 95% CIs were relatively wide.

Our results demonstrate that the LAS system significantly increased the median LAS between the pre-LAS and post-LAS cohorts. This effect was observed in the setting of a higher average number of CF and pulmonary fibrosis patients being listed per year, while the average number of COPD patients listed per year remained relatively constant. Because our listing practices have not changed at our center after LAS implementation,⁷ this trend suggests that more patients with pulmonary fibrosis and CF were referred to our center for transplantation. One explanation for this trend could be that referring centers who may have considered certain CF or pulmonary fibrosis patients too ill to accrue time on the waiting list before the LAS, now considered them potential candidates after the LAS because higher allocation scores could expedite the transplantation procedure.

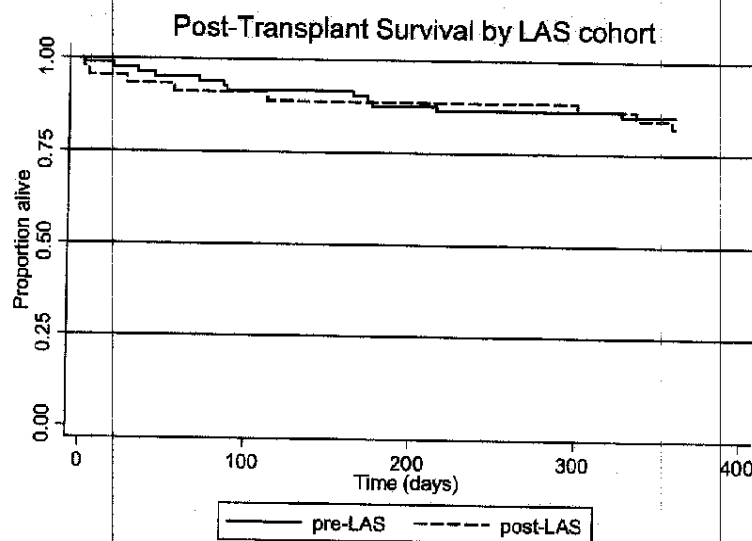


FIGURE 3. Kaplan-Meier graph of survival from time of transplantation to time of death or end of follow-up (360 days) by patients undergoing transplantation 2 years prior to (pre-LAS) and 1 year after (post-LAS) implementation of the LAS.

In addition, an increase in median LAS after implementation of the LAS system was also associated with a lower proportion of COPD patients and higher proportion of pulmonary fibrosis patients who underwent transplantation. These findings mirrored changes that were seen on a national level, including a national decrease in the percentage of emphysema patients (60 to 45%) and a national increase of pulmonary fibrosis patients (12 to 28%).¹⁰ In addition, this finding was also observed in a simulation study¹¹ that compared patients ranked by accrued waiting time compared to patients ranked by the LAS system. In this simulation, Lingaraju et al¹¹ demonstrated that compared to an allocation system based on accrued waiting time, the LAS system ranked patients with pulmonary fibrosis higher and patients with COPD lower on the waiting list. Because pulmonary fibrosis patients often have a higher acuity and higher risk of dying on the waiting list than COPD patients, these findings suggest that the LAS system has helped benefit the group of patients with the highest waiting list mortality while waiting to undergo transplantation.²

Although we were limited by a small sample size to detect significant differences, we observed similar survival estimates after listing and after transplantation between LAS cohorts. In addition, our survival estimates mirrored that of the national waiting list and posttransplant survival rates reported by OPTN for 2004.³ Observing similar survival estimates between LAS cohorts despite having higher-acuity patients listed more frequently after LAS implementation is interesting. A potential explanation for this finding is that higher-acuity patients are less likely to die on the waiting list because they are more likely to undergo transplantation. Because patients in the post-LAS cohort had a similar survival after transplantation compared to the pre-LAS cohort, our analyses suggest that performing transplantation in patients with a higher LAS and greater severity of illness does not necessarily lead to worse outcomes. In further support of this finding, other centers have reported a decrease in mortality rate (10 to 3%) after the implementation of the LAS.¹²

Our study has several limitations. Although we designed this retrospective study to observe regional changes that were not biased by changes in center practices for allocation other than LAS implementation, our ability to detect differences in survival and characteristics between diagnoses are limited by small sample size, missing data from the UNOS database, and limited follow-up time. Another limitation is that although these data represent the effect of

the LAS score on a regional level, they do represent data from a single center and generalizability may be reduced. Despite these limitations, our findings provide useful information on the impact of the LAS on survival in patients undergoing lung transplantation and may help identify directions for refining the LAS model.

In conclusion, implementation of the LAS was associated with a significantly different distribution of transplant diagnoses at our center. Although criteria for listing have not changed at our center, the median LAS has significantly increased after its adoption. Future studies with larger samples and longer follow-up in well-defined patient populations are needed to assess effects on waiting list survival and posttransplant survival.

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