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RESEARCH ARTICLE

Lung Transplantation for Chronic Obstructive Pulmonary Disease: Outcomes before and after Implementation of the UNOS Lung Allocation Scoring System

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Abstract

Background: The United Network for Organ Sharing (UNOS) Lung Allocation Score (LAS) adopted in April 2005 to prioritize lung transplantation for patients at high risk of dying without a transplant may adversely affect outcomes for patients transplanted for Chronic Obstructive Pulmonary Disease (COPD).

Methods: We reviewed the records for 141 consecutive recipients with COPD (all without alpha-1-antitrypsin deficiency) who received lung transplants at our center between January 1993 and March 2013 and compared outcomes for patients transplanted using the LAS (LAS, $n = 71$) to those transplanted prior to introduction of the LAS (pre-LAS, $n = 70$).

Results: The cohort of patients transplanted after LAS implementation had lower FVC% predicted (pre-LAS: 52 vs. LAS 46%, $p < 0.05$), lower FEV1% predicted (20 vs. 18%, $p < 0.05$), and a higher prevalence of diabetes (7 vs. 21%, $p < 0.01$). Median estimated LAS values increased significantly ($P < 0.01$) from 33.0 (pre-LAS) to 35.4 (LAS). Length of hospital stay and hospital mortality did not significantly change, and ICU length of stay decreased from 13 (pre-LAS) to 4 days (post-LAS, $p < 0.01$). However, long-term survival was significantly decreased in the LAS group with a 5-year survival of 74.2% in the pre-LAS group versus 65.0% in the LAS group ($p < 0.05$).

Conclusions: Although the mean calculated LAS value was higher for COPD patients transplanted after LAS implementation versus pre-LAS recipients, early post-transplant outcomes were not affected. However, longer term survival was decreased for LAS recipients who received Single Lung Transplants (SLT) versus the pre-LAS SLT cohort and Bilateral Lung Transplant (BLT) recipients.

Keywords

COPD, Lung allocation score, Lung transplant

List of Abbreviations

AATD: Alpha-1-Antitrypsin Deficiency; BMI: Body Mass Index; BLT: Bilateral Lung Transplant; CLAD: Chronic Lung Allograft Dysfunction; COPD: Chronic Obstructive Pulmonary Disease; CPB: Cardiopulmonary Bypass; ECMO: Extracorporeal Membrane Oxygenation; FEV1: Forced Expiratory Volume in One Second; ISHLT: International Society for Heart and Lung Transplantation; HR: Hazard Ratio; iNO: Inhaled Nitric Oxide; ICU: Intensive Care Unit; IPF: Idiopathic Pulmonary Fibrosis; IQR: Interquartile Ratio; LAS: Lung Allocation Score; LTX: Lung Transplantation; 6MWT: 6-Minute Walk Test; PAP: Pulmonary Artery Pressure; PGD: Primary Graft Dysfunction; SLT: Single Lung Transplant; UNOS: United Network for Organ Sharing

Background

The United Network for Lung Transplantation (UNOS) adopted and implemented the Lung Allocation Score (LAS) for Lung Transplantation (LTX) in the United States in 2005 with the goal of optimizing organ allocation and recipient survival [1]. Although Chronic Obstructive Pulmonary Disease (COPD) was surpassed by Idiopathic Pulmonary Fibrosis (IPF) in 2007 as the leading indication for LTX in the United States [2], COPD continues to be a major indication for LTX [3].

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Various investigations of the natural history of COPD have shown that disease progression tends to be fairly indolent with most patients manifesting relatively mild decline in lung function over time [4,5]. Even patients with advanced COPD tend to have better survival over time without transplant when compared to patients with other transplant indications such as IPF, and this accounts for comparatively lower LAS values for patients with COPD when they are placed on the lung transplant waitlist in comparison to patients with other disease indications for LTX such as IPF or cystic fibrosis.

Factors associated with poorer prognosis for patients with COPD include the presence of hypoxemia, hypercarbia, low forced expiratory volume during the first second of a Forced Expiration (FEV1), greater degree of dyspnea, more severe emphysema on radiographic imaging, pulmonary hypertension, low Body Mass Index (BMI), and poorer performance on a 6-Minute Walk Test (6MWT) [4-7]. Because these factors are of limited value in defining prognosis for individual patients, the multi-dimensional BODE Index model that uses a combination of Body Mass Index (BMI), Forced Expiratory Volume in one second (FEV1), degree of dyspnea, and 6-Minute Walk Test (6MWT) exercise capacity was created to better define the prognosis for an individual patient [8], and BODE-defined disease severity appears to be a better predictor of risk for death than individual measures [9]. Therefore, the International Society of Heart and Lung Transplantation (ISHLT) consensus guidelines have endorsed the BODE score as a principal parameter for decision-making when listing patients with COPD for LTX [10].

We reviewed the characteristics and outcomes of our patients to see if any significant differences in survival or other features could be identified for equivalent cohorts of consecutive patients with COPD transplanted before or after implementation of the LAS for prioritization of lung transplant candidates. Although we did not find significant differences in the majority of early outcome measures for the pre-LAS versus LAS cohorts, the LAS cohort of Single Lung Transplant (SLT) recipients had significantly worse long-term survival than the pre-LAS SLT cohort or the BLT recipients.

Methods

Donor and recipient characteristics

Between January 1999 and March 2013, a total of 474 patients received lungs from deceased donors at our center. Among these patients, 141 (29.7%) consecutive patients with COPD without Alpha-1-Antitrypsin Deficiency (AATD) underwent LTX. Patients transplanted using the LAS (LAS group, n = 71, May 2005-December 2013) were compared to patients transplanted prior to introduction of the LAS (pre-LAS group, n = 70, January 1999-April 2005). Patients were further stratified into Single Lung Transplant (SLT) and Bilateral Lung Transplant (BLT) groups (pre-LAS SLT n = 64, pre-LAS BLT n = 6, LAS SLT n = 37, LAS BLT n = 34). To compare the severity of illness between the groups, LAS values were calculated for the pre-LAS group using the appropriate variables available for this cohort close to the time of transplantation. Primary Graft Dysfunction (PGD) was defined and graded according to the ISHLT definition (PaO_2/FiO_2 < 300 and a chest radiograph with a characteristic diffuse infiltrate) [11], and Chronic Lung Allograft Dysfunction (CLAD) was defined by ISHLT criteria [12]. Patient demographics, donor characteristics, graft function, post-transplant complications, and graft survival rates were assessed.

Post-transplant bronchoscopy and surveillance

All recipients received surveillance bronchoscopies with bronchoalveolar lavage and transbronchial lung biopsies at post-transplant week 2, 6, 12, 18, 26, 40, and 52 to detect rejection and/or infection, and transbronchial biopsy specimens were graded according to criteria set by ISHLT Lung Rejection Study Group [13]. Bronchoscopies were also performed whenever necessary for clinical indications with follow-up bronchoscopies performed 4 weeks after a previous bronchoscopy if acute cellular rejection of any grade was detected. All biopsy results were retrospectively reviewed for this study. All patients identified as having developed CLAD had persistent decline of FEV1 below 80% of their best post-transplant FEV1 values [12].

Data acquisition and follow-up

This investigation was approved by the University of Wisconsin Human Subjects Committee (approval number M-2009-1308). Data were collected prospectively and analyzed retrospectively. The LTX database was reviewed for demographic, operative, perioperative, and outcome data. Follow-up was obtained through outpatient chart review. The longest follow-up was 5250 days (median, 3214 days [range, 0-5250] for the pre-LAS group and 1379 days [0-3246] for the LAS group).

Statistical analysis

Categorical data were summarized with frequency distributions and percentages. The mean ± standard deviation values were calculated for variables that were normally distributed, and the medians with Interquartile Ratios (IQR) were presented for those that were skewed. Continuous variables were compared by the unpaired t-test, ANOVA, or nonparametric Mann-Whitney U-test, whereas nominal variables were compared by means of Chi-Square or the Fisher exact test, as appropriate. The Kaplan-Meier method was used to assess lung allograft and recipient survival. Log-rank tests were used to assess statistical significance in survival differences between the pre-LAS and LAS groups. A p value less than 0.05 (two-sided) was considered to be statistically significant. All analyses were performed using the

SPSS Statistical Software Program (SPSS for Windows version 17.0, SPSS Inc.; Chicago, Ill.) and figures were made in GraphPad Prism (GraphPad Software, version 6.04 for Windows, La Jolla California USA, www.graphpad.com).

Results

Patient characteristics are listed in Table 1. The mean age of recipients was different between the four groups, with the oldest patients in the LAS SLT group (pre-LAS SLT 58.1, pre-LAS BLT 56.5, LAS SLT 60.7, LAS BLT 57.9, p = 0.03). Overall, differences were most notable when comparing the pre-LAS SLT and LAS SLT groups. The LAS SLT group had lower FEV1% predicted (pre-LAS SLT 20.1% vs. LAS SLT 18.1%, p = 0.04), a trend towards lower FVC% predicted (52.3 vs. 46.8%, p = 0.08), a higher prevalence of diabetes (8 vs. 32%, p < 0.01), and higher systolic and mean Pulmonary Artery Pressure (PAP) (32.8 vs. 38.9 and 25.4 vs. 27.0 mmHg, p = 0.02 and p < 0.01 respectively). Median estimated LAS values increased significantly from 32.8 for pre-LAS SLT to 36.0 for LAS SLT recipients (p = 0.03). Despite the higher LAS value for the LAS cohort, there was no significant difference in time on the waiting list between the two SLT groups (367 vs. 475 days, p = 0.50). The rate of Cardiopulmonary Bypass (CPB) increased in both LAS groups compared to pre-LAS groups (pre-LAS SLT 6%, pre-LAS BLT 50%, LAS SLT 14%, LAS BLT 97%, p < 0.001),

Table 1: Patient demographics.

	Pre-LAS SLT (n = 64)	Pre-LAS BLT (n = 6)	Post-LAS SLT (n = 37)	Post-LAS BLT (n = 34)	*p*-value
Age (y)	58.1 ± 5.5	56.5 ± 4.1	60.7 ± 4.6	57.9 ± 3.9	0.03
Gender (female)	22 (34%)	0	14 (38%)	12 (35%)	0.13
Race (Caucasian)	62 (97%)	4 (67%)	36 (97%)	30 (88%)	< 0.001
BMI (kg/m^2)	24.4 ± 4.3	25.2 ± 4.2	23.6 ± 3.6	24.5 ± 3.6	0.73
FVC (% of predicted)	52.3 ± 17.4	50.0 ± 11.4	46.8 ± 14.0	44.4 ± 15.3	0.08
FEV1 (% of predicted)	20.1 ± 6.0	16.7 ± 3.7	18.1 ± 4.7	17.4 ± 4.0	0.04
Required oxygen (L)	2.6 ± 1.3	3.8 ± 1.7	3.5 ± 3.1	3.0 ± 1.2	0.08
Assisted ventilation	6 (9%)	1 (16%)	7 (19%)	4 (12%)	0.57
Systolic PAP (mmHg)	34.8 ± 8.4	45.2 ± 8.0	38.9 ± 13.1	40.7 ± 11.1	0.02
Mean PAP (mmHg)	25.4 ± 6.5	36.6 ± 6.5	27.0 ± 8.5	28.2 ± 8.8	0.006
PCWP (mmHg)	14.2 ± 6.5	21.2 ± 9.6	13.1 ± 5.3	15.8 ± 7.4	0.03
Cardiac index (L/min/m^2)	2.9 ± 0.7	2.7 ± 1.0	2.9 ± 0.7	3.1 ± 0.7	0.6
Serum creatinine (mg/dl)	0.9 ± 0.2	1.0 ± 0.2	0.9 ± 0.2	0.7 ± 0.2	0.001
History of diabetes	5 (8%)	2 (33%)	12 (32%)	9 (27%)	0.006
Time on waiting list (d)	367 ± 258	295 ± 223	475 ± 400	410 ± 550	0.5
LAS estimation	32.8 ± 2.0	34.5 ± 1.4	36.0 ± 9.4	34.8 ± 2.3	0.03
Cardiopulmonary bypass	4 (6%)	3 (50%)	5 (14%)	33 (97%)	< 0.001
Cold ischemic time (min)	359 ± 145	492 ± 243	293 ± 101	229 ± 62	< 0.001
Donor age (y)	32.0 ± 11.9	29.0 ± 15.2	29.1 ± 16.0	36.3 ± 17.0	0.33
Donor gender (female)	20 (31%)	0	11 (30%)	11 (32%)	0.15
Donor (Caucasian)	16 (25%)	2 (33%)	26 (70%)	18 (53%)	< 0.001

LAS: Lung Allocation Score; BMI: Body Mass Index; FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in 1 second; PAP: Pulmonary Arterial Pressure; PCWP: Pulmonary Capillary Wedge Pressure.

Table 2: Postoperative outcome data.

	Pre-LAS SLT (n = 64)	Pre-LAS BLT (n = 6)	Post-LAS SLT (n = 37)	Post-LAS BLT (n = 34)	*p*-value
Primary graft dysfunction:					0.39
Grade 0 or 1	54 (84%)	3 (50%)	30 (81%)	24 (75%)	
Grade 2 or 3	10 (16%)	3 (50%)	7 (19%)	10 (30%)	
Required ECMO support	5 (8%)	0	1 (3%)	1 (3%)	0.55
Inhalation of nitric oxide	19 (30%)	3 (50%)	16 (43%)	10 (30%)	0.40
≥ 48 hrs of inhalation	10 (16%)	1 (17%)	7 (19%)	6 (18%)	0.98
Reintubation	11 (17%)	3 (50%)	8 (22%)	6 (18%)	0.065
Mechanical ventilated period (d)	4.7 (0-64)	11.1 (2-31)	1.5 (0-10)	1.6 (0-4)	0.022
≥ 48 hrs of ventilator support	25 (39%)	3 (50%)	8 (22%)	6 (18%)	0.065
Dialysis	3 (5%)	2 (33%)	2 (5%)	0	< 0.001
Length of ICU stay (d)	11 (R, 1-64)	37 (R, 3-140)	4 (R, 0-22)	4 (R, 0-34)	< 0.001
Length of hospital stay (d)	28 (9-106)	81 (19-202)	22 (6-91)	23 (0-86)	0.001
30-day mortality	0	1 (17%)	1 (3%)	1 (3%)	0.029
Readmission < 30 days	19 (30%)	2 (33%)	10 (27%)	5 (15%)	0.67

LAS: Lung Allocation Score; ECMO: Extracorporeal Membrane Oxygenation; ICU: Intensive Care Unit.

and the cold ischemic time decreased correspondingly (359 and 492 min vs. 293 and 229 min, $p < 0.001$). Importantly, there was no statistical difference in donor age or gender among the four groups.

Postoperative outcomes for COPD patients are given in Table 2. The incidence of primary graft dysfunction, use of Extracorporeal Membrane Oxygenation (ECMO) support, use of inhaled Nitric Oxide (iNO), reintubation, reoperation, and need for dialysis did not differ among the groups. The length of mechanical ventilation (4.7 and 11.1 vs. 1.5 and 1.6 days, $p < 0.05$) was significantly lower in the LAS groups, and the length of Intensive Care Unit (ICU) (11 and 37 vs. 4 and 4 days, $p < 0.01$) and hospital length of stay (28 and 81 vs. 22 and 23 days, $p < 0.01$) was significantly decreased in the LAS groups. Thirty-day mortality was significantly increased in the pre-LAS BLT cohort when compared to all others (17 vs. 0.3, and 3%, $p = 0.029$). The rate of readmission within 30 days after surgery was not significantly different among the groups.

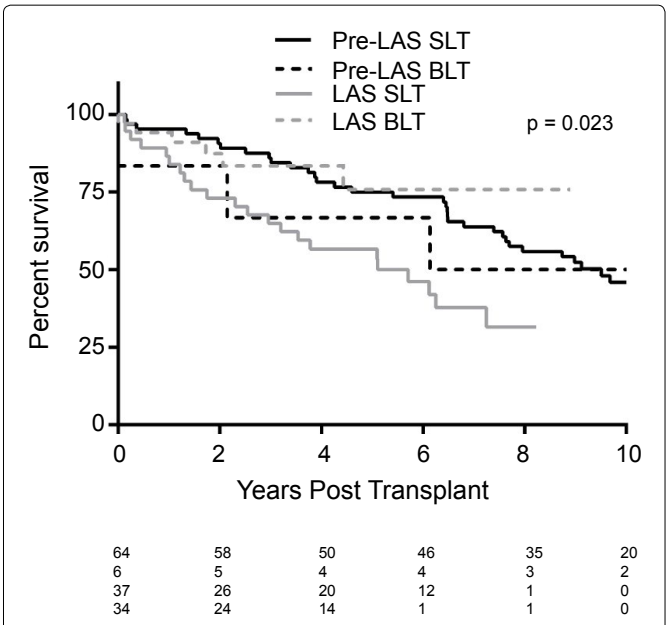

Figure 1: Post-transplant survival by Kaplan-Meier analysis.

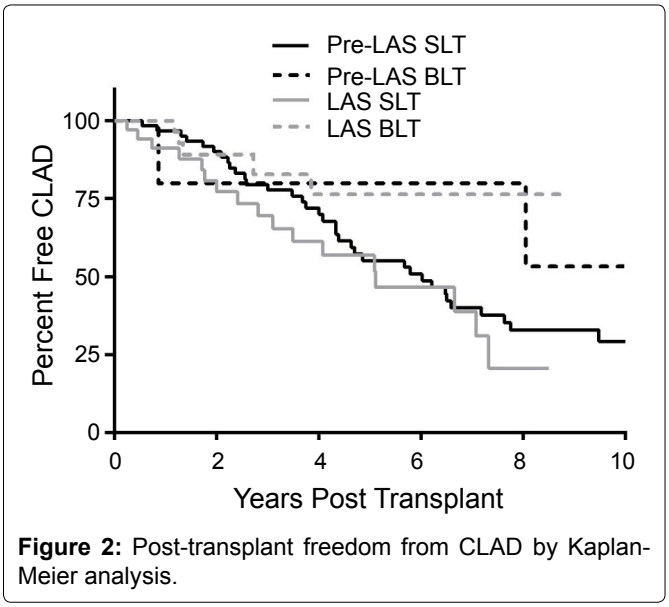

Figure 2: Post-transplant freedom from CLAD by Kaplan-Meier analysis.

The survival rate for all recipients at 1, 3, 5, and 10 years were 92.2%, 78.7%, 69.6%, and 41.1%, respectively. For the pre-LAS SLT group, actuarial survival rates at 1, 3 and 5 years were 95.3%, 85.9%, and 74.9%, respectively, and actuarial survival rates at 1, 3 and 5 years were 100%, 80.0%, and 80.0% for the pre-LAS BLT group. Actuarial survival rates at 1, 3, and 5 years were 86.5%, 64.9%, and 56.6% for the LAS SLT group and 97.0%, 85.9%, and 78.1% for the LAS BLT cohort (Log-rank test, $p = 0.01$, Figure 1). There were no significant differences among the four cohorts in the incidence of CLAD at 1, 3, and 5 years (Figure 2).

Given the statistically significant survival difference between the pre-LAS and LAS SLT groups, and the differences in patient demographics, Cox-regression analysis was used to determine the Hazard Ratio (HR) associated with SLT after implementation of the LAS system. In univariate analysis, LAS implementation in SLT patients was associated with a HR of 2.187 ($p = 0.007$) for LAS versus pre-LAS recipients. When demographic factors that differed between the two SLT groups were corrected for patient age, oxygen requirements, time on wait list, LAS, diabetes, FVC, FEV1, systolic PAP, mean PAP, and CPB, the risk associated with SLT in the LAS era remained significant with a HR of 2.05 ($p = 0.02$; Table 3). When mortality at 1 and 2 years post-transplant was assessed, the LAS SLT group had a higher risk of early mortality compared to the pre-LAS SLT group (13.5 and 27% vs.

Table 3: Multivariate cox regression analysis of risk factors for death in single lung transplant patients.

Variable	HR (95% CI)	*p*-value
Post-LAS implementation	2.05 (1.1-3.8)	0.02
Age	1.03 (0.97-1.09)	0.38
Oxygen requirements	1.36 (1.1-1.7)	0.003
Time on wait list	1.00 (0.99-1.00)	0.53
Lung allocation score	1.0 (0.92-1.09)	0.96
Diabetes	1.55 (0.78-3.10)	0.21
FVC predicted	1.0 (0.97-1.02)	0.67
FEV1 predicted	1.04 (0.98-1.11)	0.19
Systolic PAP	0.98 (0.91-1.05)	0.54
Mean PAP	0.99 (0.91-1.08)	0.83
CPB	0.77 (0.36-1.62)	0.49

HR: Hazard Ratio; LAS: Lung Allocation Score; FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in 1 Second; PAP: Pulmonary Arterial Pressure; CPB: Cardiopulmonary Bypass.

Table 4: Causes of death in single lung transplant recipients.

	Pre-LAS (n = 38)	Post-LAS (n = 22)
Malignancy	11 (29%)	2 (9%)
CLAD	7 (18%)	6 (27%)
Cardiovascular	2 (5%)	3 (14%)
Hematologic	0	1 (5%)
Infectious	10 (26%)	5 (23%)
Multi-organ failure	1 (3%)	3 (14%)
Native lung complications	1 (3%)	0
Neurologic	3 (8%)	0
Respiratory failure	1 (3%)	0
Unknown	2 (5%)	2 (9%)

4.7 and 9.4% at 1 and 2 years, p = 0.114 and 0.019, respectively). No difference in rates of CLAD between the two SLT groups was observed (Figure 2), and the overall causes of death did not differ significantly between the two SLT cohorts (Table 4).

Discussion

The LAS was devised to promote the allocation of lungs on the basis of "net transplant benefit" (the difference between predicted 1-year survival with versus without transplantation) by preferentially allocating lungs to patients with more advanced and/or rapidly progressive lung diseases who have been identified as being at significant risk of death over the coming year [1]. Therefore, due to the relatively better short-term survival of patients with COPD if they do not undergo lung transplantation, patients with COPD will generally receive lower LAS values than candidates with other indications for transplant such as Idiopathic Pulmonary Fibrosis (IPF).

Lung transplantation for COPD can significantly improve functional status and quality of life [14-16]. Whether transplantation has a significant impact on long-term survival has been less clear [17,18], although more recent analyses suggest a survival benefit for carefully selected patients [19,20]. However, if patients with more severe lung disease and higher LAS values are now preferentially receiving donor lungs, one might anticipate that post-transplant survival may decrease when patients transplanted for advanced COPD or other indications following implementation of the LAS are compared to patients transplanted before the LAS took effect. Patients with the transplant indication of COPD may be especially prone to having worsened outcomes following implementation of the LAS versus those transplanted prior to use of the LAS to allocate organs.

We found that there was a modest but significant increase in mean LAS values when estimated LAS values for the SLT pre-LAS cohort (SLT 32.8) was compared to the SLT LAS cohort (34.5). Implementation of the LAS has considerably decreased the waiting time for LTX in general [21]. In our current study, both SLT and BLT patients post-LAS implementation had longer time on waitlist, however, these differences were not significant. Adoption of the LAS has also been associated with a gradual increase in recipient age [4], and mean age increased significantly from 58.1 years for our pre-LAS SLT recipients to 60.7 years for the LAS SLT group.). Further indicators that suggest that the LAS SLT cohort had more ill patients with more advanced lung disease compared to the pre-LAS SLT group included a trend toward lower FVC, a significantly lower FEV1, and trends toward increased oxygen requirements, increased systolic and mean PAP, increased Pulmonary Capillary Wedge Pressure (PCWP), and an increased prevalence of diabetes. All of this together suggests that after LAS implementation, SLT recipients were significantly more ill than pre-LAS SLT recipients.

The increased rate of bilateral LTX that was observed in our LAS cohort can be largely explained by a shift in our institutional practice. Thabut, et al. [21] published an analysis of the International Society of Heart and Lung Transplantation registry in 2008 that showed superior survival for patients with COPD who received BLT versus SLT, and we had experienced a high degree of native lung complications with SLT at our institution (especially complications due to native lung hyperinflation). Therefore, our approach was altered to favor BLT for patients with COPD. We also simultaneously changed our approach to using elective CPB for all BLT recipients, which accounts for the corresponding increase in CPB rates in the LAS BLT group.

Despite being somewhat older and having higher LAS values than the pre-LAS recipient cohort, our LAS recipients required a significantly reduced period of post-transplant mechanical ventilatory support, had a significantly shortened length of stay in the intensive care unit, and length of stay in the hospital was reduced. Post-transplant hospital mortality rates were similar in the two time periods. Despite these early improvements since the implementation of the LAS system, long-term survival was significantly different among the four groups due to worse survival for the LAS SLT cohort. Prior to LAS implementation, nearly all lung transplants at our institution underwent SLT (91%), and these recipients had outcomes comparable to national data. Using multivariate analysis to correct for differences in baseline characteristics between pre-LAS SLT patients and LAS SLT patients failed to eliminate a difference in mortality between the two groups, and LAS SLT patients remained twice as likely to die per year when compared to their pre-LAS counterparts (HR 2.05, p = 0.02; Table 3). Furthermore, comparing the survival curves of the two groups (Figure 1) and evaluating early mortality suggested that the increased mortality in SLT patients after LAS implementation was due to increased deaths in the first one to two years after transplant, but long-term causes of mortality such as the development of CLAD did not differ between the two groups (Figure 2).

A possible factor associated with decreased long-term survival that was not controlled for in our multivariate analysis is the possibility of declining quality of donor lungs that has tended to occur since the implementation of the LAS. Although there was no difference in donor age between the two SLT recipient groups (Table 1), donor age only captures a small portion of the overall quality of donor lungs. We note that there has been a trend throughout the nation and at our own institution to accept more extended criteria donor lungs. This change has led to accepting lungs with factors which were once considered prohibitive to lung donation, such as PaO2/FiO2 at PEEP 5 cm H_2O < 300 mmHg at time of offer, presence of abnormalities on chest X-ray, significant smoking history, evidence of aspiration, presence of chest trauma, or donation after circulatory death [22]. Furthermore, the use of

extended criteria donor lungs remains controversial, with multiple studies showing either no difference in outcomes or worsened outcomes [23]. Therefore, it is possible that gradual changes in donation criteria as well as the listing of candidates who tend to have more advanced lung disease and overall poorer health status have had a negative influence on our LAS SLT cohort's long-term survival.

Our observational case series has a number of significant limitations that include its single-center, retrospective nature and relatively small number of transplant recipients. However, our general approach to the pre- and post-transplant management of LTX candidates has not changed significantly over the time period of the study. Nonetheless, incremental changes in clinical practice over the time periods assessed by our observational study may have had some impact on our findings. Although the relatively low number of recipients in the pre-LAS BLT cohort does not allow any conclusions to be drawn from comparing data for the pre-LAS and LAS BLT recipients, the size of pre-LAS and LAS SLT recipient cohorts were similar with a substantial number of recipients in both SLT groups.

Conclusions

Despite significantly older age, greater pulmonary function impairment, and higher LAS values, we did not observe a detrimental impact of LAS implementation on peri-operative and early outcomes for our LAS lung transplant recipient cohorts with COPD versus the pre-LAS recipient cohorts, and ICU and hospital length of stay were significantly decreased for the LAS recipients. Although the adoption of the LAS has shortened time-to-transplant for lung recipients while on the waiting list in general [24], the waitlist time was increased for our LAS recipient cohorts (although this did not reach statistical significance) and may reflect the generally higher scores that tend to be assigned to candidates with other transplant indications such as IPF. However, despite improved early post-transplant outcomes, there was increased mortality in the LAS SLT group compared to all other groups. When comparing these patients specifically to their pre-LAS counterparts, correction for available demographic factors failed to eliminate the increased risk of mortality. This may reflect the effects of a combination of increased age, increased prevalence of comorbidities such as diabetes, and/or increased frailty and deconditioning due to more advanced severity of COPD for the LAS recipient cohort as well as a possible decline in lung donor quality since the implementation of the LAS.

Declarations

Ethics approval and consent to participate

This investigation was approved by the University of Wisconsin Human Subjects Committee (approval number M-2009-1308).

Availability of data and materials

All data used to generate this manuscript are stored in the University of Wisconsin Society for Transplant Surgery database. Per our institutional review board, this dataset cannot be made available to third parties.

Competing interests (Financial/nonfinancial disclosures)

Dr. Meyer has been an investigator in clinical trials sponsored by Abbott, Actelion, Altana, Amgen, Asthmatx, Bayer, Boehringer-Ingelheim, Bristol Meyers Squibb, Chiron, Discovery Labs, DuPont Merck, Fibrogen, Genentech, Gilead, GlaxoSmithKline, Inspire. InterMune, Johnson & Johnson, Novartis, Nycomed, Parion, Pfizer, Pharmaxis, PreAnalytiX, Roche, Ross, Vertex, and Wyeth. Dr. Meyer has recently served on a Clinical Advisory Board for InterMune and on a clinical trial adjudication committee for Medimmune (these are no longer active). All authors do not report any other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed. No writing assistance was utilized in the production of this manuscript.

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Authors' contributions

Drs. Julliard and De Oliveira: take full responsibility for the integrity of the work as a whole, from inception to published article.

Dr. Julliard: contributed to the study design, data collection, statistical analysis, data interpretation, and manuscript composition.

Dr. Osaki: contributed to the study design, data collection, statistical analysis, data interpretation, and manuscript composition.

Dr. Maloney: contributed to the study design, data collection, data interpretation, and manuscript composition.

Dr. Cornwell: contributed to the study data collection, data interpretation, and manuscript composition.

Dr. Sonetti: contributed to the study data collection, data interpretation, and manuscript composition.

Dr. Meyer: contributed to the study design, data collection, statistical analysis, data interpretation, and manuscript composition.

Mehgan Holland: contributed to data collection and analysis and manuscript composition.

Dr. De Oliveira: contributed to the study design, data collection, statistical analysis, data interpretation, and manuscript composition.

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