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### Lung allocation score

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## ORIGINAL ARTICLE

# Lung allocation score: the Eurotransplant model versus the revised US model – a cross-sectional study

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## SUMMARY

Both Eurotransplant (ET) and the US use the lung allocation score (LAS) to allocate donor lungs. In 2015, the US implemented a new algorithm for calculating the score while ET has fine-tuned the original model using business rules. A comparison of both models in a contemporary patient cohort was performed. The rank positions and the correlation between both scores were calculated for all patients on the active waiting list in ET. On February 6th 2017, 581 patients were actively listed on the lung transplant waiting list. The median LAS values were 32.56 and 32.70 in ET and the US, respectively. The overall correlation coefficient between both scores was 0.71. Forty-three per cent of the patients had a < 2 point change in their LAS. US LAS was more than two points lower for 41% and more than two points higher for 16% of the patients. Median ranks and the 90th percentiles for all diagnosis groups did not differ between both scores. Implementing the 2015 US LAS model would not significantly alter the current waiting list in ET.

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## Key words

allocation, lung transplantation, waiting list

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## Introduction

In May 2005, the lung allocation score (LAS) was implemented in the US. This allocation system replaced a scheme solely based on waiting time. There were three objectives: reduce the number of deaths on the lung transplant waiting list; increase the survival benefit for lung recipients and ensure the efficient and equitable allocation of lungs to transplant candidates [1].

Germany was the first country to adopt the LAS on December 10, 2011; the Netherlands followed on April 22, 2014. These countries implemented the US LAS model from 2008 that incorporates the current and change of partial pressure of carbon dioxide. The German experience after introduction of the LAS was fairly similar to the US with an increase in transplants for patients with restrictive lung diseases and critically ill patients. A 26% reduction in waiting list mortality, and an improved 1-year survival post-transplant rate from 76% to 81% was observed [2].

Despite the fact that the LAS had been up and running in the US since 2005, starting the LAS scheme in the Eurotransplant (ET) countries was associated with two areas of uncertainty. Firstly, with its urgency driven allocation scheme, Germany and the Netherlands already had an urgency system in place to minimize waiting list mortality. A patient who would fulfil High Urgent (HU) criteria in the old scheme, and hence would subsequently be prioritized over elective patients, would not necessarily receive high LAS values. Secondly, in the era before LAS implementation, the German patients were sicker compared to those from the US, with 18% on ventilator support, and 7% on extra corporeal life support (ECLS), as opposed to 5.7% and 1.3% in the US [3–5]. As patients on ECLS were not accounted for in the LAS, already from the start specific business rules were introduced in ET to solve this specific European situation. This report contains a detailed description of these rules.

In February 2015, the US has implemented an update of the LAS to better cope with patients with pulmonary hypertension. Among other parameters, this new model now included cardiac index, central venous pressure and bilirubin.

The aim of this study is to compare the ET and the updated US LAS in a ET wait list cohort.

## Methods

### Definitions

Throughout this report, the name ‘ET LAS’ model will refer to the original LAS allocation scheme from 2005 with the incorporation of current partial pressure of carbon dioxide and change of partial pressure of carbon dioxide from 2008, with the inclusion of tailor-made business rules (Table 1). While the ‘US LAS’ model is the name for the LAS algorithm implemented in the US in 2015 [6,7].

Both Germany and the Netherlands use the LAS system for the national allocation of donor lungs, and in this report they will be denoted as LAS countries.

### Study population

All patients on the active waiting list in Germany and the Netherlands on February 6, 2017 are included. This is an arbitrary snapshot of the waiting list that reflects the real-life situation in ET. Based on the algorithms from both the ET LAS and the US LAS model, scores are calculated for all patients using actual clinical information available in the ET registry.

Upon listing for lung transplantation, and at regular intervals thereafter, data on LAS parameters are submitted to ET. Not all parameters needed for calculating the US LAS were available, in those cases the US LAS score was calculated using the US rules for treating missing values [6].

Patients were classified into four groups depending on their underlying disease: Group A, obstructive airway diseases (e.g. chronic obstructive pulmonary disease [COPD]); Group B, diseases of the pulmonary circulation (e.g. idiopathic pulmonary arterial hypertension (PAH)); Group C, suppurative lung diseases (e.g. cystic fibrosis [CF]) and Group D, restrictive lung diseases (e.g. pulmonary fibrosis).

## Exceptional LAS

In case the calculated LAS does not reflect the perceived idea of transplant benefit for a particular transplant candidate, it is possible to apply for an exceptional LAS. This can be done by proposing an alternative LAS value accompanied with a detailed description of the underlying reasoning. Every proposal for an exceptional LAS value will be evaluated by the LAS review board (RB). In case the RB members agree with the suggested exceptional LAS value, the value will then be assigned to the patient, where the decision of the RB members is binding. If the patient meets at least one of the following criteria, a request for an Exceptional LAS can be submitted: (i) Primary Pulmonary Hypertension types 1 and 4 [8]; (ii)

Combined lung and non-renal transplant candidates; (iii) Rare diseases; (iv) Specific situations in which the LAS does not reflect the expected urgency and benefit. In this waiting list cohort, none of the patients had an exceptional LAS value.

## Lung allocation policy changes

Prior to the introduction of the LAS in Germany, all countries in ET exchanged donor lungs cross border with high priority to patients in HU status. This HU status was agreed upon by all countries and the access to the HU list was controlled by a team of international auditors. In the LAS era, Germany and the Netherlands no longer have patients on an HU list, while this urgency tier system still exists in the other countries. Upon LAS implementation

**Table 1.** Eurotransplant lung allocation score (LAS) business rules.

### *Ventilation/extra corporeal life support (ECLS)*

If a candidate is on ECLS, the pre-ECLS settings on blood gases, oxygen and ventilator demands can be used for the LAS. If a patient on ECLS has to be re-evaluated within 6 days after getting on ECLS, the pre-ECLS settings on blood gases, oxygen and ventilator demands should be entered. If the re-evaluation takes place after at least 7 days or more, the current ventilator requirements, oxygen demand and blood gases should be entered. If weaning attempts have been made, they have to be documented.

### *Oxygen requirement at rest*

The amount of oxygen needed to maintain adequate oxygen saturation of 90–92% at rest (l/min). An additional rule for high flow oxygen therapy is introduced: High flow (HF)-oxygen therapy (=HF nasal cannula (HFNC)) is defined as an oxygen flow >15 l/min. In patients with HF-oxygen therapy, oxygen saturation (SpO<sub>2</sub>) should be measured by pulse oximetry continuously including documentation of SpO<sub>2</sub> and oxygen fraction. In case of a titrated oxygen flow of more than 15 l/min, the oxygen fraction should be entered. The maximum allowable value in the data form was reset from 26 to 15 l/min. Oxygen titration also applies to ventilated patients.

### *PCO<sub>2</sub>*

Blood gases for evaluation by LAS must adhere to all of the following criteria

- Blood gases should be of arterial or capillary origin;
- Blood gases at rest must be entered. Blood gases during or after exercise, or at night are not acceptable;
- Blood gases should be performed after titration of oxygen flow and adjusted by pulse oximetry to a target oxygen saturation of 90–92%;
- Blood gases with a pO<sub>2</sub> >60 mmHg (>8 KPa) should be repeated with oxygen titration to a target oxygen saturation of 90–92%.

### *Six-minute walk distance*

Six-minute walk distance obtained with a flow rate needed during exercise.

### *Bilirubin change*

Candidates with pulmonary hypertension in hemodynamic decompensation are eligible for an exceptional LAS value under the following rules: pulmonary arterial hypertension patients with a Cardiac Index <2 l/m<sup>2</sup> and right atrial pressure >15 mmHg or bilirubin increase by 50%/abnormal or a creatinine increase by >50%/abnormal, can be accepted with LAS value equivalent to the 95th percentile of the waiting list.

### *Creatinine and creatinine change*

A special rule for candidates with pulmonary hypertension in hemodynamic decompensation has been defined. See section on bilirubin change.

### *Cardiac index*

A special rule for candidates with pulmonary hypertension in hemodynamic decompensation has been defined. See section on bilirubin change.

### *Central venous pressure (CVP)*

A special rule for candidates with pulmonary hypertension in hemodynamic decompensation has been defined. See section on bilirubin change.

in Germany in December 2011, all countries within ET also agreed to enter LAS data on all HU patients, arbitrarily defined as those with a LAS of 50 or above, called 'high LAS'. As of that moment, the international exchange of allografts for the sickest patient was redefined from a sharing system for HU patients to sharing for patients with a high LAS value. In contrast to the US, in the ET LAS countries no local allocation was attempted first.

## Statistics

For this study, the rank positions on the waiting list are only based on the LAS values and do not take blood group rules or other allocation factors like country balances into account. Rank positions are expressed as percentiles of the combined Dutch and Germany waiting list, where the 90th percentile indicates that 10% of the patients on the waiting list at that moment had a higher LAS value.

The correlation between the ET LAS and the US LAS is measured by Spearman's rank correlation coefficient and illustrated in scatter plots. Wilcoxon signed rank test is performed for comparisons between medians. Differences between groups were evaluated by Chi-square test.

The change in LAS is obtained by subtracting the ET LAS from the US LAS values. A Bland and Altman plot is drawn to visualize agreement between the scores [9]. Differences between the ET LAS and the US LAS models are further shown by comparing median LAS values, median rank positions and percentages of patients on the active waiting list that have a calculated LAS value above the 90th percentile, according to the ET LAS and the US LAS.

For all analysis, a *p* value of  $P < 0.05$  is considered significant. All analyses are performed with SPSS v20.0.

## Results

On February 6th 2017, 581 patients were listed with an active urgency on the Dutch ( $N = 193$ ) and German ( $N = 388$ ) lung transplant waiting list. None of these patients had an exceptional LAS status. Demographic statistics are provided in Table 2.

### Correlation between the ET LAS and the US LAS

Scatter plots of the ET LAS and the US LAS percentiles by diagnosis group are given in Fig. 1. Patients with a US LAS higher than the ET LAS will appear above the 45 degree line and vice versa. The overall correlation

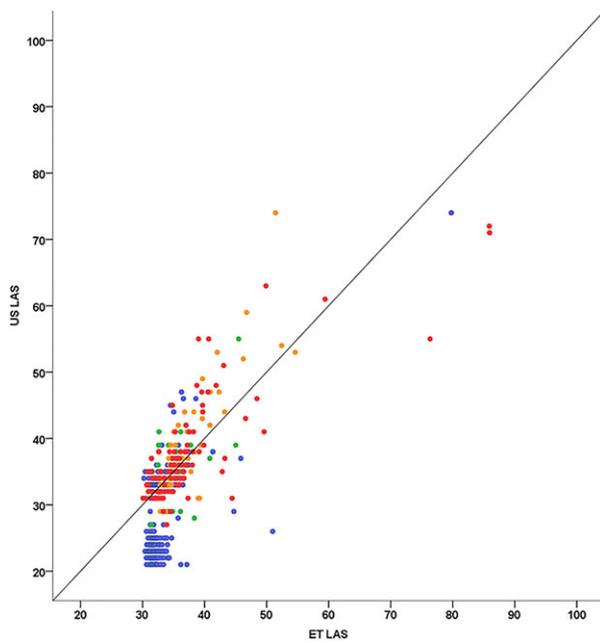
**Table 2.** Demographic statistics of the active waiting list on February 6, 2017 in the Eurotransplant (ET) lung allocation score (LAS) countries.

Variables	Number (%)/ median (IQR)
Age (years)	56 (49–61)
Body mass index	23 (20–26)
Diagnosis	
Group A	338 (58)
Group B	26 (5)
Group C	60 (10)
Group D	102 (18)
Missing	55 (9)
Assistance level with daily activities	
Total	6 (1)
Some	416 (72)
None	117 (20)
Missing	42 (7)
Diabetes	70 (12)
Continuous mechanical ventilation	4 (1)
Supplemental oxygen required at rest	282 (49)
Oxygen demand (l/min)	1.5 (1–2)
Forced vital capacity (%predicted)	46 (34–60)
Current PCO <sub>2</sub> (mmHg)	45 (38–49)
Systolic pulmonary artery pressure (mmHg)	34 (28–40)
pulmonary capillary wedge pressure (mmHg)	10 (7–13)
Cardiac Index (l/min/m <sup>2</sup> )	2.9 (2.5–3.5)
Central Venous pressure (mmHg)	6 (4–9)
6-minute walk test distance (m)	230 (139–325)
Current Serum creatinine (mg/dl)	0.8 (0.6–0.9)
Current total bilirubin (mg/dl)	0.4 (0.3–0.5)
ET LAS	32.56 (32.52–34.69)
US LAS	32.70 (23.25–34.53)

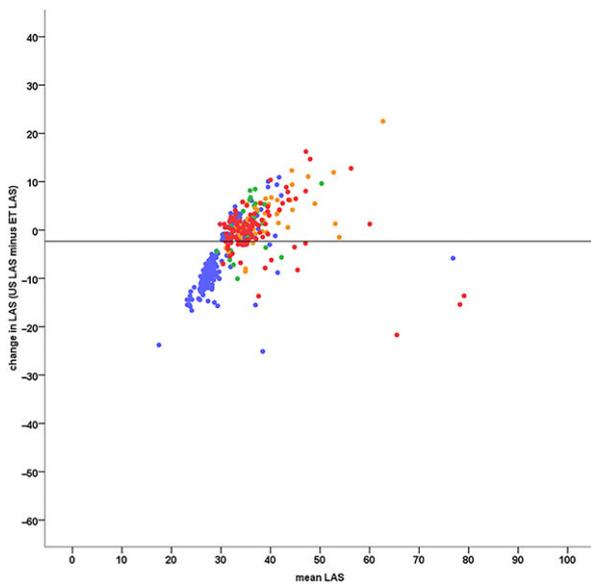
coefficient between ET LAS and US LAS is 0.71, for the diagnosis groups A, B, C and D, a correlation of 0.42, 0.14, 0.75 and 0.72 is obtained, respectively.

### Difference between the ET LAS and the US LAS

The mean change in LAS (US LAS – ET LAS) is  $-2.3$ , with a standard deviation of 6.7 (Fig. 2). Figure 3 shows that 43% of the patients had a  $< 2$  point change in their LAS. Compared to the ET LAS, the US LAS is more than two points lower for 41% and more than two points higher for 16% of the patients. The greatest increase in LAS was seen in Group B patients, where the US LAS was more than two points higher versus the ET LAS in 50%. The greatest decrease was observed in Group A patients, where 52% had a US LAS that is more than two points lower compared to the ET LAS.



**Figure 1** Scatter plot of ET and revised UNOS LAS by diagnosis group for patients on the active waiting list on February 6, 2017 in the eurotransplant LAS countries. Group A (Blue dot), Group B (Green dot), Group C (Orange dot), Group D (Red dot). Spearman's rank correlation coefficient 0.71.



**Figure 2** Scatter plot of change in LAS (US LAS minus ET LAS) by mean LAS ((US LAS + ET LAS)/2) by diagnosis group for patients on the active waiting list on February 6, 2017 in the Eurotransplant LAS countries. Group A (Blue dot), Group B (Green dot), Group C (Orange dot), Group D (Red dot).

### Median LAS by diagnosis grouping

There was a small but statistically significant lower median ET LAS of 32.56 compared to the median US LAS of 32.70 ( $P < 0.0001$ ).

Patients in Group A would obtain a lower median LAS in the US model, the value drops from 32.10 to 29.21 for the ET LAS and the US LAS, respectively ( $P < 0.0001$ ), while patients in Group C would see an increase in the median LAS in the US model, from 35.18 to 35.93 ( $P = 0.003$ ) (Fig. 4).

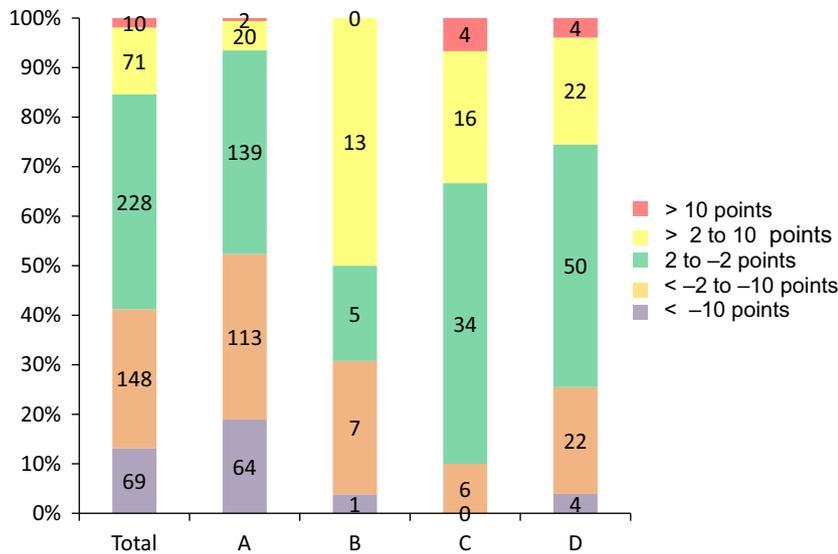
Both for Group B and Group D, the median LAS values between the ET LAS and the US LAS did not differ. For Group B patients, the ET LAS and US LAS were 34.80 and 37.25 ( $P = 0.32$ ), for Group D these median values were 35.20 for the ET LAS and 34.74 for the US LAS ( $P = 0.79$ ).

### Percentage of transplant candidates with a LAS >90th percentile

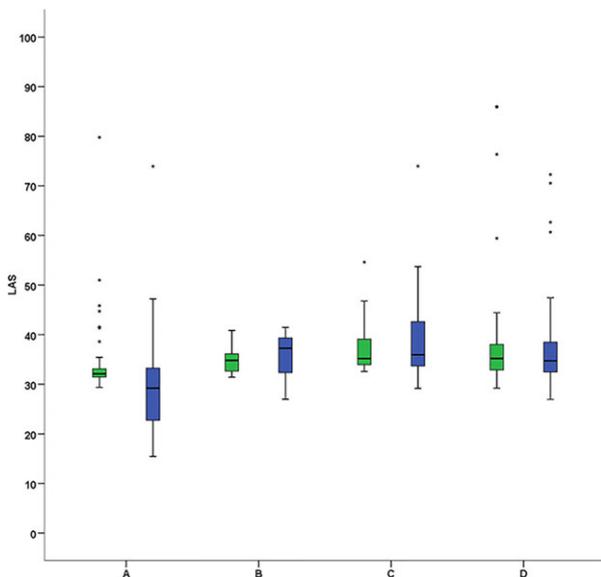
Both in the ET LAS and the US LAS, the group C was the largest group with LAS values above the threshold of the 90th percentile. 31.7% of the patients on the waiting list with group C diagnosis had an ET LAS value that placed them above the 90th percentile, followed by 23.5%, 15.4% and 2.1% of the patients with group D, B and A diagnosis, respectively (Table 3). With a LAS calculated according to the US model, the percentages of patients in each diagnosis group with LAS above the 90th percentile differed, but these differences did not reach statistical significance. According to the US LAS, the percentages of patients with a US LAS high enough to be in the top 10% of the waiting list was for Group A 2.4% (difference between ET LAS and US LAS  $P = 0.79$ ), for Group B patients 19.8% ( $P = 0.72$ ), for Group C 35% ( $P = 0.70$ ) and for Group D patients this percentage was 22.5% ( $P = 0.87$ ).

### Median ranking by diagnosis grouping

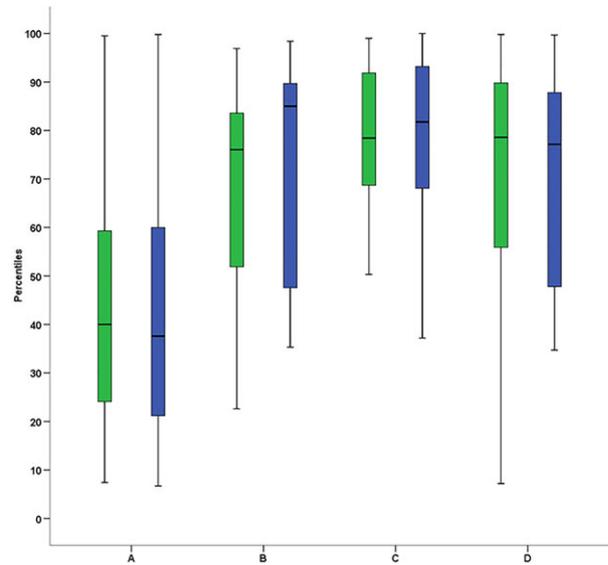
Figure 5 shows the distribution of the rank positions by diagnosis group. When sorted by their ET LAS values, patients in Group D scored highest with a median percentile of 79, followed by Group C with 78, Group B with 76 and 40 for Group A patients). Following the US LAS, the difference in median rank position according to the ET and the US LAS did not reach a statistically significant difference. The median rank positions according to the US LAS scheme were for Group A patients at the 38th percentile (difference between ET LAS and US LAS,  $P = 0.81$ ), for Group B patients this percentile was 85 ( $P = 0.29$ ), for Group C patients it was 82 ( $P = 0.19$ ) and for Group D it was 77 ( $P = 0.79$ ).



**Figure 3** Change in LAS by diagnosis group (US LAS minus ET LAS).



**Figure 4** Box plots of ET LAS and US LAS by diagnosis group. ET LAS (green), US LAS (Blue).



**Figure 5** Box plots of percentiles based on ET LAS and US LAS by diagnosis group. ET LAS (green), US LAS (Blue).

### Differences between ET and US LAS variables

The differences between ET and US LAS at variable level are listed in Tables S1–S3.

### Discussion

This is the first study comparing the ET LAS and the US LAS in a large European patient cohort. Both models were strongly correlated most closely for group C and group D patients. For all diagnosis groups in ET, switching from the ET LAS to the US LAS would not

impact statistically significant on the median ranking position and the percentage of patients that would have LAS values high enough to be placed above the 90th percentile of the waiting list would not change.

The allocation of donor lungs is governed by the LAS system in three countries in the world. Both Germany and the Netherlands allocate donor lungs according to the LAS 2008 model, while in the US an adapted model of 2015 was implemented. There were several shortcomings in the 2008 model; both the ET countries and the US have dealt with these shortcomings in a different way.

One of the major aims of the US LAS 2015 revision was to better address rapidly deteriorating PAH patients.

**Table 3.** Percentage of patients exceeding the 90th percentile of the waiting list.

Diagnosis	Eurotransplant lung allocation score (LAS), %	US LAS, %	P value
Group A	2.1	2.4	0.79
Group B	15.4	19.8	0.72
Group C	31.7	35.0	0.70
Group D	23.5	22.5	0.87

With the addition of the factors bilirubin, changes in bilirubin and creatinine as well as the factors cardiac index and central venous pressure, a higher acuity of the patient can be mapped in the US LAS. The ET LAS does not include these factors, but already from the start special business rules were introduced in ET to come to a system that would fit our population. There were several reasons for doing so. In contrast to the US, the LAS replaced an urgency tier system, where patients fulfilling strict criteria could be listed as high urgent, and receive priority upon an organ offer. Furthermore, the lung transplant candidate population in ET in 2011 was sicker compared to the patients on the list in the US in 2005. And thirdly, the US LAS model did not – and still does not – include a factor for patients on ECLS.

The results of the first 3 years of LAS in Germany show that the ET LAS model works. We observed an increase in transplants for idiopathic pulmonary fibrosis (IPF) and critically ill patients; a 26% reduction in waiting list mortality, and an improved 1-year survival post-transplant rate from 76% to 81% [2]. Hence, when the US implemented a new LAS model in 2015, there was no urgent need to follow the US and also implement this US LAS model.

The LAS model has been shown to accurately predict waiting list survival for the average PAH patient [10,11]. But identifying among these PAH candidates those who are most in need would require additional information like mean right arterial pressure and 6-minute walk test distance [12]. In ET, we adopted for a system that would allow a fast access to transplantation only for PAH patients who deteriorated quickly by granting them an exceptional LAS value; more specific the 95th percentile is assigned in case of demonstrated progressive right heart failure for PAH patients. The US LAS has introduced parameters such as cardiac index, central venous pressure and bilirubin to better cope with all group B patients. This difference in approach explains the low correlation between the ET LAS and the US LAS for group B patients.

The lack of correlation between the ET LAS and the US LAS for group A patients can be explained by the reduced influence of increasing age as well as the reduced impact of supplemental oxygen in the US LAS. In addition, a systolic pulmonary artery pressure below 40 mmHg no longer influences the LAS for group A patients which accounts for their lower US LAS values.

Since the introduction of LAS, the proportion of patients transplanted while on ECLS has increased, both in the US and in ET [13]. Although this is an unwanted effect of an allocation scheme without waiting time, several centres report good outcome for their awake ECLS patients due to expertise and quick access to transplantation [14–19]. This latter condition is facilitated in ET by allowing pre-ECLS blood gases to be used in the LAS calculation.

One of the shortcomings of the LAS 2008 model was related to huge impact of the factor oxygen requirements. In addition, there were no rules for patients requiring high flow nasal cannula (HFNC) therapy [20]. In the US LAS 2015 model, the influence of the factor oxygen in the waiting list model is reduced and the factor is added to the post-transplant model, both measures aimed at diminishing the effect of oxygen administration. In ET, the statistical model remained the same, but we defined standard titration rules, introduced a lower maximal allowed flow rate and defined special rules for patients on HFNC therapy. This results in lower median oxygen demand of 1.5 L in ET versus 4 L in the US (personal communication, Dr. Winslow J, data analyst UNOS).

In the US LAS, change in partial pressure of carbon dioxide impacts more strongly on LAS. This measure is particularly beneficial for non-IPF group D patients. In ET, we opted for not changing this factor as our patients in group D are already well served by the current LAS, instead we strictly defined and standardized the criteria under which blood gas analysis and oxygen titration should be performed.

A drawback of this study is related to the cross-sectional study design. By arbitrarily choosing a snapshot of the lung transplant waiting list not all aspects of the ET LAS model could be studied. In particular, this study cohort did not contain any patients with an exceptional LAS.

In conclusion, implementing the 2015 US LAS model in ET would not significantly impact on the current waiting list. Our data show that the ET LAS and the US LAS are correlated and median ranking positions as well as the top 10% of the waiting list are not different according to both models. However, ET is currently collecting additional parameters to build up a database that will allow further improvement of the LAS system.

## Authorship

JMS and JG: designed study. JMS, AS and DG: analysed data. EDV: collected data. JMS and JG: wrote the paper. All contributed to the creation of the ET LAS and to the discussion of this paper.

## Funding

The authors have declared no funding.

## Conflicts of interest

The authors have declared no conflicts of interest.

## SUPPORTING INFORMATION

Additional supplemental material may be found online in the Supporting Information section at the end of the article.

**Table S1.** Regression coefficients (rounded) in the ET LAS and US LAS model.

**Table S2.** Covariates in the waiting list survival model according to the ET LAS and the US LAS models.

**Table S3.** Covariates in the post-transplant survival model according to the ET LAS and the US LAS model

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