Multistate modelling of baseline lung allograft dysfunction in lung transplant recipients

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Baseline lung allograft dysfunction (BLAD) after lung transplantation (LTX) is a dynamic condition: DLTX recipients who started in BLAD frequently achieve normal baseline function whereas SLTX recipients who started in BLAD rarely do. https://bit.ly/4kKQZIB

Cite this article as: Gerckens M, Richard A, Arnold P, *et al*. Multistate modelling of baseline lung allograft dysfunction in lung transplant recipients. *ERJ Open Res* 2025; 11: 01135-2024 [DOI: 10.1183/23120541.01135-2024].

Received: 31 Oct 2024
Accepted: 2 March 2025

Abstract

Background Baseline lung allograft dysfunction (BLAD) is characterised by the failure to achieve normal baseline lung function after lung transplantation (LTX), affecting over a third of LTX recipients and conveying significant mortality. While previous studies identified BLAD as a risk factor for mortality, evolution, transitions and risk factors influencing transitions from BLAD to normal lung function or death/retransplantation remain unknown.

Methods We conducted a retrospective study of 472 LTX recipients transplanted between 2010 and 2018, using a Markov multistate model to characterise lung function evolution. The model investigated transitions between "indeterminate", "BLAD", "normal baseline lung function" and "death/retransplantation" states. We modelled state transitions, association of BLAD with mortality, and risk factors influencing transitions and mortality through respective states.

Results Our study confirms a higher mortality risk for BLAD, particularly in single LTX (SLTX) compared to double LTX (DLTX) recipients. DLTX recipients with obstructive underlying disease were more likely to recover from BLAD (hazard ratio (HR) 3.1) but faced higher mortality if remaining in BLAD (HR 2.6). Chronic lung allograft dysfunction had a strong association with mortality in patients with normal baseline lung function (HR 5.1) but also to a lesser extent in BLAD patients (HR 1.8). Longitudinal analysis demonstrated that DLTX recipients often recover from BLAD, while SLTX recipients rarely achieve normal lung function if starting in BLAD.

Conclusions Our study highlights differences in lung function evolution between SLTX and DLTX recipients and investigates for the first time prevalence and risk factors for transitions between BLAD and non-BLAD states, as well as risk factors influencing BLAD-related mortality in LTX recipients.

Introduction

Baseline lung allograft dysfunction (BLAD) complements established lung allograft dysfunction concepts such as chronic lung allograft dysfunction (CLAD). Although currently no consensus guideline exists on BLAD, it has been defined as the failure to achieve normal baseline lung function. The concept of BLAD has been applied to both double lung transplantation (DLTX) and single lung transplantation (SLTX) recipients [1, 2] and affects up to 40% of LTX recipients imposing an increased risk for mortality in all published studies [1–6].

BLAD is a dynamic condition: usually, lung function increases in LTX recipients during the first year, in some even up to 2 years until reaching their peak function [2, 7]. It is a frequent clinical observation that some LTX recipients start with an abnormal lung function and subsequently develop normal lung function. Other patients, however, start in a state BLAD and never recover, whereas others achieve normal lung function right after transplantation. BLAD trajectories, *e.g.* the recovery from baseline lung allograft dysfunction with lung function development over time, have not been investigated yet.

As BLAD or normal baseline lung function states are defined by lung function measurements and these are only available at specific timepoints, normal baseline lung function is achieved at an unknown timepoint between two lung function measurements. This phenomenon is known as interval-censored observation. Previous survival analyses are primarily based on time-to-event analysis using proportional hazards models such as Cox regression. However, these approaches do not take into account the interval-censoring of an individual's BLAD status, nor do they allow an intuitive interpretation of the estimated regression parameters when death is considered a competing risk [8]. Markov multistate models (MSM) not only enable comprehensive modelling of predefined disease states, but also simultaneously address competing risks biases and the interval-censoring of BLAD status due to intermittently performed pulmonary function tests [8]. They have previously been used, for example, to calculate time on organ transplant waiting list, to account for survivorship bias studying quality of life after LTX or to model state transitions during COVID-19 infection [9–11].

Here, we aimed to model the transitions between clinically defined states like normal baseline lung function, BLAD and death or retransplantation using MSM to gain further insights into transition frequencies and associated risk factors.

Methods

Ethics

This retrospective study was approved by the Ethics Committee of the Ludwig-Maximilians-University of Munich (#21-0020).

Patient cohort

We retrospectively reviewed all adult SLTX and DLTX recipients transplanted at our centre between 2010 and 2018. Patients were followed up until death, retransplantation or until 1 May 2024. We excluded patients who did not survive 90 days after transplantation or did not have sufficient spirometry measurements.

Standard LTX management

Treatment regimens and standardised follow-up of LTX recipients at LMU Munich were performed as previously described [12]. Lung function testing was performed according to current European Respiratory Society/American Thoracic Society guidelines [13] quarter yearly and when clinically indicated. Global Lung Function Initiative (GLI) reference equations were used according to Stanojevic *et al.* [14].

Baseline allograft dysfunction

For DLTX recipients, BLAD was defined as failure to reach both forced expiratory volume in 1 s (FEV_1) % predicted and forced vital capacity (FVC) % predicted >80% predicted on at least two consecutive tests >21 days apart [1]. For SLTX recipients, we defined BLAD as failure to reach both FEV_1 % predicted and FVC % predicted >60% predicted on at least two consecutive tests >21 days apart [2]. Further, we included another analysis with a different BLAD cut-off for SLTX recipients of FEV_1 % predicted and FVC % predicted >80% predicted on at least two consecutive tests >21 days apart. When normal baseline lung function was achieved, a state transition back to BLAD was not possible, per definition.

Chronic lung allograft dysfunction

CLAD was diagnosed according to current International Society for Heart and Lung Transplantation (ISHLT) guidelines [15]: "baseline-FEV_1" was defined as the mean of the two best post-operative FEV_1 values, measured at least 3 weeks apart. "Possible CLAD" was defined as one or more FEV_1 declines ⩽80% of "baseline-FEV_1" within 3 weeks. "Probable CLAD" was defined as two or more pulmonary function measurements with an FEV_1 ⩽80% of "baseline-FEV_1" >3 weeks and <3 months apart. "Definite CLAD" was defined as two or more pulmonary function measurements with an FEV_1 ⩽80% of "baseline-FEV_1" at least 3 months apart. For every FEV_1 decline, non-CLAD causes were excluded.

A combined state of suspected CLAD in our model comprised "definite CLAD", but also the provisional diagnosis "possible CLAD" and "probable CLAD" that could be rejected during follow-up.

States and state transitions

The "indeterminate" state was assumed if fewer than two spirometry tests, at least 21 days apart, were available. Otherwise, the baseline lung function was calculated for FEV_1 % predicted and FVC % predicted as defined in previous studies [1]. Based on these values, the state of "BLAD" or "normal baseline lung function" was determined – and treated as interval-censored observation. The state "death or retransplantation" was an absorbing state, without any possibility of a transition to another state, and the according date was recorded as an exact observation. State transitions were modelled on a timeline scaled in weeks for the first 5 years after transplantation. If a pulmonary function test did not alter the state of the patient, this was reflected in a transition towards the same state (self-loop).

Statistical analysis

For descriptive statistics, data are presented as median and interquartile range. Mann–Whitney U-test was used to compare continuous variables, not assuming normal distribution. For contingency table analysis, Chi square and Fisher's exact test were used. Multistate modelling was performed using the R package MSM, version 1.7.1 with R version 4.4.1. A multistate model was fitted on patient panel data, with BLAD, normal baseline lung function, and death or retransplantation as events of interest.

Using those observations, a time-inhomogeneous continuous Markov multistate model was fitted with time after transplantation (in weeks after transplantation) as time scale and covariate. Further covariates were "male sex" (baseline female), "single lung transplant" (baseline DLTX), "single lung transplant with obstructive underlying disease" and "double lung transplant with obstructive underlying disease" for every state transition. In further supplementary models we included the covariates transplant age (in years) and post-operative stay on intensive care unit (ICU) in weeks.

Data processing and visualisation were performed using Python 3.10 and the packages numpy (v1.22.3), pandas (v1.4.2), matplotlib (v3.5.2), seaborn (v0.11.2) and scipy (v1.8.0).

Results

Study cohort

We analysed the follow-up of all patients transplanted at our centre at LMU Munich between 2010 and 2018. 72 patients were excluded due to survival of <90 days or insufficient number of spirometries in the follow-up period. In the analysed timeframe, altogether 472 lung transplant recipients were included in the analysis: 149 SLTX and 323 DLTX recipients (figure 1) with 10 221 lung function tests. Baseline characteristics of the study cohort can be found in table 1.

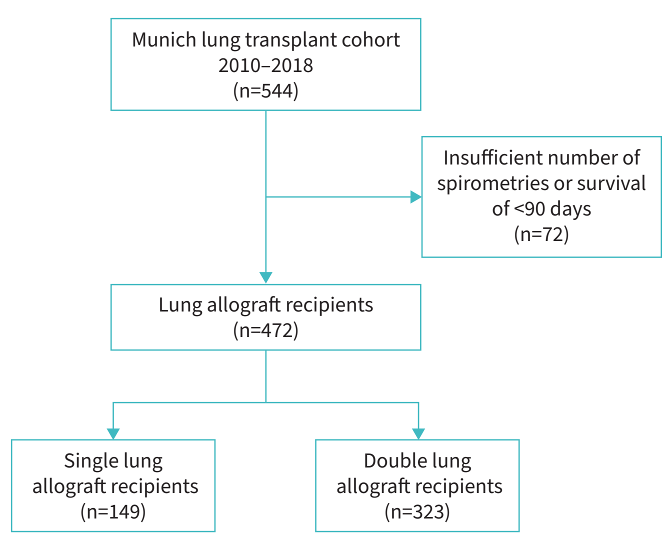

FIGURE 1 Study flow chart.

TABLE 1 Baseline characteristics of double lung allograft recipients and single lung allograft recipients recipients

	Double lung allograft recipients	Single lung allograft recipients	p-value
Case numbers			
Allografts	323 (68)	149 (32)	
Recipient characteristics			
Female sex	155 (48)	67 (45)	0.92#
Male sex	168 (52)	82 (55)	0.92#
Age at transplantation, y (median (IQR))	50 (40–57)	62 (59–64)	**<0.001**¶
Underlying disease			
COPD	67 (21)	60 (40)	**<0.001**+
ILD	158 (49)	77 (52)	
CF/NCFB	71 (22)	0	
Pulmonary hypertension	16 (5)	0	
Redo lung transplantation	7 (2)	8 (5)	
Others	4 (1)	4 (3)	
BLAD characteristics			
Normal baseline lung function	168 (52)	86 (58)	0.27#
BLAD	155 (48)	63 (42)	0.27#
Outcomes			
Death during follow-up	115 (36)	94 (63)	**<0.001**#
Retransplantation during follow-up	13 (4)	2 (1)	0.16#

Data are presented as n (%) unless stated otherwise. Bold type for p-values indicates statistical significance. IQR: interquartile range; ILD: interstitial lung disease; CF/NCFB: cystic fibrosis/non-cystic fibrosis bronchiectasis; BLAD: baseline lung allograft dysfunction. #: Fisher's exact test; ¶: Mann–Whitney U-test, +: Chi square test.

Lung function evolution and multistate modelling of BLAD and non-BLAD states in LTX recipients

After lung transplantation, patients were classified as being in an "indeterminate" state until two lung function tests at least 3 weeks apart were performed. If both FEV_1 % predicted and FVC % predicted were >80% predicted on these lung function tests in a DLTX recipient or >60% predicted in an SLTX recipient, the patient was assigned to the "normal baseline lung function" state. If these lung function requirements were not fulfilled, patients were assigned a "BLAD" status. From both BLAD and normal baseline lung function, transitions could occur towards the absorbing state death or retransplantation (figure 2). In principle, patients could also transition from indeterminate to death or retransplantation, but due to exclusion criteria for early mortality, this did not occur in our data. For better illustration, exemplary individual patient trajectories are illustrated in figure 2.

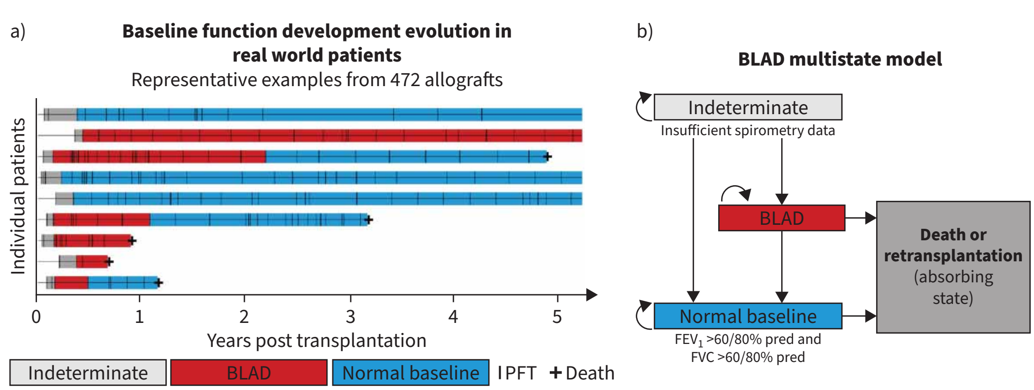

FIGURE 2 Lung function evolution and multistate modelling of baseline lung allograft dysfunction (BLAD) and non-BLAD states in lung transplantation (LTX) recipients. a) Graph depicting the evolution through different states in individual LTX recipients. b) Illustration of the BLAD multistate model with four defined states, "indeterminate", "BLAD", "normal baseline" and "death or retransplantation", as absorbing state. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; PFT: pulmonary function testing.

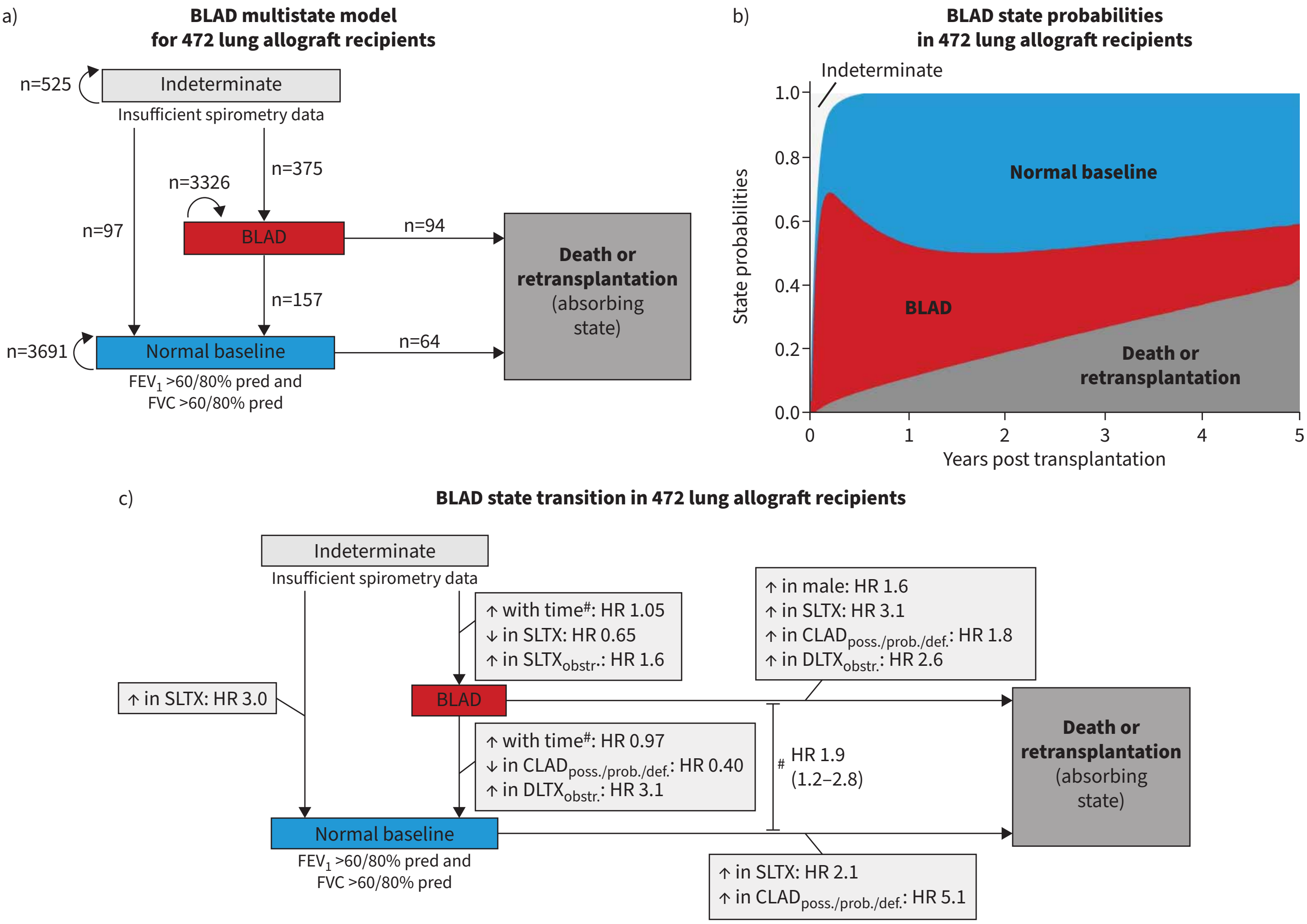

FIGURE 3 Baseline lung allograft dysfunction (BLAD) multistate modelling in lung transplantation (LTX) recipients. a) Multistate model with number of transitions between different states. b) Expected state probabilities over time depicted in the total cohort. c) Factors influencing transitions between states in LTX recipients. #: per time increment in weeks. FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; SLTX: single LTX; DLTX: double LTX; CLAD; chronic lung allograft dysfunction; HR: hazard ratio.

BLAD multistate modelling in LTX recipients

Altogether, 8327 transitions were recorded. The majority of transitions happened between the same states: 525 transitions from indeterminate to indeterminate, 3691 transitions from normal baseline lung function to normal baseline lung function, 3326 transitions from BLAD to BLAD. 97 transitions occurred directly from indeterminate to normal baseline lung function, while 375 transitions occurred from indeterminate to BLAD state. From BLAD 157 transitions occurred towards normal baseline function. 94 transitions occurred from BLAD towards death or retransplantation, whereas 64 transitions occurred from normal baseline function to death or retransplantation (figure 3a).

We modelled expected state probabilities over time, thereby illustrating state transitions over time in a cohort of LTX recipients (figure 3b). Interestingly, 119 of 157 transitions (76%) from BLAD to normal baseline lung function were observed within the first year, and 148 of 157 transitions (94%) from BLAD to normal baseline lung function were observed within the first 2 years. Only a minority of nine LTX recipients (6%) were observed to transition after 2 years after transplantation. Patients were observed to transition from BLAD to normal baseline lung function with a median of 196 days (IQR 119–358 days).

Next, we modelled hazard ratios for state transitions between different states (figure 3c). SLTX recipients had a higher probability to directly achieve normal baseline lung function after LTX (hazard ratio (HR) 3.0). Concordantly, they had a lower risk for undergoing a transition from indeterminate to BLAD (HR 0.65); however, when specifically regarding SLTX recipients with obstructive underlying disease, these had a higher risk of a transition towards BLAD (HR 1.6). Recipients with male sex (HR 1.6), suspected

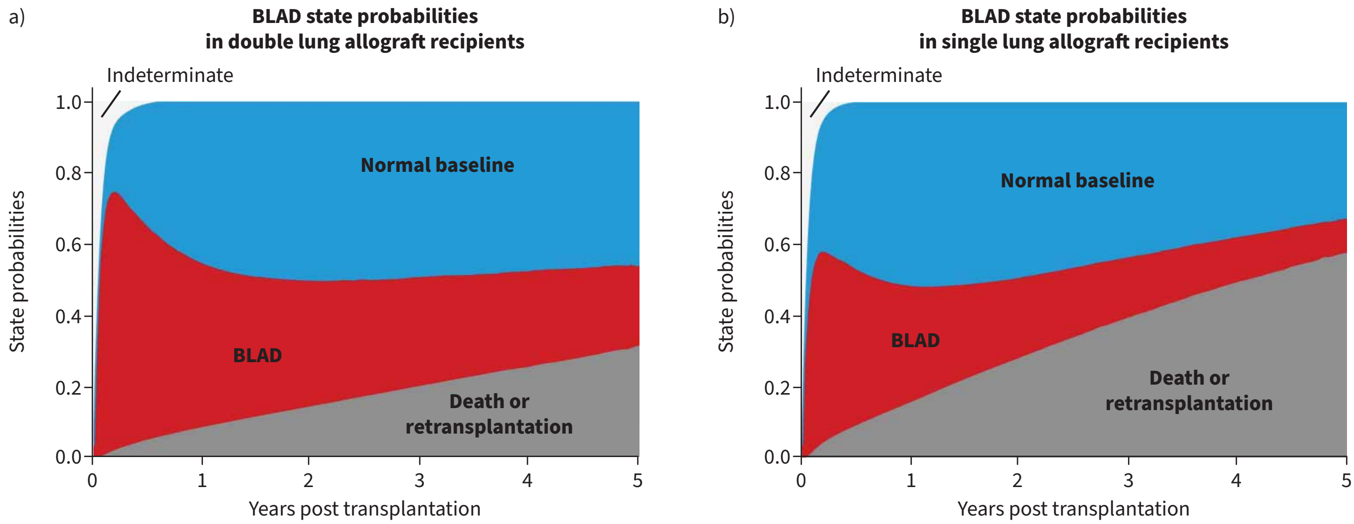

FIGURE 4 Expected state probabilities over time in a) double lung transplantation (DLTX) and b) single lung transplantation (SLTX) recipients. BLAD: baseline lung allograft dysfunction.

CLAD (*i.e.* possible, probable or definitive CLAD as per ISHLT) (HR 1.8), an underlying obstructive disease in DLTX (HR 2.6) or SLTX (HR 3.1) had significantly elevated risk for a transition from BLAD to death or retransplantation. Interestingly, DLTX recipients with underlying obstructive disease also had a significantly higher probability to undergo a transition from BLAD to normal baseline lung function (HR 3.1). Suspected CLAD reduced the probability to achieve normal baseline lung function (HR 0.4). SLTX (HR 2.1) and suspected CLAD (HR 5.1) were the strongest risk factors for death or retransplantation in LTX recipients with normal baseline lung function. LTX recipients with BLAD had a higher risk of a transition towards death or retransplantation compared to LTX recipients with normal baseline lung function (HR 1.9). As this was the first analysis of a cohort of DLTX and SLTX recipients regarding BLAD and cut-offs for SLTX recipients are currently debated, we performed another analysis with a cut-off of 80% for FEV_1% and FVC% for both DLTX and SLTX recipients (supplementary figure S1). In this model, SLTX recipients had a similar probability for a state transition from indeterminate to normal baseline lung function and from indeterminate to BLAD. Further, probability for achieving normal baseline lung function from BLAD was reduced (HR 0.56) compared to DLTX. A similar risk of death/retransplantation compared to DLTX was found once normal baseline lung function was achieved. We established further models that included transplant age (supplementary figure S2) as well as a model that included post-operative ICU stay (supplementary figure S3). Here, higher transplant age increased transition rates towards normal baseline lung function, but also increased mortality risk in patients residing in BLAD state. A longer ICU stay after transplantation was associated with a reduced transition rate to normal baseline lung function.

State probabilities over time in DLTX and SLTX recipients

Subsequently we modelled expected state probabilities over time separately for DLTX and SLTX recipients, respectively (figure 4). Compared to SLTX recipients, a higher share of DLTX recipients started in BLAD, but recovered and transitioned over time towards normal baseline lung function. SLTX recipients, however, rarely transitioned towards normal baseline lung function when started in BLAD, but rather transitioned towards death or retransplantation thereafter.

Discussion

Here, we characterised the evolution of normal baseline lung function in lung transplant recipients over time and took a close look at transitions between different clinical states and their respective risk factors using Markov multistate models.

Our approach using multistate models can also be regarded as a complementary statistical analysis to confirm previous BLAD studies [1–3]. Importantly, an increased mortality risk for BLAD in the total cohort of LTX recipients with a hazard ratio of ∼2 was found, which is in agreement with the findings of previous studies [1, 5].

Differences in lung function evolution between SLTX and DLTX recipients over time also affect the evolution of BLAD. In our longitudinal analysis of state probabilities, we observed that DLTX recipients frequently started in BLAD and transitioned towards a normal baseline lung function thereafter, even beyond the first year. In comparison, SLTX recipients rarely transitioned towards normal baseline lung function, and if they do, this primarily happened within the first 6 months. Evolution of BLAD states throughout different timepoints might impact future consensus definitions of BLAD as one of the key questions will be whether BLAD should be diagnosed at a certain timepoint or whether it should be regarded at any timepoint after LTX.

Furthermore, the transition rates of patients diverged not only according to the transplant type, but also according to their underlying disease. DLTX recipients with obstructive underlying disease had a higher rate of transitioning towards normal baseline lung function. However, DLTX recipients with obstructive underlying disease who did not transition to normal baseline lung function faced a markedly elevated mortality risk. Previous studies highlighted differences in characteristics of BLAD patients in DLTX and SLTX cohorts: in DLTX cohorts a majority of BLAD patients had underlying interstitial lung disease whereas in an SLTX cohort, BLAD patients had predominantly obstructive lung disease [1, 2, 4]. Importantly, SLTX recipients in BLAD state exhibited a significantly greater risk of death compared to their DLTX counterparts, as illustrated in figures 3c and 4.

Of note, this is the first analysis of BLAD in a combined cohort of DLTX and SLTX recipients. So far, this has not been done, as cut-offs for BLAD in SLTX recipients had not been defined. In a previous publication, we proposed a cut-off of 60% for FEV_1% and FVC% for BLAD in SLTX recipients that would equal the cut-off of DLTX recipients, based on the distribution of baseline FEV_1% and FVC% that SLTX recipients usually achieve [2]. However, it could be also argued that the expectation for a lung transplant should be to achieve normal lung function, and thus BLAD should be defined by an 80% cut-off irrespective of transplant type, well knowing that most SLTX recipients would then be classified as BLAD [16]. As there are too few studies on BLAD SLTX recipients, we found it useful to present both approaches here and believe that the lung transplant community needs further comprehensive analysis on BLAD cut-offs for SLTX recipients to establish a consensus definition.

CLAD and BLAD most likely represent two distinct entities, without a significant pathophysiological interplay [1, 5]. However, individual patients might still suffer from both entities at the same time. In a study by Darley *et al*. [4], around 30% of patients with CLAD also had BLAD, whereas the majority of CLAD patients had normal baseline lung function. In our study, patients who developed CLAD after being diagnosed with BLAD were most unlikely to return to normal baseline lung function (HR 0.4). Of note, in our model the covariate CLAD comprised not only "definite CLAD", but also "probable" and "possible CLAD" states, thus the hazard ratio of returning to normal baseline lung function from BLAD with CLAD was not zero. Further, for patients who achieved normal baseline lung function, diagnosis of CLAD still represented the highest hazard for death or retransplantation (HR 5.1), highlighting the unsolved challenges posed by CLAD in the field of LTX.

To date, the pathophysiology of BLAD remains unknown. BLAD-associated factors related to both recipient (age, BMI, underlying disease) and donor characteristics (donor smoking history, donor lung size) together with surrogates of early allograft injury (primary graft dysfunction, ventilation time, ICU time) suggest a heterogeneous condition [1–6]. Importantly, BLAD characteristics may differ according to transplant type and even underlying disease, as, for example, native lung hyperinflation is a specific risk factor for BLAD in SLTX recipients with underlying obstructive disease only [2]. The model used here illustrates that the underlying disease plays a different role in SDLTX *versus* DLTX. In SLTX, an obstructive disease (COPD) as transplant indication increases the risk of BLAD, in part mediated by native lung hyperinflation, while in DLTX, patients with underlying obstructive disease may develop better lung function. Higher transplant age was associated with an increased probability of achieving normal baseline lung function from indeterminate or BLAD states. This finding seems counterintuitive, and the reasons for it remain speculative, potentially involving confounding factors such as the impact of underlying disease or lower % predicted values in older patients. However, similar results have been observed in other cohorts [4]. Moving forward, mechanistic studies focusing on biomarkers in patient samples will be the next key step to deepen our understanding of BLAD and to guide the development of future therapeutic strategies. Novel biological findings could be included in MSM to dissect contributing factors according to underlying disease or transplant procedure.

Advantages of the current study are the use of multistate models in a large dataset, representing both DLTX as well as SLTX recipients, a large number of analysed PFTs (>10 000) for a detailed modelling of lung function trajectories and a close follow-up of these LTX recipients. However, this study also withholds several limitations: this was a single-centre, retrospective study and due its retrospective nature, data on primary graft dysfunction, an important risk factor for BLAD, were not available in sufficient granularity to include in the analysis.

To conclude, our data corroborate previous findings on the important role of BLAD in the follow-up of LTX recipients. It highlights BLAD as a dynamic rather than a static feature, with frequent transitions to normal lung function in the context of DLTX. The application of multistate models represents a novel approach in lung transplantation research, which could be extended to other forms of lung allograft dysfunction.

Data availability: The data analysed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Provenance: Submitted article, peer reviewed.

Ethics statement: This study was conducted in accordance with ethical guidelines and approved by the Ethics Committee of Ludwig-Maximilians-University of Munich (approval #21-0020). As retrospective analysis, it did not involve any direct intervention with patients. The study adhered to the principles of the Declaration of Helsinki, protecting the rights and well-being of participants.

Author contributions: Conception of the study: M. Gerckens, N. Kneidinger and C. Mümmler. Data acquisition and patient treatment: M. Gerckens, A. Richard, P. Arnold, T. Veit, J. Barton, J. Götschke, K. Milger, T. Kauke, C. Schneider, S. Michel, M. Irlbeck, A.Ö. Yildirim, J. Behr, N. Kneidinger and C. Mümmler. Data analysis and interpretation: M. Gerckens, A. Richard, M. Luecken, N. Kneidinger and C. Mümmler. Manuscript draft: M. Gerckens, A. Richard, P. Arnold, T. Veit, J. Barton, J. Götschke, K. Milger, T. Kauke, C. Schneider, S. Michel, M. Irlbeck, M. Luecken, A.Ö. Yildirim, J. Behr, N. Kneidinger and C. Mümmler.

Conflict of interest: The authors of this manuscript have no conflicts of interest to disclose.

References

1 Liu J, Jackson K, Weinkauf J, *et al.* Baseline lung allograft dysfunction is associated with impaired survival after double-lung transplantation. *J Heart Lung Transplant* 2018; 37: 895–902.

2 Gerckens M, Mümmler C, Richard A, *et al.* Characterization of baseline lung allograft dysfunction in single lung transplant recipients. *Transplantation* 2025; 109: e213–e221.

3 Li D, Weinkauf J, Kapasi A, *et al.* Baseline lung allograft dysfunction in primary graft dysfunction survivors after lung transplantation. *Respir Med* 2021; 188: 106617.

4 Darley DR, Nilsen K, Vazirani J, *et al.* Airway oscillometry parameters in baseline lung allograft dysfunction: associations from a multicenter study. *J Heart Lung Transplant* 2023; 42: 767–777.

5 Keller MB, Sun J, Alnababteh M, *et al.* Baseline lung allograft dysfunction after bilateral lung transplantation is associated with an increased risk of death: results from a multicenter cohort study. *Transplant Direct* 2024; 10: e1669.

6 Yamaguchi M, Kawashima M, Muraoka T, *et al.* Baseline lung allograft dysfunction after bilateral deceased-donor lung transplantation: a single-center experience in Japan. *Respir Investig* 2024; 62: 838–843.

7 Belloli EA, Wang X, Murray S, *et al.* Longitudinal forced vital capacity monitoring as a prognostic adjunct after lung transplantation. *Am J Respir Crit Care Med* 2015; 192: 209–218.

8 Le-Rademacher JG, Therneau TM, Ou F-S. The utility of multistate models: a flexible framework for time-to-event data. *Curr Epidemiol Rep* 2022; 9: 183–189.

9 Schwab S, Elmer A, Sidler D, *et al.* Selection bias in reporting of median waiting times in organ transplantation. *JAMA Netw Open* 2024; 7: e2432415.

10 Ursino M, Dupuis C, Buetti N, *et al.* Multistate modeling of COVID-19 patients using a large multicentric prospective cohort of critically ill patients. *J Clin Med* 2021; 10: 544.

11 Singer LG, Chowdhury NA, Faughnan ME, *et al.* Effects of recipient age and diagnosis on health-related quality-of-life benefit of lung transplantation. *Am J Respir Crit Care Med* 2015; 192: 965–973.

12 Kneidinger N, Milger K, Janitza S, *et al.* Lung volumes predict survival in patients with chronic lung allograft dysfunction. *Eur Respir J* 2017; 49: 1601315.

13 Graham BL, Steenbruggen I, Miller MR, *et al.* Standardization of spirometry 2019 update. An official American Thoracic Society and European Respiratory Society technical statement. *Am J Respir Crit Care Med* 2019; 200: e70–e88.

14 Stanojevic S, Kaminsky DA, Miller MR, *et al.* ERS/ATS technical standard on interpretive strategies for routine lung function tests. *Eur Respir J* 2022; 60: 2101499.

15 Verleden GM, Glanville AR, Lease ED, *et al.* Chronic lung allograft dysfunction: definition, diagnostic criteria, and approaches to treatment – A consensus report from the Pulmonary Council of the ISHLT. *J Heart Lung Transplant* 2019; 38: 493–503.
16 Halloran K. Finding baseline with one new lung. *Transplantation* 2025; 109: 586–587.