



# Computed Tomography-Based Body Composition is Related to Perioperative Morbidity in Older Lung Transplant Recipients

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## Abstract

**Background** In older patients, a limited physical reserve is considered a contraindication for lung transplantation (LTx). Herein, we aimed to establish a computed tomography (CT)-based quantification of physical reserve in older patients scheduled for transplantation.

**Methods** This retrospective study included patients older than 60 years who received LTx. Semiautomatic measurements of the mediastinal fat area and the dorsal muscle group area in pretransplantation CT scans were performed, and normalized data were correlated with clinical parameters.

**Results** Patients ( $n = 108$ ) were assigned into three groups (Muscle<sup>high</sup>fat<sup>low</sup> [ $n = 25$ ], Muscle<sup>low</sup>fat<sup>high</sup> [ $n = 24$ ], and other combinations [ $n = 59$ ]). The Muscle<sup>low</sup>fat<sup>high</sup> group had a significantly increased risk of wound infections ( $p = 0.002$ ) and tracheostomy ( $p = 0.001$ ) compared with Muscle<sup>high</sup>fat<sup>low</sup> patients. The median length of intensive care unit stay (25 vs. 3.5 days;  $p = 0.002$ ) and the median length of hospital stay (44 vs. 22.5 days;  $p = 0.013$ ) post-LTx were significantly prolonged in the Muscle<sup>low</sup>fat<sup>high</sup> group. Significantly more patients in this group had a prolonged ventilation time (11 vs. 0;  $p < 0.001$ ).

**Conclusion** Body composition parameters determined in pretransplant chest CT scans in older LTx candidates might aid in identifying high-risk patients with a worse perioperative outcome after LTx.

## Keywords

- ▶ lung transplantation
- ▶ body composition
- ▶ biological age
- ▶ frailty
- ▶ older patients

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## Introduction

Advanced chronological age (>65 years) is associated with an inferior outcome after lung transplantation (LTx),<sup>1</sup> requiring a thorough physical evaluation prior to LTx. Moreover, extreme frailty is considered an absolute contraindication for LTx due to the exceedingly high perioperative mortality.<sup>2</sup> Simultaneously, the age of LTx recipients is continuously rising, mirroring the demographic changes in Western societies.<sup>3</sup> From 2000 to 2012, the proportion of LTx recipients  $\geq 60$  years increased from 20% to more than 40% and of LTx recipients  $\geq 65$  years from 2.6 to 17% from 2004 to 2016.<sup>4,5</sup> Considering the disparity between chronological age and biological age, especially in the increasing group of older LTx candidates, reliable tools to quantify frailty in LTx candidates are needed.<sup>6</sup> Various clinical scores intend to describe a limited physiological reserve (e.g., the clinical frailty scale [CFS] and modified frailty index), but these are insufficient in the evaluation process for LTx candidates with end-stage lung disease.<sup>7–10</sup>

CT-based morphometric variables, such as the muscle and fat content, might be a useful tool with which to guide the selection of appropriate LTx candidates.<sup>11</sup>

Data on the objective measurement of biological age in a homogenous cohort of >60 years LTx recipients are lacking. In this study, we established an objective, CT-based quantification of body composition in a well-defined cohort of older

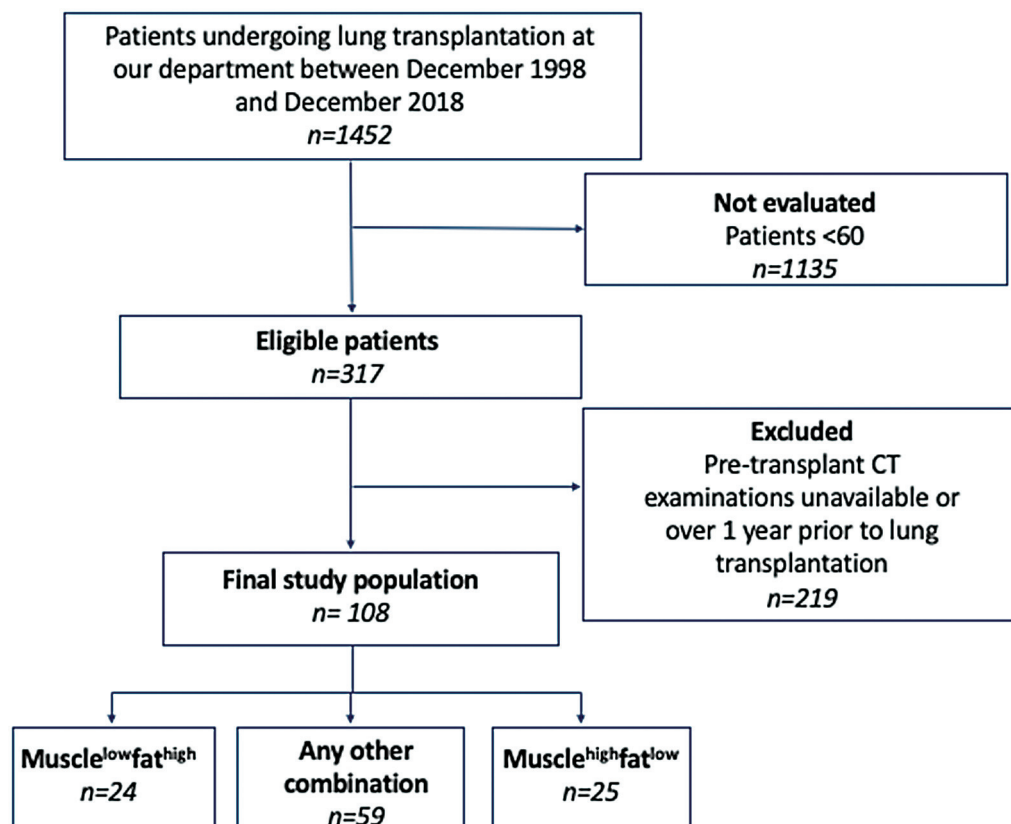
lung transplant recipients and evaluated its association with the clinical outcome after LTx.

## Materials and Methods

### Study Design

Patients  $\geq 60$  years who received lung transplantation at the Department of Thoracic Surgery at the General Hospital of Vienna from December 1998 to December 2018 were retrospectively included in this study. Inclusion criteria were age  $\geq 60$  years at the time of transplant and availability of a pretransplant CT within 1 month to 1 year before LTx. Patients were excluded if<sup>1</sup> pretransplant CT examinations were unavailable,<sup>2</sup> they received CT examinations more than 1 year or shorter than 1 month before LTx, and<sup>3</sup> CT examinations had an insufficient quality (e.g., incomplete thorax). In patients with multiple CT examinations, the last CT scan within the indicated range was used (**Fig. 1**).

Patients' clinical and demographic data including age, body mass index (BMI), sex, indication, pretransplant intensive care unit (ICU) stay (days), length of postoperative ventilation (hours), use of pre- and postoperative extracorporeal membrane oxygenation (ECMO), posttransplant ICU stay (days), complications (airway complications, renal replacement therapy, revision surgery, delirium, and wound infections), primary graft dysfunction (PGD) 72 hours post-LTx, FEV1, pretransplant corticosteroid therapy, national high-urgency status, and the lung allocation score (LAS; range 0–100) at the



**Fig. 1** Flowchart illustrating inclusion and exclusion criteria for the final study cohort ( $n = 108$  patients).

time of LTx were retrieved from the patient records. Patients with LAS scores >49 were considered “high urgent.” The pre-LAS high-urgency status was provided by the transplant center. Based on the clinical information, two frailty scales were determined: the nine-point CFS comprising nine levels of physical fitness from 1 (very fit) to 9 (terminally ill with a life expectancy <6 months; ▶ **Supplementary Table S1**, available in the online version); and the modified frailty index comprising 11 components including patients' medical history besides physical activity (▶ **Supplementary Table S2**, available in the online version).<sup>8,12</sup>

The Ethics Committee of the Vienna approved this study (EK 2283/2018) and waived the need for written informed consent.

### Primary Graft Dysfunction Scoring

PGD scores were calculated for the 72 hours post-LTx time point based on International Society of Heart and Lung Transplantation (ISHLT) guidelines using the partial pressure of arterial oxygen/fraction of inspired oxygen ratios and chest radiograph interpretation. For those patients who were on posttransplantation ECMO, the PGD score was deemed ungradable if the chest radiographs were clear or classified as PGD 3 in the presence of bilateral infiltrations. Patients who had been extubated were not assigned a PGD score.<sup>13,14</sup>

### Evaluation of Chest Computed Tomography Scans

All CT examinations were performed in deep, sustained inspiration over the whole thorax in the supine position. Each CT examination scan was reconstructed with thin slices in a soft-tissue (mean 60 Hounsfield units [HUs]; width 360 HU) window setting. The acquired datasets were exported to the Digital Imaging Communications in Medicine viewer (OsiriX, version 10.14, Pixmeo SARL, Bernex, Switzerland), to measure the cross-sectional mediastinal fat area (MFA) and total muscle area (TMA) of the dorsal muscle group (DMG).<sup>15</sup> For all measurements, axial plane reconstructions were used. Semiautomated measurements of the MFA were performed using attenuation thresholds of −190 to −30 HUs at the level of the carina (first slice depicting the carina).<sup>16–18</sup> We performed semiautomated measurements of the DMG area using attenuation thresholds of −29 to 150 HUs at the level of the 12th thoracic vertebral body (T12).<sup>17</sup> The boundaries of the DMG area were defined by the spine, the ribs, and the lateral edges of the *M. erector spinae*. If necessary, tissue borders were corrected manually.

### Adjustments and Stratification

To assess the skeletal muscle indices (SMI) of the DMG at the 12th thoracic vertebral body and the mediastinal fat index (MFI) at the level of the carina, TMA and MFA were normalized by height, as previously described<sup>15,19</sup>:

$$SMI = \frac{TMA}{m^2} \quad MFI = \frac{MFA}{m^2}$$

To normalize the LTx recipients' diversity, measurements were standardized by gender. The height and gender-corrected median was used to dichotomize the fat and muscle

area measurements (low versus high). Patients were assigned to three body composition groups according to the dichotomized parameters: patients with mediastinal fat values higher than the median and DMG values lower than the median were assigned to the Muscle<sup>low</sup>fat<sup>high</sup> group ( $n = 24$ ), the Muscle<sup>high</sup>fat<sup>low</sup> group contained patients with DMG values higher than the median and mediastinal fat values lower than the median ( $n = 25$ ). Patients in the third group had any other combination ( $n = 59$ ).

Patients were assigned into three groups based on their BMI: underweight (<18.5 kg/m<sup>2</sup>); normal weight (>18.5–<25 kg/m<sup>2</sup>); or overweight (>25 kg/m<sup>2</sup>).<sup>20,21</sup>

### Statistical Analysis

All statistical tests were performed using the SPSS Statistics for Windows version 24.0 (IBM, Armonk, NY, United States) and GraphPad Prism (La Jolla, CA, United States). Continuous variables including the MFI and DMG index were tested for normal distribution using the Kolmogorov–Smirnov test. Continuous variables are described using the median (interquartile range). Categorical variables are described using absolute frequencies and percentages. To compare the three groups, Fisher–Freeman–Halton tests were calculated for categorical variables and (due to heterogeneous variances) Kruskal–Wallis tests for metric data. Pearson correlations were used to assess the correlation between two metric variables. Survival outcomes were calculated using the Kaplan–Meier method. The log-rank test was used to compare the survival of the groups. Multivariable Cox-regression was performed to evaluate the influence of clinical variables on overall survival (OS). To assess the interreader variability, two-way random intraclass correlation coefficients for absolute agreement were used. Two-sided  $p$ -values <0.05 were considered statistically significant.

## Results

### Patients' Demographics

In total, 108 patients were included in the final study cohort: 103 (95%) patients received a bilateral LTx and 5 (5%) patients a single LTx. Of the included patients, 81 (75%) were male and 27 (25%) were female. The mean age was  $63.8 \pm 2.7$  years. The two most frequent diagnoses were chronic obstructive pulmonary disease (51.9%) and lung fibrosis (40.7%). The mean time from the CT examination to LTx was  $175.3 \pm 96.4$  days. Detailed patient baseline characteristics, frequency of complications, hospital stay, ICU stay, and ventilation duration are provided in ▶ **Tables 1** and **2**. Overall, male lung transplant recipients showed higher values for both body composition parameters (▶ **Supplementary Table S3**, available in the online version).

### Interreader Reliability

The MFA and DMG area measurements (▶ **Fig. 2**) were performed independently by two independent readers. To assess the inter-reader reliability, 20 patients were randomly chosen. The intra class correlation coefficient (two-way random effects for absolute agreement) for MFA was 0.893 and for DMG 0.832.

**Table 1** Patient characteristics

Characteristic	Total study cohort ( <i>n</i> = 108)	
	<i>n</i>	%
Age at Tx (mean ± SD)	63.8 ± 2.7	
Sex		
Male	81	75.0
Female	27	25
Diagnosis		
COPD	56	51.9
Fibrosis	44	40.7
PAH	4	3.7
Alpha1 antitrypsin deficiency	2	1.9
Sarcoidosis	1	0.9
CTEPH	1	0.9
Complications and clinical variables		
Wound infection/VAC treatment	14	13
Revision surgery	16	14.8
Reintubation	15	13.9
Thromboembolic event	4	3.7
PRES	2	1.9
PEG feeding tube	3	2.6
Hemofiltration/Dialysis	16	14.8
Delirium	23	21.3
Tracheostomy	26	24.1
ECMO pre-Tx	9	8.3
ICU pre-Tx	12	11.1
Prolonged ECMO	7	6.5
Readmission ICU	6	5.6
HU-status	23	21.3
Pre-Tx corticosteroid therapy	49	45.4
Prolonged ventilation (>24 h)	79 ( <i>n</i> = 106)	74.5
PGD at 72 h post-Tx	6	5.5
Pre-Tx FEV1% (median; IQR)	34.3 (31.1)	
Length of ICU stay after Tx (median, IQR in days)	8 (15)	
Length of hospital stay after Tx (median, IQR in days)	27 (23.5)	
Duration ventilation (median, IQR in hours)	46 (92)	
Lung allocation score (median, IQR, <i>n</i> = 70)	40.3 (13.8)	
Modified frailty index (median, IQR, <i>n</i> = 84)	2 (1)	
Clinical frailty scale (median, IQR, <i>n</i> = 83)	6 (2)	

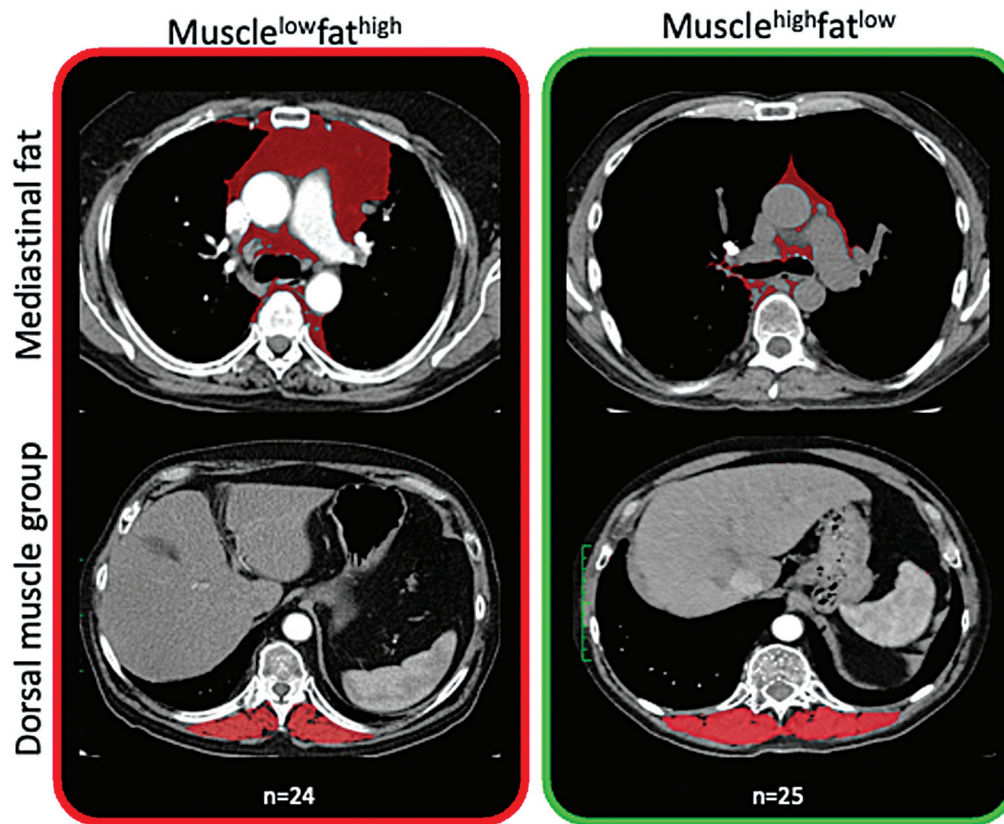
Abbreviations: COPD, chronic obstructive pulmonary disease; CTEPH, chronic thromboembolic pulmonary hypertension; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IQR, interquartile range; PAH, pulmonary arterial hypertension; PEG, percutaneous endoscopic gastrostomy; PRES, posterior reversible encephalopathy syndrome; PGD, primary graft dysfunction; Tx, transplantation; VAC, vacuum-assisted closure therapy.

**Table 2** Association of diagnosis, complications, and clinical variables with body composition types

	Muscle <sup>low</sup> fat <sup>high</sup> n = 24 (22)	Any other combination n = 59 (55)	Muscle <sup>high</sup> fat <sup>low</sup> n = 25 (23)	p-Value
Age at Tx (mean ± SD)	64.1 ± 2.8	63.7 ± 2.7	63.6 ± 2.6	0.823
Sex (f/m)	6/18	15/44	6/19	1.000
<b>Diagnosis</b>				
COPD (n;%)	6 (25)	35 (59.3)	15 (60)	0.026
Fibrosis (n;%)	15 (62.5)	20 (33.9)	9 (36)	
PAH (n;%)	3 (12.5)	1 (1.7)	0	
CTEPH (n;%)	0	1 (1.7)	0	
Sarcoidosis (n;%)	0	1 (1.7)	0	
Alpha1 antitrypsin deficiency (n;%)	0	1 (1.7)	0	
<b>Complications</b>				
Revision surgery				
VAC treatment (n;%)	8 (33.3)	6 (10.2)	0	0.002
Hemothorax (n;%)	4 (16.7)	10 (16.9)	2 (8)	0.628
Re-intubation (n;%)	4 (16.7)	10 (16.9)	1 (4)	0.315
Thromboembolic event (n;%)	3 (12.5)	1 (1.7)	0	0.062
PRES (n;%)	1 (4.2)	0	1 (4)	0.204
PEG feeding tube (n;%)	1 (4.2)	2 (3.4)	0	0.790
Hemofiltration/Dialysis (n;%)	6 (25)	8 (13.6)	2 (8)	0.274
Delirium (n;%)	9 (37.5)	11 (18.6)	3 (12)	0.079
Acute rejection (n;%)	3 (12.5)	3 (5.1)	2 (8)	0.420
Tracheostomy (n;%)	13 (54.2)	9 (15.3)	4 (16)	0.001
Prolonged ventilation (>24 h; n; %)	11 (45.8)	6 (10.2)	0	<0.001
PGD at 72 h post-Tx (n;%)	2 (8.3)	3 (5.1)	1 (4)	0.737
<b>Clinical variables</b>				
ECMO pre-Tx (n;%)	5 (20.1)	4 (6.8)	0	0.022
Prolonged ECMO (n;%)	3 (12.5)	3 (5.1)	1 (4)	0.501
Readmission ICU (n;%)	4 (16.7)	2 (3.4)	0	0.037
ICU pre-Tx (n;%)	6 (25)	6 (10.2)	0	0.017
In-hospital death (n;%)	3 (12)	6 (10.2)	3 (12)	0.922
BMI (mean ± SD)	24.6 ± 3.1	23.6 ± 3.7	22.8 ± 3.6	0.152
In-hospital stay (median; IQR in days)	44 (61)	27.5 (18.8)	22.5 (11.3)	0.013
30 d mortality (n, %)	1 (4.2)	2 (3.4)	3 (12)	0.279
ICU stay (median; IQR in days)	25 (42)	7.5 (9.5)	3.5 (5.8)	0.002
Pre-Tx corticosteroid therapy (n;%)	11 (45.8)	26 (44)	12 (48)	0.901
Pre-Tx FEV1% (median; IQR)	40.5 (20.2)	35 (41.4)	25.6 (35.7)	0.414
HU- status (n; %)	12 (50)	9 (16.4)	2 (8.7)	0.001
Lung allocation score (median; IQR)	53.3 (23.4) (n = 17)	38.8 (10.2) (n = 39)	36 (6.9) (n = 14)	0.014
Modified frailty index (median; IQR)	3 (2) (n = 17)	2.5 (2) (n = 47)	2 (2) (n = 20)	0.378
Clinical frailty scale (median; IQR)	7 (1) (n = 17)	6 (1) (n = 46)	4.5 (2) (n = 20)	0.017

Abbreviations: COPD, chronic obstructive pulmonary disease; CTEPH, chronic thromboembolic pulmonary hypertension; ECMO, extracorporeal membrane oxygenation; FEV1%, forced expiratory volume; HU, high urgency; ICU, intensive care unit; IQR, interquartile range; PAH, pulmonary arterial hypertension; PEG, percutaneous endoscopic gastrostomy; PGD, primary graft dysfunction; PRES, posterior reversible encephalopathy syndrome; Tx, transplantation; VAC, vacuum-assisted closure-therapy.





**Fig. 2** Representative measurements of patients in the Muscle<sup>lowfat</sup><sup>high</sup> and Muscle<sup>highfat</sup><sup>low</sup> groups based on the measurement of cross-sectional muscle and MFAs on chest CT scans.

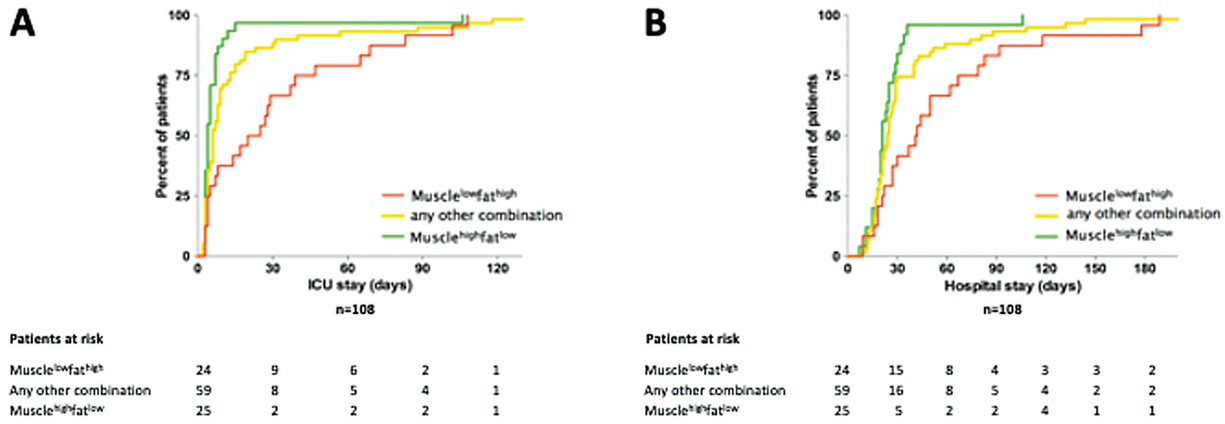
### Association of Body Composition with Clinical Variables

During the wait for LTx, significantly more patients in the Muscle<sup>lowfat</sup><sup>high</sup> group compared with the Muscle<sup>highfat</sup><sup>low</sup> group deteriorated and were bridged to transplantation using ECMO (5 vs. 0 patients;  $p=0.022$ ) or were admitted to ICU at the time of LTx (6 vs. 0 patients;  $p=0.017$ ). Compared with patients in the Muscle<sup>highfat</sup><sup>low</sup> group, patients in the Muscle<sup>lowfat</sup><sup>high</sup> group showed a significantly increased risk for wound infections requiring vacuum-assisted closure therapy (8 vs. 0 patients,  $p=0.002$ ) or tracheostomy (13 vs. 4 patients;  $p=0.001$ ). The Muscle<sup>lowfat</sup><sup>high</sup> phenotype was associated with re-admission to ICU after LTx (4 vs. 0 patients;  $p=0.037$ ). Significantly more patients in the Muscle<sup>lowfat</sup><sup>high</sup> group compared with the Muscle<sup>highfat</sup><sup>low</sup> group had a prolonged ventilation time (>24 hours; 11 vs. 0;  $p<0.001$ ). Moreover, the stay in the ICU (25 vs. 3.5 days;  $p=0.002$ ) and the stay in the hospital (44 vs. 22.5 days;  $p=0.013$ ) were significantly longer in Muscle<sup>lowfat</sup><sup>high</sup> patients, compared with Muscle<sup>highfat</sup><sup>low</sup> patients (→Fig. 3). Patients in the Muscle<sup>lowfat</sup><sup>high</sup> group had a significantly higher LAS at the time of LTx than patients in the Muscle<sup>highfat</sup><sup>low</sup> group (53.3 vs. 36;  $p=0.014$ ) and, therefore, were listed significantly more often as high-urgency patients (12 vs. 2 patients;  $p=0.001$ ). Furthermore, patients in the Muscle<sup>lowfat</sup><sup>high</sup> group had a significantly higher mean nine-point CFS score than patients in the Muscle<sup>highfat</sup><sup>low</sup> group

(7 vs. 4.5;  $p=0.017$ ), whereas the modified frailty index did not differ between groups ( $p=0.378$ ). A detailed overview of the association of clinical variables with body composition types is provided in →Table 2. →Supplementary Tables S4 and S5 (available in the online version) show the association of clinical variables, the MFI and DMG index. We did not find any significant relationship between the BMI and clinical variables, except for diagnosis ( $p<0.001$ ), LAS ( $p=0.012$ ), and FEV1 ( $<0.001$ ) (→Supplementary Tables S6 and S7, available in the online version).

### Survival after Transplantation

Median OS in the cohort was 103 months (95% confidence interval [CI], 40.5 to 165 months). The Kaplan–Meier survival analysis revealed no difference in the OS between the different body composition groups (log-rank test,  $p=0.397$ ; →Supplementary Fig. S1, available in the online version). Furthermore, the BMI had no impact on survival (log-rank test,  $p=0.687$ ). On multivariable Cox-regression, tracheostomy (HR [95% CI], 3.26 [1.39–7.68],  $p=0.007$ ), acute rejection (HR [95% CI], 4.26 [1.37–13.32],  $p=0.013$ ), type of transplantation, bilateral LTx versus single LTx (HR [95% CI], 0.12 [0.02–0.58]),  $p=0.008$ ), and pre-LTx FEV1 (HR [95% CI], 1.02 [1.01–1.03]) were independent predictors of the OS. None of the other post-LTx complications had any significant influence on the OS (→Supplementary Tables S8 and S9, available in the online version).



**Fig. 3** Duration of ICU (A) and hospital stay (B) depending on body composition types. Patients in the Muscle<sup>low</sup>fat<sup>high</sup> group had a significantly prolonged ICU and hospital stay compared with patients in the Muscle<sup>high</sup>fat<sup>low</sup> group ( $p = 0.002$  and  $p = 0.013$ ). 33.3% of patients in the Muscle<sup>low</sup>fat<sup>high</sup> group and 80% of the patients in the Muscle<sup>high</sup>fat<sup>low</sup> were dismissed from the ICU within 1 week after LTx. 42% of patients in the Muscle<sup>low</sup>fat<sup>high</sup> group and 84% of the patients in the Muscle<sup>high</sup>fat<sup>low</sup> were dismissed from the hospital within 1 month after LTx.

**Comment**

Here, we demonstrated that patients with a specific body composition type, characterized by low muscle mass and high mediastinal fat content, experienced more complications after LTx. Moreover, the prolonged postoperative course is reflected by a significantly increased duration of mechanical ventilation and ICU and hospital stay.

A variety of tools for the assessment of the physical capacity (e.g., grip strength, six-minute-walk test [6MWT]) can be used in the evaluation process for post-LTx.<sup>2,22</sup> However, the 6MWT does not provide accurate information about the reason for decreased physical activity and can be easily influenced by daily constitution and cardiopulmonary and musculoskeletal limitations.<sup>23</sup> Furthermore, it cannot be used to assess immobilized patients referred for possible transplantation, for example, patients at the end stage of their chronic disease who are not able to easily perform physical activities and those bridged to LTx by mechanical ventilation or ECMO.

Besides, LTx recipients can also be stratified according to their BMI. Although exceedingly high or low BMI values are considered a contraindication for LTx, the BMI does not properly reflect body composition as it does not discriminate between muscle and fat.<sup>2,24,25</sup> Also, in our study, the pre-LTx BMI did not correlate with either the morphometric phenotype or the clinical outcome after LTx. Furthermore, we observed a significant association of the CT-based phenotype with only one of the two available frailty scores.

In contrast, a chest CT scan provides easily available, objective information about the current muscle and fat composition even of immobilized patients, and therefore might serve as an adjunct tool in LTx candidate selection.<sup>26</sup> Unlike our current study on older patients, previous publications have assessed the prognostic impact of CT-based morphometric variables on the post-LTx outcome mostly in patients of heterogeneous age groups.<sup>16,24,26</sup>

The herein described stratification based on the muscle/fat phenotype allowed the identification of patients

who are at high risk of rapid deterioration while on the waiting list for transplantation. Significantly more patients in the Muscle<sup>low</sup>fat<sup>high</sup> group required a bridge to transplant on ECMO ( $p = 0.022$ ) or were admitted to ICU before LTx ( $p = 0.017$ ). Also, during the postoperative course, patients with the Muscle<sup>low</sup>fat<sup>high</sup> phenotype had significantly prolonged weaning from the respirator ( $p < 0.001$ ), reflecting the reduced muscular reserve in these patients. Using the lean psoas area to identify frail LTx recipients, an inverse association with dependency on tracheostomy (odds ratio: 0.41 [0.17–1.00];  $p = 0.035$ ) and mechanical ventilation ( $p = 0.0031$ ), ICU stay ( $p = 0.018$ ), and hospital stay ( $p = 0.005$ ) was previously demonstrated.<sup>24</sup> Together with our results, this demonstrates the crucial role of well-preserved core muscles for LTx in elderly. Furthermore, a positive correlation between the mediastinal fat volume and length of hospital stay ( $p = 0.002$ ) was previously found but could not demonstrate an association between the DMG and postoperative complications.<sup>26</sup>

Our data suggest that maintaining fitness, reflected by a beneficial body composition before LTx, could significantly decrease postoperative morbidity, thus sparing medical resources at transplant centers. In agreement, it was previously found that the pretransplant physical fitness correlated inversely with the length of hospital stay after LTx ( $p = 0.003$ ).<sup>27</sup>

Patients in the Muscle<sup>low</sup>fat<sup>high</sup> group required prolonged ventilation, ICU and in-hospital stays but still had a good long-term outcome (median survival: 71.5 months), which did not differ from the other subgroups. Similar to our results, no impact of the lean psoas area on 1-year survival was previously found.<sup>24</sup> In contrast, others demonstrated a significantly longer median survival in LTx recipients with interstitial pulmonary fibrosis and low anterior mediastinal fat (AMF) compared with patients with high AMF (8.5 vs. 2.5 years;  $p < 0.001$ ).<sup>28</sup>

This study has several limitations. Ideally, CT should be performed closest to the transplantation date as these are most reliably associated with patients' pretransplant

condition. However, the unpredictability of transplantations makes the implementation of CT scans prior transplantation rather difficult. Nevertheless, to minimize this possible confounder, we excluded patients with CT scans performed more than 1 year before transplantation. Another limitation of this study is that the underlying diagnosis, a rapid deterioration before the transplantation, a prolonged postoperative course, and morphometric variables are highly associated with each other. However, much larger sample sizes are required to address this potential multicollinearity. The relatively small sample size did not allow to further elaborate to which degree the morphometric characteristics in contrast to correlating clinical variables such as pretransplant ICU stay, or diagnosis contribute to the diminished clinical outcome. Beyond the herein used muscle area, the muscle density (i.e., composition of fat, connective tissue and muscular fibers within the muscle area) might reflect muscular fitness even more reliably. However, this would require standardized CT protocols under the same conditions, including the use of intravenous contrast agent, which would have required a prospective collection of data instead. Last, the evaluation process for lung transplant candidates as well as the clinical management of these patients might vary over time as the inclusion period was overlooking two decades.

In summary, we demonstrate in a well-defined cohort of older LTx recipients that a quantitative measurement of morphometric parameters using chest CT scans can be used to identify patients at higher risk of experiencing postoperative complications. This emphasizes the crucial role of preserving the physical fitness and metabolic reserve of older patients prior to LTx.

#### Abbreviations

6MWT, six-minute-walk test  
 AMF, anterior mediastinal fat  
 BMI, body mass index  
 CA, chronological age  
 COPD, chronic obstructive pulmonary disease  
 CT, computed tomography  
 DMG, dorsal muscle group  
 ECMO, extracorporeal membrane oxygenation  
 FEV1, forced expiratory volume  
 HU, Hounsfield units  
 ICU, intensive care unit  
 LAS, lung allocation score  
 LTx, lung transplantation  
 MFA, mediastinal fat area  
 PGD, primary graft dysfunction  
 SMI, skeletal muscle indices  
 TMA, total muscle area

#### Conflict of Interest

None declared.

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