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Muscle Composition and Gas-Transfer Impairment in Idiopathic Pulmonary Fibrosis: A CT-Based Study

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Abstract

Background

Muscle abnormalities and myosteatosis are increasingly recognized as important extrapulmonary features in patients with idiopathic pulmonary fibrosis (IPF). However, their relationship with pulmonary function is not fully understood. This study aimed to investigate the association between CT-derived myosteatosis and pulmonary function, including vital capacity and gas-transfer impairment, in patients with IPF.

Methods

Eighty-five patients with multidisciplinary diagnoses of IPF were retrospectively evaluated. Myosteatosis Index, a relative muscle-associated adiposity measure, and erector spinae muscle index (ESMI), a muscle-quantity measure, were derived from chest CT. The primary analysis related baseline Myosteatosis Index to diffusing capacity for carbon monoxide (DLCO). Linear models adjusted for age, sex, interstitial lung disease extent, emphysema, body mass index (BMI), and smoking exposure. Baseline ESMI and follow-up forced vital capacity (FVC) were evaluated separately. Exploratory analyses examined both indices against baseline and follow-up DLCO and FVC and compared their associations with BMI.

Results

Seventy-eight patients were included in the primary analysis. Median age was 68 years and median DLCO was 51.4% predicted. Each 1-standard-deviation higher Myosteatosis Index was associated with 4.99 percentage points lower DLCO after multivariable adjustment (95% confidence interval − 9.30 to − 0.69; p = 0.024). This association remained consistent in sensitivity analyses. Adding the index to a model containing BMI and the other covariates increased explained DLCO variance from 16.1% to 23.0%. Baseline ESMI was not significantly associated with follow-up FVC (n = 80; −0.09 percentage points per 0.01 L/m²; 95% confidence interval − 0.38 to 0.20; p = 0.525).

Conclusions

Increased CT-derived Myosteatosis Index was independently associated with lower DLCO in patients with IPF, even after adjustment for pulmonary disease extent, BMI, and smoking exposure. These findings suggest that muscle-related body composition changes may provide additional information in the multidimensional assessment of patients with IPF.

Background

Idiopathic pulmonary fibrosis (IPF) is a progressive interstitial lung disease with a heterogeneous clinical course and substantial functional burden [1, 2]. Patients may experience markedly different rates of irreversible lung function decline, ranging from slowly progressive deterioration to more rapid functional loss [3]. Forced vital capacity (FVC) and diffusing capacity of the lung for carbon monoxide (DLCO) capture related but distinct aspects of this physiological impairment. FVC primarily reflects ventilatory restriction, whereas DLCO provides a broader measure of gas-transfer efficiency and may also be influenced by pulmonary vascular involvement and coexisting emphysema [4, 5]. Beyond their physiological relevance, both measures are clinically important prognostic markers; in the IPF-PRO Registry, baseline DLCO, oxygen use, and FVC were among the leading variables associated with long-term survival [6].

Although IPF primarily affects the lungs, extrapulmonary manifestations may also occur [2]. Therefore, abnormalities in body composition and skeletal muscle quality have gained increasing attention. Sarcopenia, defined by the European Working Group on Sarcopenia in Older People 2 (EWGSOP2) as reduced muscle strength accompanied by low muscle mass or impaired muscle quality, is increasingly recognized as an important manifestation of biological ageing and chronic disease including interstitial lung disease (ILD) [7, 8].

Chronic hypoxaemia, systemic inflammation, physical inactivity, and enhanced protein catabolism may promote muscle loss and impair muscle repair, while reduced muscle strength may further limit exercise capacity, respiratory muscle performance, and overall functional status. This bidirectional interaction may contribute to a progressive cycle of declining pulmonary and physical function [9, 10]. Evidence from IPF-specific cohorts supports this relationship. Reduced muscle mass and clinically defined sarcopenia have been associated with impaired gas transfer, more advanced disease and lower physical activity; body mass index (BMI) did not distinguish patients with and without sarcopenia in the prospective cohort [11, 12]. A recent meta-analysis, mostly including patients with IPF, reported lower FVC and DLCO in individuals with low muscle mass or consensus-defined sarcopenia, although substantial heterogeneity existed in the definitions and assessment methods used [10].

Nevertheless, most previous studies have focused primarily on muscle quantity, whereas muscle quality may provide additional and potentially distinct information. Myosteatosis, characterized by pathological fat accumulation within skeletal muscle, is increasingly recognized as a marker of impaired muscle quality and metabolic dysfunction; however, its role in IPF has not yet been fully clarified. Quantitative computed tomography (CT)-based assessment offers an opportunity to characterize these changes using routinely acquired thoracic imaging and may provide complementary information beyond conventional measures of muscle mass or BMI alone [13].

Up to now, various CT-based approaches have been used to assess myosteatosis. Reduced skeletal muscle attenuation is commonly used as a surrogate of fatty infiltration, whereas volumetric methods quantify muscle-associated adipose tissue together with other adipose compartments [14, 15]. In IPF, an association between a volumetric myosteatosis index and survival has been reported [16]. Subsequent

studies using paravertebral muscle attenuation or muscle-based fat fractions have similarly demonstrated associations between impaired muscle quality and short-term mortality [17, 18]. In a cohort of 307 patients with IPF, the subgroup with the greatest loss of CT-derived body fat during the first year had poorer transplant-free survival after adjustment for pulmonary function and CT disease extent, whereas changes in BMI were not prognostic [19]. Similarly, comprehensive nutritional assessment identified early functional or nutritional abnormalities in nearly half of patients considered normally nourished at the time of IPF diagnosis [20]. Collectively, these findings support the evaluation of body composition and tissue distribution rather than reliance on body weight, BMI, or muscle volume alone.

These findings suggest that skeletal muscle involvement may represent an integral component of the IPF disease phenotype rather than simply an age-related comorbidity. This study aimed to investigate the association between CT-derived myosteatosis and pulmonary function, including vital capacity and gas-transfer impairment, in patients with IPF. We distinguished muscle-associated adipose composition, assessed by the Myosteatosis Index, from muscle quantity, assessed by the erector spinae muscle index (ESMI). The primary analysis focused on contemporaneous DLCO, whereas the key exploratory analysis related baseline ESMI to baseline-adjusted follow-up FVC. To examine both functional domains consistently, additional exploratory analyses evaluated each index against both baseline and follow-up DLCO and FVC.

Methods

Study design and participants

This single-centre retrospective cohort study included adults followed for IPF in the Department of Pulmonary Medicine at Dokuz Eylül University Hospital, İzmir, Türkiye. IPF diagnoses were established through multidisciplinary assessment involving pulmonologists and radiologists, with histopathology when clinically indicated, in accordance with international diagnostic criteria [1, 2]. The source cohort comprised 87 patients with baseline and follow-up thorax CT examinations and corresponding pulmonary function assessments. Baseline CT examinations were obtained from 19 September 2013 to 13 January 2025, and follow-up examinations extended to 7 January 2026.

Baseline was defined as the assessment performed at the time of IPF diagnosis, whereas follow-up was defined as the last available paired clinical assessment. Chest CT and pulmonary function tests were considered matched when performed within ± 15 days of each other. Eligibility required adulthood, multidisciplinary IPF diagnosis, and evaluable baseline and follow-up CT–pulmonary function assessments. The available source cohort had already been restricted to patients with paired assessments. Two records were excluded because pulmonary function measurements could not be reliably reconciled: one had an unresolved extreme baseline DLCO value and the other an unresolved longitudinal DLCO pattern. The final study cohort comprised 85 patients; analysis-specific missingness was handled separately.

The present study represents a post hoc analysis of the original thesis cohort. The specific focus on myosteatosis and the sequence of multivariable adjustment were developed after completion and review of the original thesis analyses. All eligible source records were included, without a formal a priori sample-size calculation.

Clinical variables and pulmonary function

Age at baseline thorax CT, sex, smoking history, cumulative smoking exposure, height, BMI and initial antifibrotic treatment were obtained from the clinical and imaging datasets. FVC was obtained by spirometry and DLCO from carbon monoxide transfer testing, with measurement definitions and interpretation described in the relevant ATS/ERS technical standards [4, 5, 21]. The primary outcome was baseline DLCO expressed as percent predicted; values were harmonised using the European Community for Steel and Coal 1993 reference equations during preparation of the analysis dataset [22]. FVC percent predicted was taken from the locked clinical dataset. The key exploratory longitudinal outcome was FVC percent predicted at the final assessment. Baseline FVC and the interval between the paired thorax CT examinations were included in longitudinal models. Baseline FVC and follow-up DLCO were also evaluated in the complementary analyses of both body-composition measures.

CT-derived body composition

Routine-care thoracic CT examinations were analysed using an automated three-dimensional body-composition workflow based on the method described by Pu and colleagues [15]. The available thoracic CT volume was used to quantify skeletal muscle and adipose tissue compartments.

The primary exposure was the Myosteatosis Index, calculated as 100 × IMAT/(IMAT + SAT + VAT), where IMAT represents muscle-associated adipose tissue volume, SAT subcutaneous adipose tissue volume, and VAT visceral adipose tissue volume. The index represents the proportion of IMAT relative to the three measured adipose tissue compartments and should not be interpreted as either muscle attenuation or an intramuscular fat fraction. The terminology follows previous volumetric myosteatosis literature [16], while the exact formula and exported variables used in the present study are detailed in Additional file 1. The Myosteatosis Index was analysed as a continuous variable, without application of a diagnostic cut-off, thereby avoiding reliance on a cohort-derived threshold [10]. The anatomical compartments and index calculation are illustrated in Fig. 1.

Erector spinae muscle index (ESMI) was calculated by dividing erector spinae muscle volume, expressed in litres, by height squared in metres. Effect estimates were reported per 0.01 L/m² increase in ESMI. ESMI was considered a measure of muscle quantity rather than a diagnostic measure of sarcopenia, as current consensus definitions of sarcopenia require assessment of muscle strength, with physical performance used to grade severity [7].

Automated quantification of pulmonary disease burden

Pulmonary disease burden was quantified using automated volumetric outputs from the same baseline CT examination. The ILD-specific model, developed by the University of Pittsburgh group, was trained on 100 ILD cases and segmented abnormal interstitial regions as a single class without separating individual radiological patterns. The output was therefore interpreted as overall ILD extent rather than a fibrosis-specific measure.

The group's published methodological work includes U-Net-based lung-boundary and central-vessel segmentation combined with automated quantification of parenchymal abnormalities [23], and three-dimensional convolutional neural-network analysis of infiltrative lung patterns [24]. These reports provide methodological background; the ILD-specific implementation and the relationship of its outputs to the cited methods are described in Additional file 1, section S2.

ILD extent and emphysema fraction were normalised to the corresponding total lung volume:

ILD extent (%) = 100 × ILD abnormality volume / total lung volume

Emphysema fraction (%) = 100 × emphysema volume / total lung volume

Both measures were included as continuous baseline adjustment covariates to account for the proportions of lung affected by interstitial abnormalities and emphysema in the body-composition–DLCO analysis.

Statistical analysis

Continuous variables were summarized as median and interquartile range (IQR), and categorical variables as number and percentage. Zero-coded height, BMI and DLCO values were treated as unavailable. Complete-case analyses were performed without imputation. The primary model sequence used the same 78 participants throughout.

The association between baseline DLCO and the Myosteatosis Index was assessed using linear regression. Sequential models were constructed as follows: Model 0 was unadjusted; Model 1 was adjusted for age and sex; Model 2 additionally included CT-derived ILD extent and emphysema fraction; and Model 3 additionally included BMI and smoking exposure (pack-years). The Myosteatosis Index was standardized, and effect estimates are reported as the percentage-point difference in DLCO per 1-standard deviation (SD) increase in the index. Heteroskedasticity-consistent type 3 (HC3) standard errors were used to calculate 95% confidence intervals (CIs) and two-sided p values with t-based inference.

Sensitivity analyses included 5000 participant-level bootstrap resamples, leave-one-out analysis, and additional adjustment for baseline FVC and CT acquisition parameters. The latter comprised exported slice thickness and the number of contributing CT series. The primary model was also repeated after

reinstating the record excluded for an unresolved longitudinal DLCO pattern. The exploratory ESMI analysis evaluated follow-up FVC conditional on baseline FVC, follow-up duration, age, sex, initial antifibrotic treatment and ILD extent, with emphysema added in a further model. The estimates describe baseline-adjusted follow-up function, not annualised decline.

To address the complementary roles of muscle composition, muscle quantity and body size, univariable associations of age, sex, smoking exposure, BMI, ILD extent, emphysema, Myosteatosis Index and ESMI with baseline DLCO and FVC were examined using a common complete-case sample for each outcome. Pearson correlations were calculated for Myosteatosis Index, ESMI and BMI; paired participant-level bootstrap intervals compared the absolute correlation magnitudes. The increase in model R^2 after adding each CT measure to the clinical model containing BMI was reported as incremental explained variance. Both CT measures were also examined against each baseline and baseline-adjusted follow-up pulmonary function outcome. These additional analyses were exploratory; no adjustment for multiple comparisons was applied. Full specifications and results are provided in Additional file 1.

All statistical analyses were performed using Python version 3.13 with NumPy, pandas and SciPy. A two-sided p value < 0.05 was considered statistically significant for the primary analysis. Executable analysis code, dependency versions and aggregate reference outputs are provided in Additional file 2.

Use of AI-assisted tools

OpenAI ChatGPT was used to assist with language editing, literature identification, code review and consistency checks. Consensus was used for literature discovery, with supporting claims checked against accessible original publications. AI-assisted code was executed against the study dataset during preparation of the analysis package. The authors retain responsibility for the scientific content and interpretation; AI tools are not listed as authors.

Results

Study population

The final cohort included 85 patients, of whom 64.7% were male and 61.2% had a history of smoking. The median age was 68.0 years (IQR 64.0–74.0). Median BMI was within the overweight range at 26.9 kg/m² (IQR 23.9–29.5; n = 80). Baseline pulmonary function parameters, CT-derived ILD extent, ESMI, and Myosteatosis Index are summarized in Table 1. Median follow-up duration was 1.87 years (IQR 1.05–3.05).

Table 1
Clinical and body-composition characteristics of the study cohort

Characteristic	n	Value
Age, years	85	68.0 (64.0–74.0)
Male sex	85	55 (64.7%)
Smoking history	85	52 (61.2%)
Smoking exposure, pack-years	85	20.0 (0–30.0)
BMI, kg/m²	80	26.9 (23.9–29.5)
Baseline FVC, % predicted	85	79.0 (67.0–89.0)
Baseline DLCO, % predicted	78	51.4 (41.2–61.1)
CT-derived ILD extent, % lung volume	85	47.4 (35.6–59.8)
Emphysema fraction, % lung volume	85	5.7 (3.1–10.3)
Myosteatosis Index, %	85	10.50 (8.94–12.37)
ESMI, L/m²	80	0.087 (0.052–0.124)
Follow-up interval, years	85	1.87 (1.05–3.05)

Values are median (IQR) or n (%). Percentages use the available denominator. BMI, body mass index; CT, computed tomography; DLCO, diffusing capacity of the lung for carbon monoxide; ESMI, erector spinae muscle index; FVC, forced vital capacity; ILD, interstitial lung disease; IQR, interquartile range.

Myosteatosis and gas-transfer impairment

Higher baseline Myosteatosis Index was consistently associated with lower DLCO across all regression models (Table 2). In the unadjusted analysis, each 1-SD increase in the Myosteatosis Index, corresponding to 2.63 percentage points, was associated with a 4.51 percentage-point lower DLCO (95% CI − 7.89 to − 1.13). The association remained similar after adjustment for age, sex, ILD extent, and emphysema.

Table 2
Association between baseline Myosteatosis Index and baseline DLCO

Model and adjustment	n	Difference[1]	95% CI	p value
Model 0: unadjusted	78	−4.51	−7.89 to −1.13	0.010
Model 1: age and sex	78	−5.22	−8.87 to −1.57	0.006
Model 2: Model 1 + ILD extent and emphysema fraction	78	−5.34	−8.90 to −1.77	0.004
Model 3: Model 2 + BMI and pack-years	78	−4.99	−9.30 to −0.69	0.024

[1] DLCO percentage-point difference per 1-SD higher Myosteatosis Index. All models use the same 78 complete cases; 1 SD = 2.63 index percentage points. Confidence intervals and p values use HC3 standard errors with t-based inference. In Model 3, the difference per one-percentage-point higher index was − 1.90 DLCO percentage points (95% CI − 3.53 to − 0.26). BMI, body mass index; CI, confidence interval; DLCO, diffusing capacity of the lung for carbon monoxide; HC3, heteroskedasticity-consistent type 3; ILD, interstitial lung disease; SD, standard deviation.

In the fully adjusted model, which additionally included BMI and smoking exposure, each 1-SD increase in the Myosteatosis Index was associated with a 4.99 percentage-point lower DLCO (95% CI − 9.30 to − 0.69; p = 0.024). On the original scale, each one-percentage-point increase in the Myosteatosis Index corresponded to a 1.90 percentage-point lower DLCO (95% CI − 3.53 to − 0.26). The observed and adjusted associations are shown in Fig. 2.

The inverse association remained consistent across sensitivity analyses (Fig. 3 and Additional file 1, Table S1). Similar results were obtained after leave-one-out analysis, additional adjustment for baseline FVC and CT acquisition parameters, and inclusion of the previously excluded record. These findings support the robustness of the association between higher Myosteatosis Index and lower DLCO.

Univariable associations and comparison with BMI

Univariable associations with baseline DLCO and FVC are presented in Table 3. In the same 78 patients, baseline DLCO correlated with Myosteatosis Index (r = − 0.26) and ESMI (r = 0.24), whereas the correlation with BMI was small (r = 0.03). The correlation magnitudes were numerically greater for the CT measures, but paired bootstrap intervals for their differences from BMI included zero. Adding Myosteatosis Index to the clinical model containing BMI increased R^2 from 0.161 to 0.230 (ΔR^2=0.070); adding ESMI yielded R^2=0.213 (ΔR^2=0.053). Correlations and incremental model results are provided in Additional file 1, Tables S5–S7.

Table 3
Univariable associations with baseline DLCO and FVC

Variable and increment	DLCO difference (95% CI), n = 78	p value	FVC difference (95% CI), n = 80	p value
Age, per 10 years	2.27 (− 2.03 to 6.57)	0.296	0.84 (− 3.53 to 5.21)	0.702
Female vs male	−1.50 (− 9.27 to 6.28)	0.703	4.96 (− 2.23 to 12.15)	0.174
Smoking exposure, per 10 pack-years	−1.08 (− 2.45 to 0.28)	0.116	−0.14 (− 1.54 to 1.27)	0.845
BMI, per 1 kg/m²	0.12 (− 0.72 to 0.96)	0.775	−0.47 (− 1.27 to 0.33)	0.242
ILD extent, per 10 pp	−3.21 (− 6.05 to − 0.37)	0.027	−2.55 (− 4.20 to − 0.90)	0.003
Emphysema fraction, per 5 pp	−0.95 (− 4.97 to 3.07)	0.640	1.98 (− 0.72 to 4.68)	0.148
Myosteatosis Index, per 1 SD	−4.51 (− 7.89 to − 1.13)	0.010	−0.08 (− 3.17 to 3.01)	0.958
ESMI, per 0.01 L/m²	0.74 (− 0.25 to 1.73)	0.143	0.09 (− 0.48 to 0.67)	0.743

Separate univariable linear models with HC3, t-based 95% CIs. Differences are pulmonary-function percentage points. A common complete-case population was used for all variables within each outcome. One Myosteatosis Index SD was 2.63 percentage points for DLCO and 2.66 for FVC. These descriptive associations were not used to select covariates. BMI, body mass index; CI, confidence interval; DLCO, diffusing capacity of the lung for carbon monoxide; ESMI, erector spinae muscle index; FVC, forced vital capacity; ILD, interstitial lung disease; pp, percentage points; SD, standard deviation.

Exploratory analysis of muscle quantity and follow-up FVC

Among 80 patients with available ESMI data, baseline ESMI was not significantly associated with follow-up FVC after adjustment for baseline FVC and relevant clinical covariates. Each 0.01 L/m² increase in ESMI was associated with a − 0.09 percentage-point difference in follow-up FVC (95% CI − 0.38 to 0.20; p = 0.525). Further adjustment for emphysema did not materially alter the result (Additional file 1, Table S2).

The Myosteatosis Index and ESMI were weakly inversely correlated (r = − 0.23).

The complementary adjusted analyses did not identify an association of either CT measure with baseline FVC or baseline-adjusted follow-up FVC or DLCO. ESMI was also not significantly associated with baseline DLCO after full adjustment. These comparisons used the same participants for the two CT measures within each outcome; all coefficients and confidence intervals are reported in Additional file 1, Table S8.

Discussion

Skeletal muscle abnormalities are increasingly recognized as relevant extrapulmonary features of IPF, but the contribution of muscle quality to physiological impairment remains incompletely understood. In particular, the relationship between CT-derived myosteatosis and pulmonary function has received limited attention.

In this clinically characterised IPF cohort, a higher Myosteatosis Index was consistently associated with lower DLCO. Each 1-SD increase in the index was associated with approximately five percentage points lower DLCO after adjustment for age, sex, ILD extent, emphysema, BMI, and smoking exposure. In contrast, baseline ESMI was not associated with baseline-adjusted follow-up FVC, highlighting the distinction between muscle composition and muscle quantity, as well as between current physiological impairment and subsequent functional change.

DLCO is particularly relevant for evaluating the relationship between body composition and pulmonary function in IPF because it reflects several components of gas exchange, including effective alveolar volume, alveolar–capillary membrane diffusion, and pulmonary capillary blood volume, rather than ventilatory restriction alone [4, 5]. In our study, the association between a higher Myosteatosis Index and lower DLCO persisted after adjustment for CT-derived ILD extent and emphysema. Additional adjustment for baseline FVC also had little effect on the estimate. These findings suggest that the observed association is not fully explained by the extent of parenchymal lung disease, emphysema, or body size. However, this was a cross-sectional between-patient association and should not be interpreted as evidence of longitudinal decline or treatment response. Its main relevance is that CT-derived body composition may provide complementary information to established physiological measures used in IPF assessment.

The most comparable previous study is the 79-patient analysis by Salhöfer and colleagues, in which a volumetric muscle-associated fat index was independently associated with overall survival after adjustment for FVC, DLCO, and clinical characteristics [16]. Although that study used a different automated segmentation method and adipose tissue definition, both studies point to a similar clinical concept: the distribution of adipose tissue within and around skeletal muscle may capture aspects of the IPF phenotype that are not reflected by BMI or muscle quantity alone. Our findings extend this concept by showing an association between a volumetric Myosteatosis Index and contemporaneous gas-transfer impairment after accounting for quantified pulmonary abnormalities.

Other studies have reported similar findings, although differences in imaging methods and clinical outcomes should be considered. Bernardinello and colleagues found that low paravertebral muscle attenuation was associated with two-year mortality in 96 patients with IPF receiving antifibrotic treatment, although it was not associated with overall survival [17]. Sanmartín-Sánchez and colleagues also reported an association between a CT-derived muscle-fat fraction at the T12 level and 12-month mortality [18]. However, their metric differed from ours because muscle and muscle-associated fat were included in the denominator, whereas our Myosteatosis Index is based on the relative distribution of measured adipose tissue compartments. These measures therefore reflect related but distinct aspects

of muscle composition. Collectively, these studies support the clinical relevance of CT-derived muscle composition in IPF, while also highlighting the need for caution when comparing thresholds or prognostic effects across different methods.

Our findings are also consistent with the broader literature on musculoskeletal involvement in fibrotic ILD. In a cohort of 115 patients with fibrotic ILD, including 40 with IPF, Guler and colleagues showed that greater physiological disease severity was associated with lower muscle quantity, while muscle strength and physical performance provided additional information beyond body composition alone [25]. Similarly, Sridhar and colleagues reported associations of low muscle mass and sarcopenia with reduced DLCO in IPF, whereas frailty was related to a wider range of functional and patient-reported outcomes [11]. Together, these findings suggest that muscle quantity, muscle composition, muscle strength, and physical function represent complementary dimensions of musculoskeletal health. Our study adds CT-derived muscle composition to this framework and should not be interpreted as replacing direct assessment of muscle strength, sarcopenia, or frailty.

The persistence of the association and additional explained variance after adjustment for BMI are clinically relevant because changes in adipose tissue and skeletal muscle composition may occur without major changes in overall body weight. Weight loss itself has prognostic importance in fibrotic ILD [26], but body weight does not indicate which tissue compartments are affected. In the study by Lee and colleagues, poorer outcomes were associated with the subgroup showing the greatest CT-derived fat loss, whereas continuous fat change was not independently associated with prognosis after multivariable adjustment [19]. This finding suggests that changes in adipose tissue should be interpreted in the context of tissue distribution rather than assuming that lower fat mass is uniformly adverse. In our study, a higher Myosteatosis Index may result from greater IMAT, lower SAT or VAT, or a combination of these changes. The index should therefore be interpreted as a relative body-composition phenotype rather than as a direct measure of total adiposity.

Several clinical mechanisms may contribute to this association. Greater physiological impairment may be accompanied by reduced physical activity and nutritional vulnerability, both of which can adversely affect muscle composition. Nutritional and functional abnormalities may also be present in patients who appear to have normal nutritional status based on conventional assessment [20]. Together, these observations support a possible interaction between pulmonary impairment, physical inactivity, nutritional status, and altered body composition. Because these factors were not directly measured in our study, prospective studies combining CT-based body-composition analysis with activity monitoring, muscle strength testing, and nutritional assessment are needed to clarify these relationships.

Previous studies have shown that lower muscle mass and reduced physical activity are associated with worse outcomes in IPF [12, 27–29]. However, several of these studies focused on mortality and used area-based muscle measurements. In our study, volumetric ESMI was evaluated in relation to follow-up FVC and was not significantly associated with this outcome. The additional analyses of both CT

measures across FVC and DLCO did not identify longitudinal associations. Thus, a relationship with contemporaneous physiology should be distinguished from prediction of subsequent functional change.

The weak correlation between ESMI and the Myosteatosis Index also suggests that muscle quantity and muscle composition represent different aspects of body composition. Future studies should evaluate both measures together with muscle strength and physical performance to determine their relative clinical value in IPF.

Strengths of this study include multidisciplinary confirmation of IPF, close temporal matching of CT and pulmonary function tests, and assessment of both pulmonary and body-composition measures from the same baseline period. The Myosteatosis Index was analysed as a continuous variable, avoiding the need for a study-specific cut-off. The use of the same complete-case population across sequential models also allowed direct comparison of adjusted estimates, and sensitivity analyses supported the stability of the main finding.

Several limitations should be acknowledged. This was a retrospective, single-centre study with a relatively small sample size, which limits generalisability. Inclusion required available CT and pulmonary function data, which may have introduced selection bias. The analysis was post hoc, and missing data were handled by complete-case analysis. CT acquisition protocols were not fully standardised, and variation in imaging parameters may have influenced body-composition measurements [30]. In addition, the historical data did not allow confirmation of the exact software model version used, and manual validation of the automated segmentation was not available for this cohort. Important factors such as physical performance, nutritional status, haemoglobin, and pulmonary haemodynamics were also not included and may have contributed to residual confounding. Prospective multicentre studies using standardised imaging and concurrent functional assessment are needed to confirm these findings and clarify their clinical significance.

Conclusions

A higher CT-derived Myosteatosis Index was associated with lower DLCO in patients with IPF, independent of ILD extent, emphysema, and relevant clinical characteristics. These findings suggest that muscle composition may provide additional information beyond conventional measures of pulmonary disease and body size.

Further studies are needed to determine whether CT-derived myosteatosis can help identify patients who would benefit from more detailed nutritional or functional assessment. At present, this index should be considered an investigational marker rather than a standalone tool for rehabilitation referral or treatment decisions.

Abbreviations

BMI

body mass index
CI
confidence interval
CT
computed tomography
DLCO
diffusing capacity of the lung for carbon monoxide
ESMI
erector spinae muscle index
FVC
forced vital capacity
HC3
heteroskedasticity-consistent type 3
ILD
interstitial lung disease
IMAT
muscle-associated adipose tissue
IPF
idiopathic pulmonary fibrosis
IQR
interquartile range
SAT
subcutaneous adipose tissue
SD
standard deviation
VAT
visceral adipose tissue.

Declarations

Ethics approval and consent to participate

The Dokuz Eylül University Non-Interventional Research Ethics Committee approved the study on 8 October 2025 (decision 2025/34-23) and waived individual informed consent because of the retrospective design and use of pseudonymised routinely collected data. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable. No identifiable participant information is included. The illustrative CT image is de-identified.

Availability of data and materials

The participant-level data are not publicly available because of participant privacy and institutional data-sharing restrictions. They are available from the corresponding author on reasonable request, subject to approval by the local ethics committee and institution. The executable analysis code is provided in Additional file 2.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

EB contributed to conceptualisation, data curation, formal analysis, investigation, project administration, visualisation and writing the original draft. GÖŞ contributed to conceptualisation, methodology, supervision, validation and manuscript review. AÖA contributed resources, supervision, validation and manuscript review. KCT and CS contributed to methodology, validation and manuscript review. NSG contributed to data curation, investigation, methodology, project administration, resources, supervision, validation, visualisation and manuscript review. GK contributed to data curation, formal analysis, software, validation, visualisation and manuscript review. JP contributed to methodology, resources, software, supervision, validation and manuscript review. EB is the guarantor.

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Figures

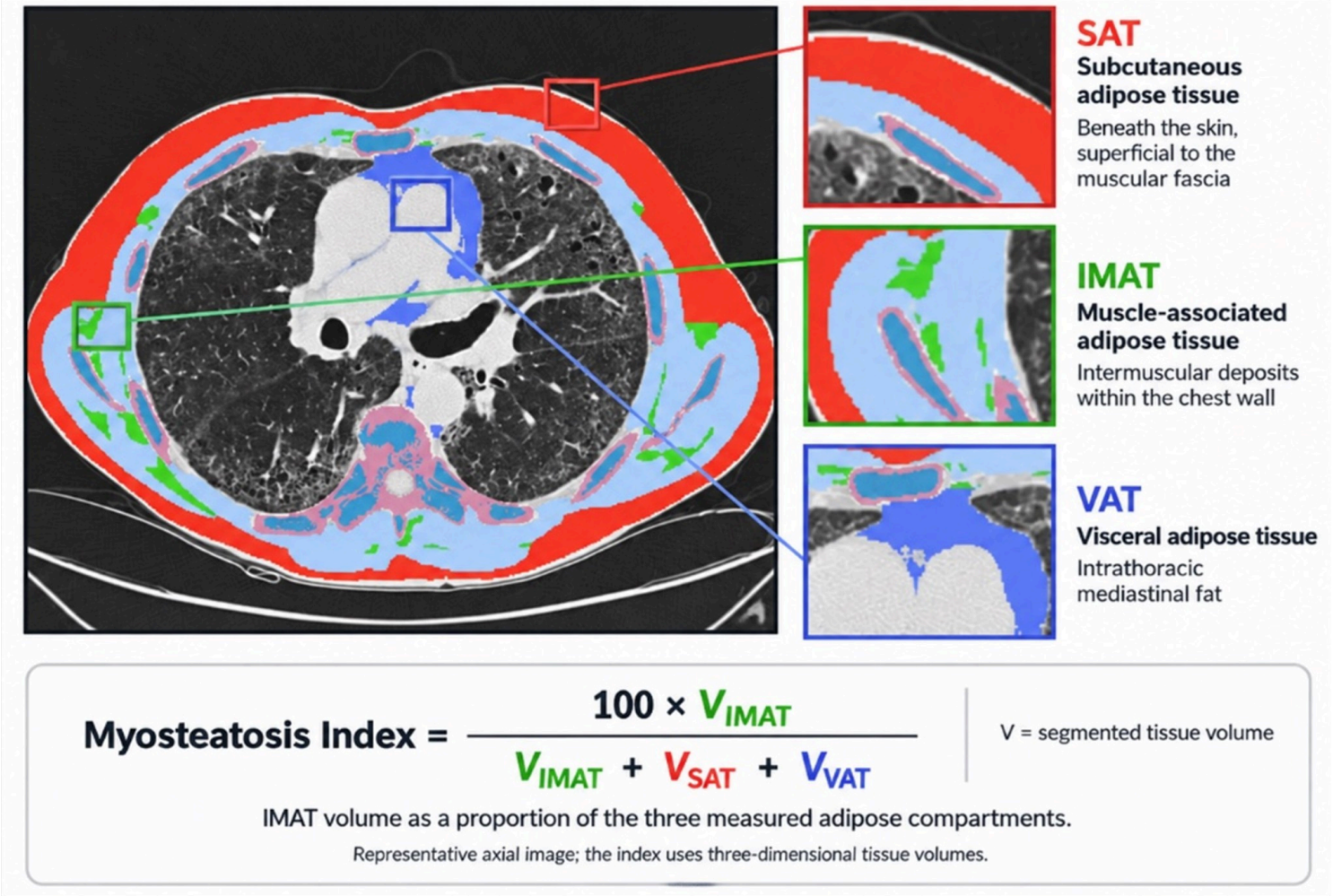


Figure 1

CT-derived adipose compartments and the Myosteatosis Index.

Illustrative axial chest CT with colour-coded adipose compartments and magnified detail views. Subcutaneous adipose tissue (SAT; red) lies beneath the skin, superficial to the muscular fascia. Muscle-associated adipose tissue (IMAT; green) is illustrated by intermuscular deposits in the chest wall. Visceral adipose tissue (VAT; blue) is illustrated by intrathoracic mediastinal fat. The Myosteatosis Index is defined as 100 × VIMAT/(VIMAT + VSAT + VVAT), where V denotes segmented tissue volume. The axial view illustrates anatomical correspondence; the study index was calculated from three-dimensional tissue volumes across the available chest CT, not from the area of this single image.

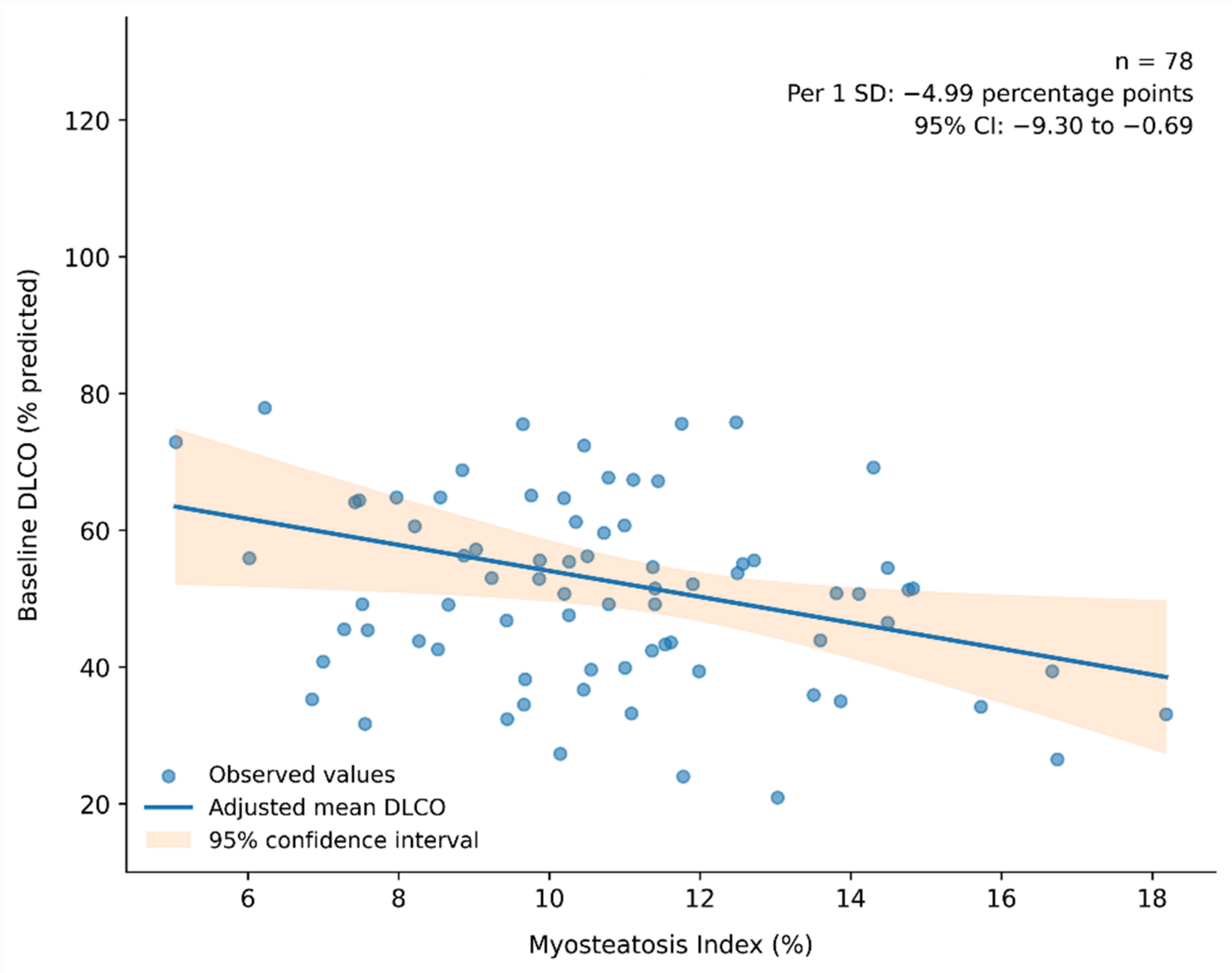
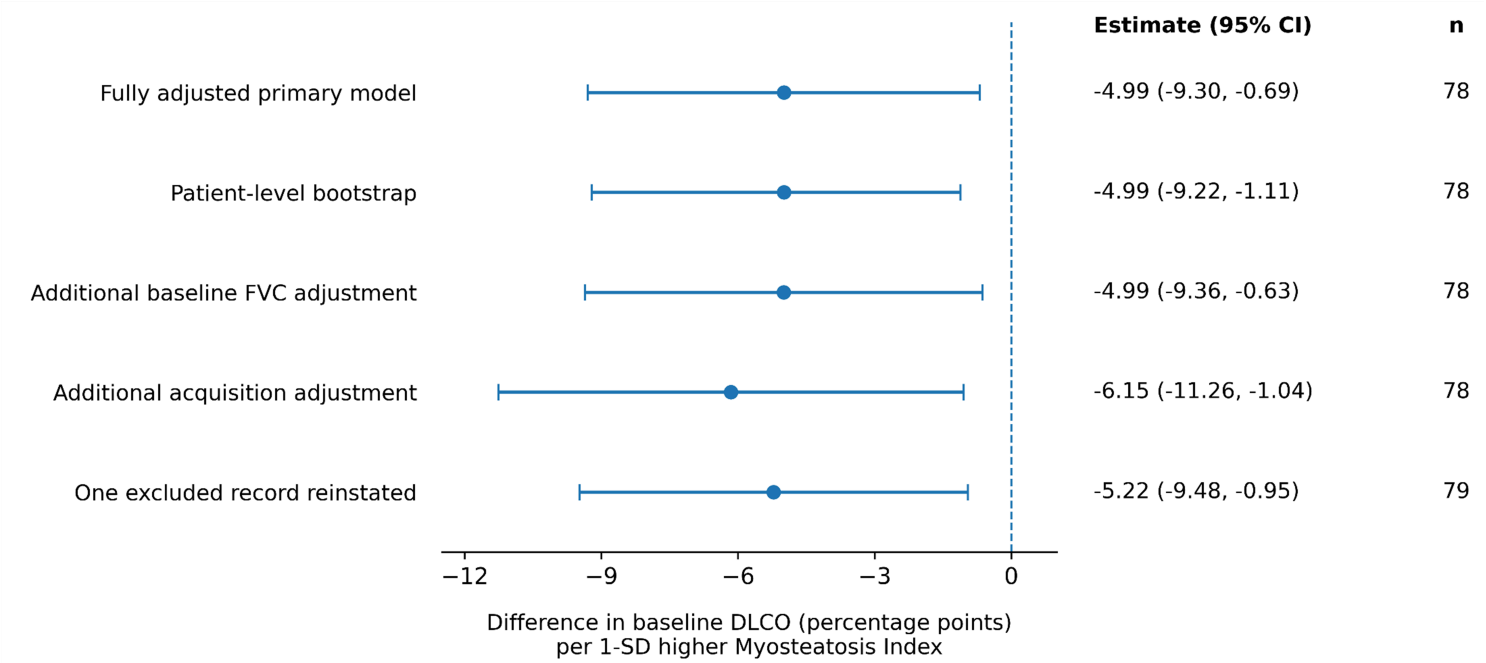


Figure 2

Myosteatosis Index and baseline DLCO.

Points show observed values in the fixed complete-case population (n=78). The line represents the adjusted mean DLCO from Model 3, averaging predictions over the observed distribution of age, sex, ILD extent, emphysema fraction, BMI and pack-years. Shading denotes the HC3-based 95% confidence interval for the adjusted mean, not a prediction interval for an individual patient. One SD of the Myosteatosis Index was 2.63 percentage points. BMI, body mass index; CI, confidence interval; DLCO, diffusing capacity of the lung for carbon monoxide; HC3, heteroskedasticity-consistent type 3; ILD, interstitial lung disease; SD, standard deviation.



HC3 intervals except the bootstrap. Acquisition adjustment includes exported slice thickness and number of CT series.

Figure 3

Fully adjusted and sensitivity estimates.

Points show the baseline DLCO difference per 1-SD higher Myosteatosis Index, and horizontal lines show 95% confidence intervals. The primary model adjusted for age, sex, ILD extent, emphysema fraction, BMI and pack-years. Additional adjustment models separately included baseline FVC or exported slice thickness and the number of CT series contributing to the examination-level output. The final row reinstates the record excluded for an unresolved longitudinal DLCO pattern. HC3 intervals are shown except for the percentile bootstrap interval, based on 5,000 patient-level resamples with seed 20260919. The index SD was held fixed during resampling and recalculated in the expanded sensitivity population. CI, confidence interval; CT, computed tomography; DLCO, diffusing capacity of the lung for carbon monoxide; FVC, forced vital capacity; HC3, heteroskedasticity-consistent type 3; SD, standard deviation.

Supplementary Files

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