Monaldi Archives for Chest Disease

eISSN 2532-5264 https://www.monaldi-archives.org/

Monaldi Arch Chest Dis 2024 [Online ahead of print]

To cite this Article:
Bešić E, Muršić D, Jalušić Glunčić T, et al. **Prediction of spirometry outcome in Croatian patients with chronic obstructive pulmonary disease.** *Monaldi Arch Chest Dis* doi: 10.4081/monaldi.2024.3099

Prediction of spirometry outcome in Croatian patients with chronic obstructive pulmonary disease

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Contributions: EB, DM, MS, AVD, equally contributed to the conception and design of the article and revising it critically for important intellectual content; DM, TJG, JO, SSC, MD, NKL, AVD, contributed to the acquisition of the data and revising the article critically for important intellectual content; EB, DM, AVD, contributed to the acquisition, analysis, and interpretation of the data, as well as drafting the article. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Conflict of interest: the authors declare that they have no competing interests, and all authors confirm accuracy.

Ethics approval and consent to participate: the study protocol was approved by the Ethical Review Committee of the University of University Hospital Centre Zagreb (ID 02/18 AG) as well as by the Ethical Committee of the University Hospital Centre Rijeka, the University Hospital Centre Osijek and Zadar General Hospital.

Informed consent: written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article. The manuscript does not contain any individual person's data in any form..

Funding: none.

Availability of data and materials: data and materials available from the corresponding author upon request.

Abstract

The current study offers an extensive examination of the influence of 29 diverse parameters on spirometry measurement variables in a cohort of 534 patients with chronic obstructive pulmonary disease (COPD) from five different centers in Croatia. The study elucidates both the magnitude and direction of the effect exerted by the 29 predictors on forced vital capacity (FVC), forced expiratory volume in one second (FEV1), the ratio FEV1/FVC, and predicted forced expiratory flow at 50% of FVC. Additionally, the development of prediction models for these parameters has been undertaken using several statistical methods.

The study identifies fat-free mass index, 6-minute walk distance, predicted diffusing capacity of the lung for carbon monoxide, arterial partial pressure of oxygen, and both arterial and tissue hemoglobin oxygen saturation percentage as robust positive predictors for all four spirometry parameters. Body mass index is recognized as a weak positive predictor for FEV1 and FEV1/FVC, commonly observed in COPD patients. As expected, smoking years is identified as a strong negative predictor for all four spirometry parameters, while age and illness duration exhibit strong predictive negative associations. Furthermore, modified medical research council, arterial partial pressure carbon dioxide, St George's respiratory questionnaire, COPD assessment test, depression anxiety stress scales, and nutritional risk screening are identified as weak negative predictors. Charlson comorbidity index, phase angle, and number of comorbidities do not exhibit a significant impact on spirometry variables.

Ultimately, the performed factorial analysis categorized the 29 parameters into five groups, which were identified as relating to lung function, health status, nutritional status, age, and smoking. Multiple regression analysis, including four newly derived parameters based on the results of factorial analysis, identified nutritional status as a positive predictor for spirometry readings, while smoking, poor health status, and age were identified as negative predictors in successive order.

Key words: COPD, spirometry parameters, general linear model, multiple linear regression, stepwise regression, factorial analysis.

Introduction

Chronic obstructive pulmonary disease (COPD) is a prevalent lung ailment characterized by constrained airflow and respiratory difficulties. COPD is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production and/or exacerbations) due to abnormalities of the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction. It stands as one of the top three leading causes of mortality worldwide, imposing a substantial burden on global healthcare systems and public health. The progressive nature of COPD, coupled with its significant impact on quality of life and mortality rates, underscores the critical need for effective prevention, diagnosis, and management strategies [1-4].

Spirometry test variables are crucial in diagnosing and managing respiratory conditions, particularly COPD and asthma. Key variables include forced vital capacity (FVC), which measures the maximum amount of air a person can forcibly exhale after a full inhalation and forced expiratory volume in one second (FEV1), which measures the amount of air exhaled in the first second of the FVC manoeuvre. The ratio FEV1/FVC helps determine the presence and severity of airway obstruction. These spirometry variables are essential for assessing lung function, monitoring disease progression, evaluating treatment efficacy, and guiding clinical decision-making [5-8].

An overview of studies examining the relationships between lung function and various contributing factors has revealed a complex structure underlying the conditioning of FEV1, FVC, and FEV1/FVC [9-11]. The multifaceted nature of factors influencing lung function highlights the challenges in determining accurate and reliable predicted values for FEV1, FVC, and FEV1/FVC [12]. Most equations used to estimate predicted values of spirometry parameters typically incorporate a limited number of predictors [13]. However, it is evident that expanding the number of predictors in predictive models for spirometry parameters enhances their robustness and accuracy in clinical applications. Incorporating a broader array of predictors allows for a more comprehensive evaluation of lung function, considering both clinical and physiological variables [14].

Several studies have advocated for the inclusion of additional predictors beyond conventional factors such as age, sex, and height, to improve the accuracy of spirometry prediction equations [5,10,15,16]. For instance, factors like smoking history, comorbidities, body composition metrics, and respiratory symptoms have been shown to contribute significantly to lung function variability [17,18]. By incorporating these factors into predictive models, clinicians can obtain more personalized and precise estimates of spirometry parameters for individual patients [19].

Recently, a multicenter study was conducted across four different regions of Croatia, where COPD patients were recruited and evaluated regarding 29 various parameters. The study included 534 patients, of whom 325 (60.9%) were men and 209 (39.1%) were women, with a mean age of (66.7±8.3) years. The mean duration of the disease was (6.9±1.2) years. Most patients exhibited a moderate to severely abnormal obstructive pattern with a reduced 6-minute walk distance (6MWD) ((396.5±110.8) meters). The patients were predominantly overweight or obese, with an average body mass index (BMI) of (26.4±5.5) kg/m^2, and demonstrated satisfactory values for nutritional status variables, including fat-free mass index (FFMI), skeletal muscle mass index (SMMI), and phase angle (PhA). Primarily, the study was designed to assess the nutritional status of COPD patients and to investigate the association between nutritional status, disease severity, and exercise capacity in four different regions of Croatia [20]. The subsequent publication delves into a more targeted investigation, specifically examining obese patients diagnosed with chronic obstructive pulmonary disease, investigating aspects related to body composition, pulmonary function tests, exercise capacity, and quality of life in these patients [21]. However, within these two publications stemming from the same cohort of COPD patients, we undertook preliminary investigations to ascertain which among the 29 measured parameters assessed exerted an influence on spirometry outcomes.

Therefore, the present study aims to elucidate the factors impacting variables derived from pulmonary function tests and to determine both the magnitude and direction (whether positive or negative) of the effects exerted by numerous predictors on each spirometry parameter. To achieve this objective, several statistical analyses were employed, including general linear models, stepwise regression models, and multiple regression models guided by the findings of factorial analysis.

Materials and Methods

Patients

This multicenter study involved a cohort of 534 patients diagnosed with COPD, who were recruited and assessed in the years 2018 and 2019. The study encompassed five distinct centers, comprising two from the Mediterranean region and three from continental Croatia. Patients with COPD were screened for eligibility and recruited during ambulatory visits at outpatient clinics. Consecutive patients, predominantly current or former smokers aged 45 to 90 years, with a confirmed COPD in accordance with the GOLD guidelines, were included. All COPD patients enrolled in the study were required to be in a stable phase of the disease, defined as having no exacerbations for at least the preceding month, with no changes in respiratory medication and no symptoms indicative of a lower respiratory tract infection. Additional exclusion criteria included recent exacerbations, active malignant diseases,

uncontrolled arterial hypertension (systolic pressure >180 mmHg, diastolic pressure >100 mmHg), presence of a pacemaker, or finger amputation. Ethical approval for the study protocol was obtained from the respective Ethics Committees, and all participating individuals provided informed consent. Diagnosis of COPD was established in accordance with the 2019 GOLD guidelines. Patients exhibiting indications of asthma or positive bronchodilator responses were excluded from the study, as were those with musculoskeletal, neurological, or other conditions that might influence the results of the 6MWD test.

For each participant, data encompassing 29 distinct parameters were meticulously collected. In addition to recording the age, sex, and the disease duration of the patients, the evaluation included a comprehensive suite of assessments: pulmonary function tests, the 6-minute walking test, BMI and body composition via bioelectrical impedance analysis, which provided measurements such as FFMI, SMMI, and PhA. Oxygenation status was assessed through arterial hemoglobin oxygen saturation percentage (a-Sa(Hb)-O_2%) and tissue hemoglobin oxygen saturation percentage (t-Sa(Hb)-O_2%), both measured using pulse oximetry.

Furthermore, the study captured data on smoking habits (including smoking status, smoking years, and pack-years), parameters reflecting gas exchange efficiency in the lungs — such as the predicted diffusing capacity for carbon monoxide (DLCO%), the predicted carbon monoxide transfer coefficient (KCO%), and the partial arterial pressures (PO_2) and carbon dioxide (PCO_2) — as well as measures of oxygenation status: arterial hemoglobin oxygen saturation percentage (a-Sa(Hb)-O_2%) and tissue hemoglobin oxygen saturation percentage (t-Sa(Hb)-O_2%).

Additional assessments included various validated questionnaires and indices to gauge psychological, respiratory, nutritional status, and quality of life. These included the Depression Anxiety Stress Scales (DASS), St George's Respiratory Questionnaire (SGRQ-C), Nutritional Risk Screening (NRS-2002), the Body mass index/airflow Obstruction/Dyspnea/Exercise capacity index (BODE), Charlson Comorbidity Index (CCI), Global initiative for chronic Obstructive Lung Disease classification (GOLD (I-IV)), the COPD Assessment Test (CAT), and the modified Medical Research Council dyspnea scale (mMRC).

Methods

Spirometry and the measurement of lung diffusing capacity for carbon monoxide (DLCO) were conducted in accordance with the standards set by the American Thoracic Society/European Respiratory Society (ATS/ERS). The 6-minute walk test was administered following the guidelines provided in the ATS/ERS statement.

Bioelectrical impedance analysis (BIA) is a widely accepted method for assessing body composition in patients with COPD. In this study, body composition measurements were

obtained using the TANITA MC-780MA P device, which employs an eight-contact electrode system. The procedures were performed according to the manufacturer's instructions and the recommendations outlined by Kyle et al [22].

Statistical analysis

Statistical analysis was performed using Minitab 17 statistical software. For the evaluation of the effect of various predictors on each of the four dependent spirometry variables, a general linear model with three predictors (factors: predictor, sex, age) was used. Modelling the linear regression model for each of the dependent spirometry variables, which included a reduced number of predictors, was performed using the stepwise method. To condense 29 variables into a smaller number of factors, factor analysis followed by varimax rotation was employed. Multiple linear regression was utilized to create a model for spirometry variables incorporating four of the five newly derived factors resulting from the factorial analysis. P-values less than 0.05 were considered statistically significant in all statistical methods used in this study.
All computer outcomes are provided in the *Supplementary Material*.

Results and Discussion

All measured values were numerical, with most exhibiting a symmetrical or normal distribution. To determine the normality of the given dataset, the Shapiro-Wilk test was employed ($\alpha = 0.05$). All non-normally distributed variables (Shapiro-Wilk: $p > 0.001$) were log-transformed before inclusion in multivariable models to approximate a normal distribution. The distributions for the parameters NRS-2002, BODE, DASS and SGRQ-C significantly deviated from normality (Shapiro-Wilk: $p < 0.001$), yet they were still included in the parametric linear regression analysis alongside other parameters. Additionally, outcomes for GOLD(I-IV) were converted to numerical data (GOLD I = 1, GOLD II = 2, GOLD III = 3, GOLD IV = 4) and treated as discrete numerical variables. The same treatment was applied to smoking status (non-smokers = 1, ex-smokers = 2, smokers = 3). Accordingly, caution should be exercised when interpreting results obtained for these six predictors.
Descriptive statistics for all 29 parameters are displayed in Table 1. Normally distributed variables are reported as the mean ± standard error, whereas non-normally distributed data are presented as the median and interquartile range. Results for gender-sensitive parameters are listed separately for males and females.
Initially, we investigated the impact of each individual parameter (referred to as independent variables or predictors or factors) on the four spirometry variables (FVC, FEV1, FEV1/FVC, and FEF50%). Opting for a simple general linear model proved to be the most appropriate method for modelling a single independent quantitative variable with multiple quantitative dependent

variables (the predictor itself, age, and sex). Moreover, utilizing the data in their original, non-standardized form would hinder direct comparisons across different independent variables due to disparities in their scales. Additionally, such variables would not facilitate comparative assessments of the effects of one independent variable in relation to another within the model. Consequently, the general linear model was conducted using standardized variables. This approach yielded standardized regression coefficients (betas), which denote the alteration in the dependent variable associated with a one-unit change in the corresponding independent variable, while maintaining other variables constant. These coefficients quantitatively capture the influence of each independent variable, delineating both its direction and magnitude.

The results of the general linear model for FVC, FEV1, FEV1/FVC, and FEF50% are presented in *Tables S1-S4* in the *Supplementary Material*, respectively, accompanied by Figure 1, as well as *Figures S1-S4* provided in the *Supplementary Material*. Positive standardized beta coefficients are highlighted in blue in *Tables S1-S4*, while negative beta coefficients are marked in red. Predictors with non-statistically significant beta coefficients are indicated in black. For more detailed information on the general linear model conducted, one can refer to the program outputs provided in the *Supplementary Material*.

The systematic presentation of all quantitative data presented in Tables S1-S4 has been qualitatively organized in Table 2. Table 2 categorizes the predictors for all four spirometry parameters into strong, moderate, and weak (both positive and negative) categories. Strong predictors are defined as those with an absolute value of the beta coefficient greater than 0.5 ($|\beta| > 0.5$), moderate predictors are those with a beta coefficient value between 0.3 and 0.5 in absolute terms ($0.3 \quad |\beta| \quad 0.5$), and weak predictors are those with an absolute value of the beta coefficient less than 0.3 ($|\beta| < 0.3$).

As anticipated, a general linear model analysis demonstrated a strong positive association among all four spirometry parameters, indicating a high degree of mutual correlation. The 6MWD emerged as a weak positive predictor for FEV1/FVC and FEF50%, but a strong positive predictor for FVC and FEV1. These findings are consistent with previous studies that have also reported a positive association between 6MWD and spirometry variables [23-25].

Moderately positive predictors of FEV1 and FEV1/FVC include DLCO%, PO_2, a-Sa(Hb)-O_2%, and t-Sa(Hb)-O_2%. Several studies have reported positive associations between DLCO% and spirometry parameters [26-29]. All these studies provide robust support for the positive relationships between DLCO% and various spirometry parameters, confirming the findings in this study. Moreover, lower DLCO% and lower FEV1 were associated with significantly increased morbidity in COPD patients compared to the reference group [30]. The positive relationship between oxygenation parameters (PO_2, a-Sa(Hb)-O_2%, and t-Sa(Hb)-O_2%) and spirometry values is a well-documented concept in the field of pulmonary medicine

[23,31,32]. Additionally, FFMI was shown to be a weak positive predictor for all four spirometry outcomes, while SMMI was a weak positive predictor for FEV1 and FEV1/FVC. There is considerable evidence that both FFMI and SMMI have a positive impact on spirometry outcomes [33-35], although their predictive strength can be weak, especially in the context of multifactorial influences in COPD patients.

BMI was identified as a weak positive predictor of FEV1 and FEV1/FVC. However, the beta coefficients for BMI in relation to FVC and FEF50% were not statistically significant. These findings are consistent with our previously reported results, indicating that FEV1, FEV1/FVC, and DLCO values in pulmonary function tests were significantly higher in obese COPD patients compared to non-obese patients, whereas the FVC values were similar across all groups [21]. This outcome is commonly documented among individuals diagnosed with chronic obstructive pulmonary disease [36-39].

Regarding negative predictors, strong negative predictors for spirometry outcomes include smoking-related factors, such as the number of years of smoking, pack-years, and smoking status. It is also evident that the BODE index and GOLD classification, relying extensively on FEV1 measurements, demonstrate significant negative influence on spirometry parameters. Age and duration of illness have emerged as moderate negative predictors for spirometry readings, aligning with established findings in the field [40-42]. SGRQ-C, PCO_2, CAT, and mMRC were found to be weak predictors, consistent with previously published findings [43-46].

Factors such as the number of comorbidities, CCI, and PhA were found to have no significant impact on spirometry outcomes. Several studies have explored the relationship between these parameters and spirometry outcomes, yielding mixed results. For instance, the number of comorbidities, as measured by tools such as the CCI, has been reported to have varying impacts on spirometry outcomes. While some research indicates no significant effect, others suggest correlations between higher comorbidity scores and poorer lung function [47,48]. Phase angle, a parameter derived from bioelectrical impedance analysis and often used as an indicator of nutritional status and overall health, has similarly been studied for its potential impact on lung function. Again, findings are mixed, with some studies indicating significant associations with spirometry variables, while others not [49,50]. These discrepancies highlight the complexity of understanding how these factors influence respiratory health and suggest that further research is needed to clarify these relationships and their underlying mechanisms.

To further explore the issues being investigated, our objective was to develop a predictive model for the spirometry variables under consideration. Despite predictive models traditionally serving as indicators for the onset of illness, the development of predictive regression models among patients already affected by illness can prove highly advantageous. This approach holds

significant potential for enhancing healthcare outcomes, optimizing resource management, and improving the effectiveness of medical interventions.

Particularly, our goal was to establish a predictive model using a reduced set of the most impactful predictors to select the best subset of predictors from a larger set of predictors. To achieve this, we employed stepwise regression, a method that sequentially selects predictors based on some statistical criteria. To mitigate bias in variable selection inherent to the stepwise method and to isolate the influence on each spirometry outcome from factors independent of the spirometry test itself, we initially excluded five predictors highly correlated with each spirometry variable. These predictors encompassed the remaining three spirometry outcomes, as well as the BODE and GOLD (I-IV) scores, which integrate FEV1 within their scoring systems.

The results of the linear regression model using the stepwise method are presented in Table 3. Indication I pertain to the stepwise regression conducted with standardized variables, aiming to determine comparable beta coefficients. Positive predictors of FVC, FEV1, and FEV1/FVC are indicated in blue in the table, while negative predictors are highlighted in red. As expected, excluding five influential factors affecting the spirometry variables under investigation led to a decrease in the adjusted R-squared, which remains around 0.65 across the three models presented. The R-squared for modelling FEF50% was below 0.5, thus rendering this analysis unreliable, and it has been excluded. In Table 3, indication II denotes the results of stepwise regression analysis conducted on unstandardized variables, aimed at establishing practical regression equations (1), (2), and (3), which can be found in the *Supplementary Material*.

After excluding five spirometry-related parameters, FFMI and 6MWD emerge as the stronger positive predictors for all three spirometry readings considered in the modelling. Other positive predictors include DLCO% and a-Sa(Hb)-O_2%. PO_2 is a statistically significant positive predictor for FVC, while BMI is a significant positive predictor for FEV1 and FEV1/FVC. The strongest negative predictor of spirometry variables is smoking years, with other statistically significant negative predictors including age, illness duration, mMRC, CAT, PCO_2, and SGQR-C.

To mitigate the complexity and intricacy associated with data processing and foster a more profound comprehension of interrelationships among variables within a dataset, factorial analysis is undertaken. Based on the scree plot (see *Supplementary Material*), it has been demonstrated that selecting five factors represents the optimal choice. This selection ensures a balanced representation of underlying structures while effectively capturing a satisfactory amount of variance (62%) within the dataset. After the initial extraction of factors in factor analysis, varimax rotation is employed to simplify and enhance the interpretability of the factor

structure by maximizing the variance of squared loadings on each factor and ensuring orthogonality among factors.

Rotated factor loadings and communalities following varimax rotation are displayed in Table 4. The highest factor loadings for Factor 1 include spirometry parameters, BODE, GOLD (I-IV), a-Sa(Hb)-O_2%, t-Sa(Hb)-O_2%, PO_2, PCO_2, DLCO%, and KCO%. Based on this, Factor 1 can be concluded to be associated with lung function. Factor 2 exhibits highest loadings for CAT, DASS, mMRC, SGRQ-C, and NRS-2002, broadly reflecting health status of the patients. Factor 3 is characterized by highest loadings for FFMI, SSMI, BMI, and PhA, indicating its association with nutritional status. Factor 4 appears to be linked to age, as reflected by the highest loadings of age, illness duration, CCI, and 6MWD. Lastly, Factor 5 clearly pertains to smoking, with the highest loadings for pack-years, smoking years, and smoking status. Ultimately, factor analysis divided the 29 variables under consideration into five factors, respectively related to lung function (Factor 1), health status (Factor 2), nutritional status (Factor 3), age (Factor 4), and smoking (Factor 5). The highest loadings for each factor are highlighted in bold in Table 4, with different colours indicating each factor (Factor 1 – black, Factor 2 – blue, Factor 3 – red, Factor 4 – green, Factor 5 – purple).

Following factorial analysis, four new variables were generated: health status (Factor 2), nutritional status (Factor 3), age (Factor 4), and smoking (Factor 5). This was achieved by combining individual variables with the highest loadings within each factor. Specifically, each given variable was multiplied by its respective loading; the products of the loadings and variable values were summed and then divided by the sum of the loadings, considering the sign of the loadings. This procedure was undertaken to create a new model for three pulmonary variables (FVC, FEV1, FEV1/FVC), with the four newly created variables serving as predictors. The variables from Factor 1 were not consolidated into a new variable since they exhibit strong intercorrelations and are related to lung function, like the variables for which the model is being developed.

The results of the multiple linear regression with the four newly formed predictors are presented in Table 3, indicated by indicator III. As can be observed, for all three spirometry variables, the results are consistent — nutritional status (Factor 3) is a positive predictor of spirometry outcomes, while poorer health status, age, and smoking are negative predictors. It is important to note that in mathematical terms, an increase in the health status variable (mMRC, CAT, DASS, SGRQ-C, and NRS-2002) corresponds to a decrease in the dependent variables (FVC, FEV1, FEV1/FVC).

In conclusion, following the factorial analysis and multiple linear regression conducted with the four newly formed factors, it can be stated that spirometry outcomes are most significantly influenced by smoking (negatively), followed by poor health status (negatively), nutritional

status (positively), and finally age (negatively). The regression equations for FVC (4), FEV1 (5), and FEV1/FVC (6) can be found in the *Supplementary Material*.

Conclusions

In the current study, encompassing a large cohort of 534 COPD patients from five distinct centers in Croatia, the prediction of spirometry functional test parameters (specifically FVC, FEV1, FEV1/FVC, and FEF50%) was conducted, involving 29 different variables. This prediction was achieved through the application of several statistical methods, including a general linear model, stepwise regression, and subsequent multiple regression models followed by the results of factorial analysis.

Although the findings of the study align with established knowledge regarding factors influencing spirometry pulmonary test parameters in patients diagnosed with COPD, it is important to note that this study precisely determined the magnitude of these variables' impacts, as well as predictive models for spirometry outcomes in patients already diagnosed with COPD.

The study also demonstrated that smoking has the most detrimental effect on spirometry variables, followed by poor health status, and then the age of the patients. Good nutritional status positively affects spirometry variables. However, patients with a higher BMI exhibit better FEV1 and FEV1/FVC outcomes as has been documented in a considerable number of studies."

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Online supplementary material:
Table S1. Predictors of forced vital capacity.
Table S2. Predictors of forced expiratory volume in one second.
Table S3. Predictors of forced expiratory volume in one second/forced vital capacity ratio.
Table S4. Predictors of forced expiratory flow at 50% of forced vital capacity.
Figure S1. Patient flow chart.
Figure S2. Standardized beta coefficients with 95% confidence intervals for the effect of various predictors on FEV1. Only statistically significant predictors are shown.
Figure S3. Standardized beta coefficients with 95% confidence intervals for the effect of various predictors on FEV1/FVC. Only statistically significant predictors are shown.
Figure S4 forced expiratory volume in one second. Standardized beta coefficients with 95% confidence intervals for the effect of various predictors on FEF50%. Only statistically significant predictors are shown.
Supplementary material. Computer outcomes for forced vital capacity in relation to predictor, age and sex.

Table 1. Descriptive statistics of measured variables.

Variable	
Age (years)	66.65±0.36
BMI (kg/m^2)	26.36±0.24
Diagnosis (years)	5.00 (3.00)
Smoking (years)	35.00 (10.00)
Pack–year	45.00 (17.50)
FVC (L) – total	2.81±0.04
FVC (L) – men	3.14±0.05
FVC (L) – women	2.30±0.05
FEV1 (L) – total	1.45±0.03
FEV1 (L) – men	1.60±0.04
FEV1 (L) – women	1.22±0.04
FEV1/FVC – total	0.52±0.01
FEV1/FVC – men	0.50±0.01
FEV1/FVC – women	0.54±0.01
FEF50% – total	23.31±0.78
FEF50% – men	22.47±0.84
FEF50% – women	24.63±1.51
DLCO%	57.56±0.90
KCO%	68.99±1.00
t–Sa(Hb)–O_2%	94.52±0.12
a–Sa(Hb)–O_2%	94.07±0.11
PO_2 (mmHg)	72.57±0.45
PCO_2 (mmHg)	39.49±0.25
6MWD (m) – total	396.53±4.80
6MWD (m) – men	397.07±6.18
6MWD (m) – women	395.70±7.65
Number of comorbidities	2.00 (1.00)
FFMI – total	19.88±0.14
FFMI – men	20.60±0.16
FFMI – women	18.75±0.27
PhA – total	6.00 (1.10)
PhA – men	6.00 (1.00)
PhA – women	5.75 (1.50)
SMMI	7.73±0.06
SMMI – men	8.23±0.08
SMMI – women	6.94±0.07
GOLD(I–IV)	2.00 (1.00)
mMRC	2.00 (1.00)
CAT	15.00 (10.00)
DASS	10.00 (14.00)
SGRQ–C	39.12 (31.00)
NRS–2002	1.00 (2.00)
BODE	3.00 (3.00)
CCI	4.00 (1.00)

BMI, body mass index; diagnosis, number of years since first diagnose; FVC, forced vital capacity; FEV1, forced expiratory volume in one second; FEV1/FVC, FEV1/FVC ratio; FEF50%, forced expiratory flow at 50% of FVC; DLCO%, predicted diffusing capacity for carbon monoxide; KCO%, predicted carbon monoxide transfer coefficient; t-Sa(Hb)-O_2%, tissue hemoglobin oxygen saturation percentage; a-Sa(Hb)-O_2%, arterial hemoglobin oxygen saturation percentage; PO_2, arterial partial pressure of oxygen; PCO_2, arterial partial pressure carbon dioxide; 6MWD, 6-minute walk distance; FFMI, adjusted fat–free mass index; PhA, phase angle; SMMI, skeletal muscle mass index; GOLD(I-IV), global initiative for chronic obstructive lung disease; mMRC, modified medical research council; CAT, COPD assessment test; DASS, depression anxiety stress scales; SGRQ-C, St George's respiratory questionnaire; NRS-2002, nutritional risk screening; BODE, body mass index/airflow obstruction/dyspnea/exercise capacity index; CCI, Charlson comorbidity index.

Table 2. **Predictors of forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FEV1/FVC, and forced expiratory flow at 50% of FVC.**

	FVC	**FEV1**	**FEV1/FVC**	**FEF50%**
strong positive predictors	FEV1	FVC FEV1/FVC FEF50%	FEV1 FEF50%	FEV1 FVC FEV1/FVC
moderate positive predictors	6MWD FEF50%	6MWD DLCO% PO_2 t–Sa(Hb)–O_2% FFMI	DLCO% KCO% t–Sa(Hb)–O_2% PO_2 a–Sa(Hb)–O_2%	—
weak positive predictors	FFMI PO_2 a–Sa(Hb)–O_2% FEV1/FVC DLCO% t–Sa(Hb)–O_2%	KCO% a–Sa(Hb)–O_2% SMMI BMI	FVC FFMI 6MWD BMI SMMI FVC	DLCO% PO_2 KCO% t–Sa(Hb)–O_2% a–Sa(Hb)–O_2% 6MWD FFMI PhA
strong negative predictors	Smoking years Pack–year Smoking status GOLD (I–IV)	GOLD (I–IV) BODE Pack–year Smoking status Smoking years	GOLD (I–IV) Smoking years Smoking status BODE Pack–year	Pack–year Smoking years Smoking status GOLD (I–IV)
moderate negative predictors	BODE Age	mMRC Diagnosis SGRQ–C Age	Diagnosis mMRC SGRQ–C	BODE Diagnosis Age
weak negative predictors	CAT mMRC SGRQ–C PCO_2 DASS	CAT PCO_2 Diagnosis DASS	CAT Age NRS–2002 PCO_2 DASS	mMRC SGRQ–C CAT PCO_2 NRS–2002
not statistically significant	KCO% PhA CCI SMMI NRS–2002 BMI Comorbidities Diagnosis	NRS–2002 CCI Comorbidities PhA	CCI Comorbidities PhA	Comorbidities CCI BMI SMMI DASS

Table 3. The results of statistical modeling using stepwise regression and multiple linear regression following factorial analysis.

STAT. METHOD*	INDEP. VAR.	DEP. VAR.**	BETA	SE	p	R^2 adj (%)	REGR. EQUAT.
I	FVC	FFMI	0.358	0.060	0.000	67.50	
		6MWD	0.280	0.037	0.000		
		PO_2	0.212	0.051	0.000		
		DLCO%	0.145	0.052	0.005		
		a–Sa(Hb)–O_2%	0.079	0.034	0.020		
		mMRC	–0.116	0.035	0.001		
		CAT	–0.122	0.036	0.001		
		Age	–0.147	0.036	0.000		
		SMMI	–0.167	0.035	0.000		
		PCO_2	–0.168	0.033	0.000		
		Smoking years	–0.558	0.034	0.000		
II							(1)
I	FEV1	FFMI	0.243	0.046	0.000	67.76	
		6MWD	0.216	0.054	0.000		
		DLCO%	0.175	0.039	0.000		
		a–Sa(Hb)–O_2%	0.134	0.038	0.000		
		BMI	0.104	0.053	0.014		
		Diagnosis	–0.093	0.039	0.018		
		mMRC	–0.095	0.046	0.041		
		CAT	–0.113	0.046	0.014		
		Age	–0.114	0.037	0.002		
		PCO_2	–0.134	0.034	0.000		
		SGRQ–C	–0.146	0.039	0.000		
		Smoking years	–0.387	0.036	0.000		
II							(2)
I	FEV1/FVC	FFMI	0.233	0.047	0.000	65.37	
		t–Sa(Hb)–O_2%	0.199	0.046	0.000		
		6MWD	0.179	0.053	0.000		
		BMI	0.168	0.043	0.000		
		DLCO%	0.122	0.076	0.027		
		a–Sa(Hb)–O_2%	0.112	0.044	0.010		
		Diagnosis	–0.085	0.039	0.032		
		SGRQ–C	–0.132	0.053	0.012		
		DASS	–0.153	0.046	0.001		
		Age	–0.239	0.057	0.000		
		Smoking years	–0.288	0.042	0.000		
II							(3)
III	FVC	Factor 3	0.132	0.015	0.014	60.81	
		Factor 4	–0.138	0.012	0.002		
		Factor 2	–0.145	0.011	0.000		
		Factor 5	–0.242	0.018	0.000		
IV							(4)
III	FEV1	Factor 3	0.157	0.016	0.000	59.24	
		Factor 4	–0.126	0.012	0.037		
		Factor 2	–0.174	0.011	0.000		
		Factor 5	–0.220	0.019	0.000		
IV							(5)
III	FEV1/FVC	Factor 3	0.170	0.017	0.000	54.84	
		Factor 4	–0.123	0.020	0.042		
		Factor 2	–0.182	0.012	0.000		
		Factor 5	–0.207	0.013	0.000		
IV							(6)

Factor 2, HEALTH STATUS; Factor 3, NUTRITION STATUS; Factor 4, AGE; Factor 5, SMOKING. *Parameters strongly related to independent variable (the rest of the three spirometry parameters, BODE and GOLD(I–IV)) have been excluded in regression models as predictors; ** only statistically significant predictors are shown. I, stepwise regression with standardized variables; II, stepwise regression with unstandardized variables; III, multiple linear regression (using four new parameters from factorial analysis as predictors) with standardized variables; IV, multiple linear regression (using four new parameters from factorial analysis as predictors) with unstandardized variables. STAT. METHOD, statistical method; INDEP. VAR., independent variable; DEP. VAR., dependent variable; SIGNIF. PREDIC., predictor with statistically significant beta; p, p–value; SE, standard error for beta; REGR. EQUAT., multiple regression equation.

Table 4. Rotated factor loadings and communalities (varimax rotation).

	Variable	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Communality
1	Age	–0.026	–0.133	–0.017	**0.852**	0.042	0.747
2	BMI	–0.007	–0.038	**0.844**	0.012	–0.140	0.733
3	Smoking status	0.162	0.034	–0.129	–0.411	**0.533**	0.497
4	Smoking years	–0.023	0.033	–0.009	0.094	**0.782**	0.743
5	Pack–year	–0.096	0.044	0.078	0.122	**0.856**	0.644
6	Diagnosis	–0.109	0.194	–0.100	**0.384**	–0.131	0.224
7	mMRC	–0.390	**0.694**	–0.007	0.108	0.076	0.652
8	CAT	–0.215	**0.757**	–0.008	0.030	–0.038	0.621
9	GOLD(I–IV)	**–0.776**	0.206	–0.087	0.087	0.045	0.661
10	FVC	**0.520**	–0.115	0.084	–0.261	0.390	0.450
11	FEV1	**0.834**	–0.172	0.093	–0.090	–0.050	0.745
12	FEV1/FVC%	**0.714**	–0.114	0.200	–0.106	–0.219	0.621
13	FEF50%	**0.539**	–0.116	0.101	–0.172	–0.157	0.368
14	DLCO%	**0.496**	–0.218	0.445	0.017	–0.287	0.575
15	KCO%	**0.345**	–0.203	0.482	0.207	–0.344	0.554
16	t–Sa(Hb)–O_2%	**0.577**	–0.050	–0.054	–0.095	0.030	0.348
17	a–Sa(Hb)–O_2%	**0.705**	0.117	–0.073	0.188	0.121	0.566
18	PO_2	**0.699**	0.118	–0.048	0.122	0.120	0.534
19	PCO_2	**–0.339**	0.066	0.131	–0.016	–0.113	0.149
20	6MWD	0.371	–0.389	–0.068	**–0.407**	0.017	0.459
21	Comorbidities	–0.013	0.265	**–0.518**	–0.246	0.040	0.401
22	DASS	0.045	**0.758**	–0.055	0.017	0.056	0.583
23	SGRQ–C	–0.338	**0.690**	0.006	0.027	0.062	0.596
24	NRS–2002	0.128	**0.634**	0.041	–0.107	–0.018	0.431
25	BODE	**–0.659**	0.469	–0.182	0.201	0.054	0.730
26	CCI	0.006	–0.099	0.043	**0.776**	0.046	0.617
27	SMMI	–0.047	0.002	**0.868**	–0.039	0.064	0.761
28	PhA	0.054	0.065	**0.353**	–0.115	0.078	0.151
29	FFMI	–0.048	–0.015	**0.869**	0.004	0.039	0.759
	Variance	5.058	3.290	3.002	2.298	2.207	15.855
	% Variance	0.184	0.133	0.124	0.091	0.088	0.616

Factor 1, lung function; factor 2, health status (questionnaires and tests – higher values indicate poorer health status); factor 3, nutritional status; factor 4, age; factor 5, smoking.

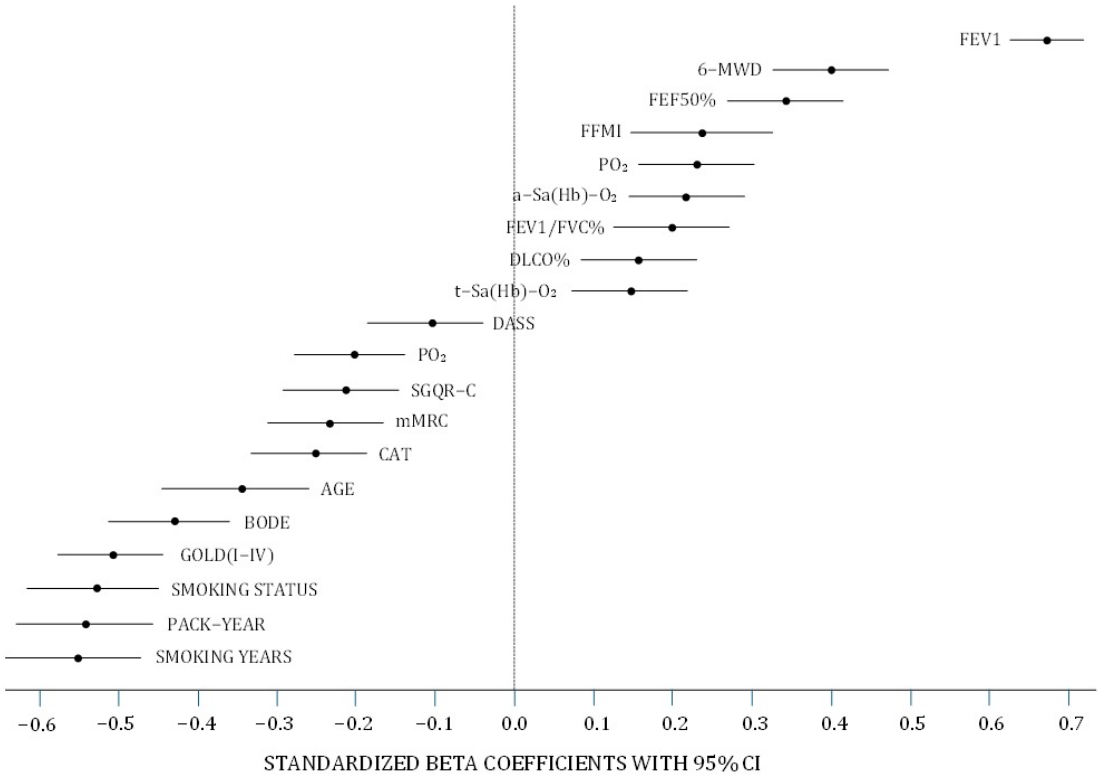

Figure 1. Standardized beta coefficients with 95% confidence intervals for the effect of various predictors on forced vital capacity. Only statistically significant predictors are shown.