

The Impact of Body-Weight Components on Forced Spirometry in Healthy Italians

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Abstract. Many studies have investigated lung function in relation to age and height among Caucasians, however, most of these studies did not consider the individual components of body weight. The objective of the present study was to study the effect of body weight components [bone-free lean body mass (BF-LBM), bone mineral content (BMC), and fat mass (FM)] measured by dual x-ray absorptiometry (DXA) on the lung-function variables (FVC, FEV1, and PEF) and to derive prediction equations for these variables in healthy adult Italians. Dynamic spirometric tests and body composition analysis by DXA were performed on 58 nonsmoking males, mean age (\pm SE) 26.72 ± 1.98 years and BMI 25.51 ± 0.64 kg/m², and 60 nonsmoking females matched for age and BMI (29.61 ± 1.65 years and 26.45 ± 1.05 kg/m², respectively). Bivariate linear regression analysis showed the variables age, height, BF-LBM, BMC, and the interaction term BF-LBM*Height, but not weight and FM, to correlate significantly with lung-function variables for males and for females separately. Multiple linear regression analysis showed that sex, age, height, and BF-LBM*Height were significantly associated with FVC, FEV1, and PEF. The prediction equations developed for FVC, FEV1, and PEF on the basis of the independent variables i.e. sex, age (y), height (m), and BF-LBM*Height (kg · m) had a significantly higher cumulative correlation coefficient and a lower SEE compared with those based on age and height only. The present report suggests that the BF-LBM, expressed independently from height, can be considered for predicting lung-function variables.

Key words: Body Composition—Bone-free lean body mass—Dual X-ray absorptiometry—Prediction equation

Introduction

Dynamic spirometric tests are commonly used in assessing respiratory status, and they have become part of routine health examinations in occupational and sports medicine, public-health screening, and clinical case management [1]. The results of spirometric tests are interpreted in relation to normal-range reference values [4], yet they can be affected by many sorts of variations (e.g., procedure, observer bias, and biological variations within an individual, among individuals, and among populations). With regard to inter-individual variability in lung function, the most important determinants are sex, size, aging, race, and current and past health. Other determinants of variability include environmental factors such as geographic, exposure to environmental and occupational pollution (e.g., active and passive smoking), and socioeconomic status [1, 28, 30].

Although many studies have investigated lung function in relation to age and height among Caucasians [14, 19, 25, 26, 28, 29], and lung-function reference values have been reported for a variety of race/ethnic groups and age ranges in males and females [3, 7, 9, 16, 21, 33], only weak or nonsignificant associations have been observed for body weight and body mass index (BMI) after accounting for the effects of age and height in linear regression models [1, 8, 23]. However, these studies did not consider the individual components of body weight. Only one study [23] has evaluated the effect of these components [i.e., fat mass (FM) and fat-free mass (FFM)], yet they were estimated on the basis of skinfold thickness measurements. The importance of the quantity and distribution of FM [5] has been recognized in a range of chronic diseases, including cardiovascular disease and abnormalities of glucose tolerance (diabetes and insulin resistance) [10], and FFM has been found to be associated with immune competence, functional status, and survival [31].

The objectives of this study were to investigate the relation between lung-function variables [i.e., forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and peak expiratory flow (PEF)] and body weight components measured by dual x-ray absorptiometry (DXA) [i.e., bone-free lean body mass (BF-LBM), bone mineral content (BMC), and FM], in addition to age and height, and, based on this relation, to develop prediction equations for calculating normal-range spirometric reference values for Italian adults. These equations will contribute to the understanding of the influence of body muscular mass and fat-mass distribution on lung function.

Methods

Study Population

The study population consisted of healthy, nonsmoking Italian Caucasian volunteers aged 18–58 years living in Rome. The age range was comparable to those reported in two previous studies of Caucasian

(Italian and Spanish) populations [26, 29]. The population was comprised of 58 men [mean age (\pm SE) 26.72 ± 1.98 years, BMI 25.51 ± 0.64 kg/m²] and 60 women matched for age (29.61 ± 1.65 years) and BMI (26.45 ± 1.05 kg/m²), respectively. Volunteers were recruited randomly from among persons participating in various health programs carried out at the Human Physiology Division of the University of Rome "Tor Vergata." Informed written consent was obtained from all participants. The Ethics Committee of the University of Rome "Tor Vergata" approved the study protocol.

All participants had clinical examinations before undergoing spirometry. Following the American Thoracic Society (ATS) recommendations [1], the exclusion criteria were tobacco smoking (whether current or past, including occasional), current or past cardiorespiratory or abdominal symptoms (i.e., chronic cough, wheezing, hemoptysis, dyspnea), neuromuscular disease, thoracic wall deformities, pregnancy, high-risk for occupational lung disease, a known systemic disease, and drug use.

Lung-Function Measurements

Dynamic spirometric tests were performed using a portable open-circuit spirometer (KIT-Cosmed spirometer, Cosmed, Rome, Italy), which was known to fulfill the ATS recommendations [2, 11]. To obtain precise measurements, the instrument was calibrated for every individual as recommended by the manufacturer. The individuals were seated and fitted with a nose clip, and were told to avoid extension or flexion of the neck. The individuals were also instructed to perform three acceptable and reproducible maneuvers, ensuring that they produced the highest possible peak flows and that the expiration continued for ≥ 6 sec, as recommended by the ATS and ERS [2, 28]. Measurements were obtained for men and women in a randomized order to avoid any sequence effect. A single physician (C. Maiolo) performed the flow/volume spirometry for all participants, which ensures an intra-observer coefficient of variation for FEV₁ during the study period as low as 2.5%–5.0%, with a mean value of 4.0%.

The best of three repeated forced expiratory maneuvers obtained from maximum expiratory flow volume was considered for FVC and FEV₁ analysis [1]. The largest two FVC from acceptable tests were compared and the largest two measures of FEV₁ were compared and their respective differences did not exceed 200 ml [2]. The PEF was measured on the basis of the flow-volume curve with the largest sum of FVC and FEV₁. The operator used the computer during the test, it provided feedback messages, which allow for the on-line control of compliance with ATS criteria [2]. Individuals who had FEV₁/FVC < 76% were excluded from the study population, their data were applied to a comparable Italian population in a previous study [26].

Anthropometric and Body-Composition Measurements

Anthropometric and body-composition variables were measured for all participants. Specifically, body weight (kg) (participants clothed in underwear, bare feet) was measured using a digital scale sensitive to the nearest 0.01 kg (Body Master, Rowenta, Germany). Height (m) was measured using a stadiometer. BMI was calculated as weight/height² (kg/m²). Total BF-LBM, total BMC, and total FM were measured using DXA total body scan (Lunar DPX Densitometer, Lunar Radiation Corp., Madison, WI, USA) as previously detailed for standard measurements in our laboratory [12].

Statistical Analysis

Data analysis was carried out using the StatView statistical software package (SAS Institute Inc., NC, USA). Descriptive statistics were calculated for all relevant variables and their frequency distributions were examined. Analysis of the continuous variables showed them to be normally distributed. Unpaired Student's *t*-test of significance was used to compare differences between male and female

participants for various variables (anthropometric, body composition, and respiratory). Differences were considered to be significant at $p \leq 0.05$.

Bivariate linear regression analysis was performed to examine the interrelations among variables using simple and partial correlation coefficients (R). The associations between each forced spirometric variable (i.e., FVC, FEV1, and PEF) and anthropometric variables (i.e., sex, age, weight, and height) and body-composition variables (BF-LBM, BMC, and FM) in various powers and interactions were modeled using multiple linear regression analysis. Statistical significance and fraction of explained variability of lung function were the main criteria for selecting independent variables. To reduce collinearity among higher order and cross-product terms, the independent variables were centered by subtracting the variable mean from its observed values, as explained elsewhere [21]. The assumptions for linearity were also tested. Significance was accepted at $p \leq 0.05$ for single terms and $p \leq 0.10$ for interaction terms. The regression coefficient (β), standard error of estimation (SEE), and significance level (p) were determined for independent variables added simultaneously.

To investigate the complementary effects of BF-LBM and other body-weight components (i.e., BMC and FM) on the fraction of observed variability of lung-function variables, sensitivity analysis with each variable added separately to the initial regression model were carried out. The effect of other confounding variables [e.g., age² and ln (height)], which have been previously shown to contribute significantly to the explained variance of lung-function variables [21], was also investigated. Based on these analyses, gender-specific prediction formulae for FVC, FEV1, and PEF based on two independent variables (i.e., age and height) as well as prediction equations based on four independent variables (i.e., sex, age, height, and the interaction term BF-LBM*Height) were developed and their cumulative correlation coefficients (R) and SEE were calculated. Sex was included as a variable in the final prediction equations, which was coded as 1 for men and 2 for women, to avoid developing separate prediction equations of every lung-function variable for males and for females. The prediction equations were used to simulate observed FVC, FEV1, and PEF measurements and the difference between predicted and observed values was given as mean squared. Errors generated by the prediction equations were calculated using the weighed sum of squared errors (χ^2) formula [20], given by

$$\chi^2 = \sum_{i=1}^n [(SV_i(Pred) - SV_i(Obs))/\sigma_i]^2 \quad (1)$$

where $SV_i(Pred)$ and $SV_i(Obs)$ are the predicted and observed forced spirometric variable, respectively, and σ_i is the standard error of $SV_i(Pred)$. Prediction plots for the forced spirometric variables as a function of BF-LBM were produced for male and female participants of average age and height.

Results

The characteristics of the study participants are presented by gender in Table 1. Significant differences between males and females were found for the weight ($p < 0.05$) and its components (i.e., FFM and FM). Males had a significantly higher FFM (65.82 ± 1.24 kg, compared with 43.42 ± 0.93 kg for females, $p < 0.0001$) and a significantly lower FM (13.64 ± 1.63 kg compared with 25.39 ± 2.52 kg for females, $p < 0.0001$), indicating that FFM (the sum of BF-LBM and BMC) and FM depend on gender. The forced spirometric variables (i.e., FVC, FEV1, and PEF) were also significantly higher for males than for females ($p < 0.0001$).

The bivariate linear regression analysis showed that the variables age, height, BF-LBM, BF-LBM*Height, and BMC, but not weight and FM, were correlated significantly ($p < 0.0001$ for all associations) with FVC ($R = 0.30, 0.75, 0.65, 0.80$, and 0.65 , respectively, for males and $R = 0.59, 0.68, 0.35, 0.49$, and 0.45 , re-

Table 1. Anthropometric, body composition, and forced spirometric variables of the studied participants

	Males (58)		Females (60)	
N				
Age (year)	26.72 ± 1.98	(18.00–58.00)	29.61 ± 1.65	(19.00–42.00)
Weight (kg)	79.76 ± 1.96*	(61.00–102.00)	71.09 ± 2.90	(47.70–97.00)
Height (m)	1.77 ± 0.01**	(1.65–1.96)	1.64 ± 0.01	(1.56–1.78)
BMI (kg/m ²)	25.51 ± 0.64	(19.25–34.48)	26.45 ± 1.05	(18.31–34.68)
BF-LBM (kg)	62.28 ± 1.19**	(51.19–75.54)	40.91 ± 0.89	(33.41–51.46)
BMC (kg)	3.54 ± 0.09**	(2.58–4.73)	2.50 ± 0.06	(2.02–3.20)
FFM (kg)	65.82 ± 1.24**	(54.11–79.40)	43.42 ± 0.93	(35.68–54.65)
FM (kg)	13.64 ± 1.63**	(4.41–42.78)	25.39 ± 2.52	(3.34–48.55)
FVC (L)	5.32 ± 0.15**	(3.61–7.52)	3.66 ± 0.10	(2.68–4.62)
FEV1 (L)	4.34 ± 0.11**	(3.00–5.43)	2.89 ± 0.07	(2.06–3.51)
PEF (L/sec)	9.51 ± 0.32**	(6.29–12.46)	5.65 ± 0.26	(3.99–8.90)

Values are expressed as mean ± SE and numbers in brackets are variable ranges (minimum-maximum).

* $p < 0.05$ and ** $p < 0.0001$ vs females.

BMI: body mass index, BF-LBM: bone-free lean body mass, BMC: bone mineral content, FFM: fat free mass, FM: fat mass, FVC: forced vital capacity, FEV1: forced expiratory volume in 1 second, PEF: peak expiratory flow.

spectively, for females). Similar correlations were found for the same variables with FEV1 and PEF for males and for females. Sensitivity analysis of the weight and its components (i.e., BF-LBM, BMC, and FM) added separately to age and height in the initial regression model showed BF-LBM rather than FM and BMC to contribute significantly to the observed variability of FVC, FEV1, and PEF.

An initial multiple linear regression model was used to determine the effect of simultaneously adding the covariates sex, age, height, weight, BF-LBM, BF-LBM*Height, BMC, and FM on FVC, FEV1, and PEF, respectively, as the dependent variables. Table 2 shows that sex, age, height, and BF-LBM*Height were significantly associated with lung-function variables, yet neither the weight nor its components (i.e., BF-LBM, BMC, or FM), except for BF-LBM when associated with FVC, attain statistical significance for associations in the studied population. The sex and interaction term BF-LBM*Height were used in the analysis so that the results of FVC, FEV1, and PEF can be presented in a single regression model, rather than separated by sex. The variables age², ln (height), and BMI were not included in the regression model because they did not provide additional explanatory power if BF-LBM*Height was included as a covariate. Statistical analysis showed all residuals to be normally distributed.

Table 3 shows the continuous prediction equations developed for FVC, FEV1, and PEF based on 2 independent variables (age and height), for males and for females separately, and those based on 4 independent variables (sex, age, height, and BF-LBM*Height). The prediction equation based on 4 independent variables for FVC had a significantly higher cumulative correlation coefficient ($R = 0.94$, $p < 0.0001$) compared with prediction equations based on 2

Table 2. Coefficients of initial multiple linear regression for predictors of FVC, FEV1, and PEF added simultaneously

	FVC (L)		FEV1 (L)		PEF (L/sec)	
	β (SEE)	<i>P</i> Value	β (SEE)	<i>P</i> Value	β (SEE)	<i>P</i> Value
Sex (M/F)	-0.207 (0.230)	0.0051	-0.743 (0.179)	< 0.0001	-2.932 (0.740)	0.0002
Age (year)	-0.013 (0.005)	0.0046	-0.016 (0.004)	< 0.0001	-0.024 (0.015)	0.0500
Height (m)	4.522 (0.907)	< 0.0001	3.543 (0.704)	< 0.0001	4.748 (2.931)	0.0510
Weight (kg)	-0.012 (0.012)	0.3486	-0.007 (0.010)	0.4542	-0.001 (0.039)	0.9736
BF-LBM (kg)	0.037 (0.017)	0.0319	0.006 (0.013)	0.6604	-0.162 (0.120)	0.1799
BMC (kg)	0.100 (0.184)	0.5894	0.075(0.143)	0.6022	0.315 (0.592)	0.5963
FM (kg)	0.007 (0.012)	0.5631	0.008 (0.009)	0.3797	-0.007 (0.039)	0.8662
BF-LBM*						
Height	0.124 (0.037)	0.0013	0.103 (0.029)	0.0006	0.264 (0.198)	0.1076

FVC: forced vital capacity, FEV1: forced expiratory volume in one second, PEF: peak expiratory flow, β : regression coefficient, SEE: standard error of estimation, BF-LBM: bone-free lean body mass, BMC: bone mineral content, FM: fat mass. Sex is coded as 1 for males and 2 for females.

Table 3. Final prediction equations based on 2 and 4 independent variables for FVC, FEV1, and PEF of study participants

Prediction Equation	R	SEE	χ^2
2 Independent variables			
FVC = -10.212 - 0.001 \times Age + 8.786 \times Height (Males)	0.75	0.56	25.86
= -2.759 - 0.016 \times Age + 4.204 \times Height (Females)	0.77	0.37	38.57
FEV1 = -6.771 - 0.014 \times Age + 6.484 \times Height (Males)	0.84	0.35	13.47
= 0.049 - 0.016 \times Age + 2.017 \times Height (Females)	0.72	0.29	49.92
PEF = -2.840 - 0.029 \times Age + 7.391 \times Height (Males)	0.39	1.68	182.01
= 3.572 - 0.031 \times Age + 1.904 \times Height (Females)	0.42	1.07	257.90
4 Independent variables			
FVC = -1.701 - 0.284 \times Sex - 0.016 \times Age + 2.942 \times Height + 0.023 \times BF-LBM*Height	0.94*	0.43 ^o	12.77*
FEV1 = -0.237 - 0.686 \times Sex - 0.016 \times Age + 2.767 \times Height + 0.007 \times BF-LBM*Height	0.95*	0.34	11.90*
PEF = 5.907 - 3.073 \times Sex - 0.029 \times Age + 4.375 \times Height - 0.003 \times BF-LBM*Height	0.85*	1.33 ^o	35.17*

* $p < 0.0001$ vs respective 2 independent variables formulae for males and females and ^o $P < 0.05$ versus respective male formulae. FVC: forced vital capacity (*liter*), FEV1: forced expiratory volume in 1 second (*liter*), PEF: peak expiratory flow (*liter/sec*), Age (*y*), Height (*m*), BF-LBM: bone-free lean body mass (*kg*), Sex is coded as 1 for males and 2 for females. *R*: cumulative correlation coefficient, *SEE*: standard error of estimation; χ^2 : weighed sum of squared errors.

independent variables ($R = 0.75$ for males and 0.77 for females, respectively). The analysis of simulations carried out using the prediction equation based on 4 independent variables for FVC observed values, showed that the *SEE* of predictions was significantly lower than that based on 2 independent variables for males ($p < 0.05$), being comparable with that for females (0.43 versus 0.56 and 0.37, respectively). However, the χ^2 of predictions using the same 4 independent

variables equation was significantly lower than those produced using prediction equations based on 2 independent variables (12.77 versus 25.86 for males and 38.57 for females, $p < 0.0001$). Similar profiles of difference between prediction equations based on 4 independent variables and 2 independent variables were also recognized for FEV1 and PEF (Table 3).

The effect of BF-LBM*Height on FVC, FEV1, and PEF for males and females, as modeled by the prediction equations based on 4 independent variables, is shown in Figure 1. A clear separation between BF-LBM*Height levels for males and for females is evident by the dispersion plots. The solid and broken lines represent predictions computed for the average age and height for males and for females, respectively.

Discussion

We found no significant linear correlation between the forced spirometric variables FVC, FEV1, and PEF and the body weight, for males or for females, although some nonlinear association may well exist [27], yet we observed significant correlations with the weight components BF-LBM and BMC. We have developed prediction equations for the FVC (L), FEV1 (L), and PEF (L/sec) based on the independent predictors sex, age (y), height (m), and BF-LBM*Height ($\text{kg} \cdot \text{m}$).

Most mathematical equations developed to predict lung-function variables have been based on two predictors: age and height [3, 19, 26, 29], neglecting the role of body weight. Most authors [15, 18] have reported no significant association between body weight and lung function after accounting for age and height. Although the effect of body weight on lung function is detectable, the additional variance explained by body weight (or BMI) in linear regression models has been found to be modest in both adults [6] and children [22].

Lazarus et al. [23] have underlined the effect of body weight components (FFM and FM) on the lung-function variables (represented by the variable FVC) for a random population sample of male and female adult Australians. They calculated FFM and FM indirectly using published regression equations based on skinfold-thickness measurements. It is well known, as even reported by the same authors, that skinfold-thickness measurements are associated with a greater measurement error compared with available techniques for the direct evaluation of body composition (e.g., DXA). In the present report, we studied the effect of body weight components (especially BF-LBM and FM) measured using the DXA technique on the forced spirometric variables FVC, FEV1, and PEF.

It has been found previously that body weight components measured using DXA (i.e., BF-LBM, BMC, and FM) were significantly different for males than for females [12, 31], which means that these differences derive from weight and height significant differences between males and females. The BF-LBM adjusted for the effect of height (given as the cross-product term BF-LBM*Height) was accompanied by better associations with FVC, FEV1, and PEF than simple BF-LBM or BF-LBM adjusted for the effect of weight. Thus, the direct association

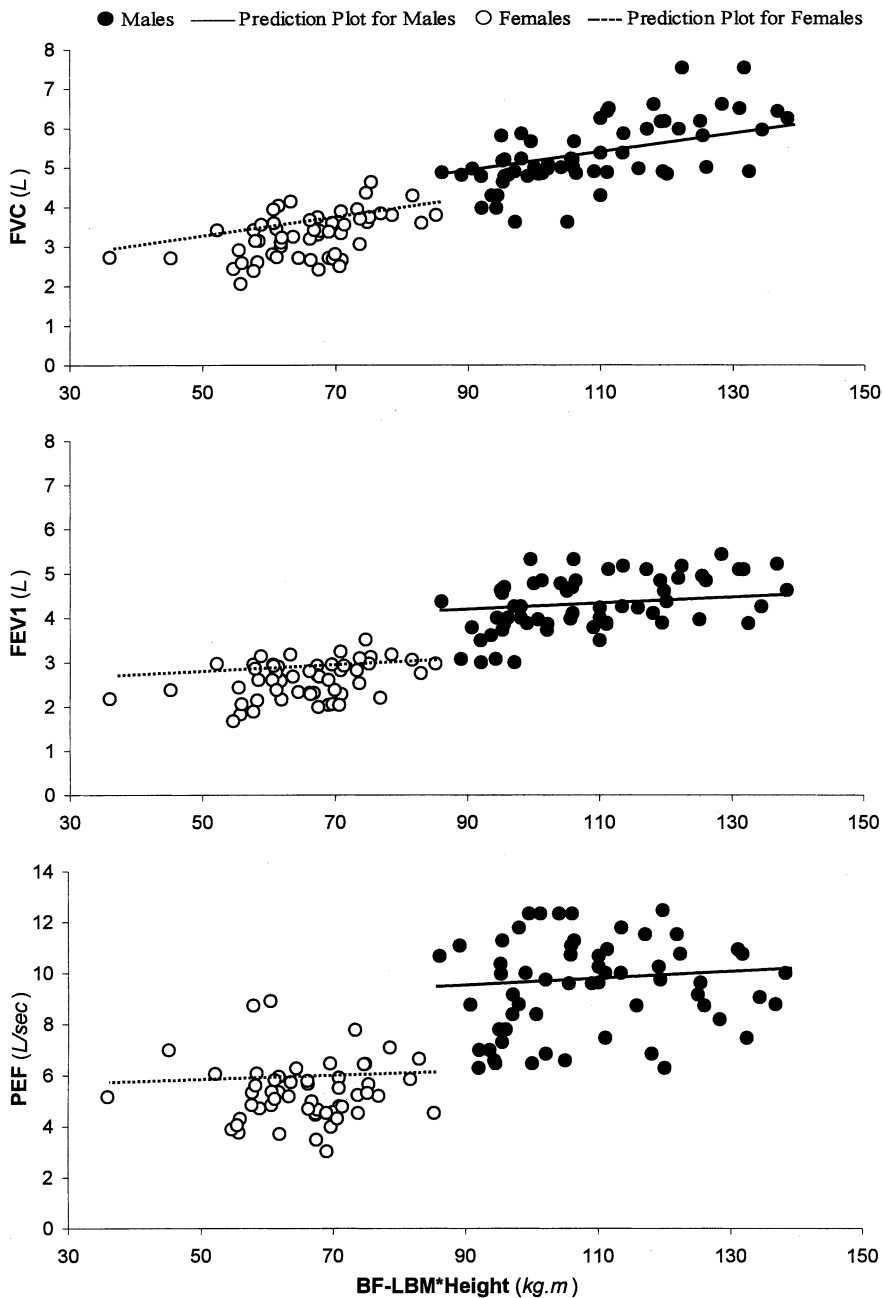


Fig. 1. Effect of the cross-product term bone-free lean body mass adjusted for the effect of height (BF-LBM*Height) on lung function variables [forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV1), and peak expiratory flow (PEF)] for male and female participants as modeled by 4 variables (sex, age, height, and BF-LBM*Height); prediction equations for average age and height for males (26.72 year and 1.77 m, respectively) and for females (29.61 year and 1.64 m, respectively).

between BF-LBM*Height and lung-function variables did not derive from the significant height and/or weight differences between males and females, but rather from the direct effect of the muscular mass. This is in line with the associations between respiratory muscle strength and ventilatory function reported previously, across all age strata for both males and females, suggesting that the association is independent of age and sex [17]. In fact, the ventilatory function requires muscular contraction to overcome air pressure on the large surface area of the chest wall.

Neither simple FM nor FM adjusted for the effect of height or weight differences between males and females were associated with FVC, FEV1, and PEF in a significant way, which confirms the fact that the effect of body fat on ventilatory function is limited to obese individuals. Furthermore, in two previous studies, we found associations between truncal fat mass and lung-function variables in healthy obese adults [13] and in type 2 diabetic obese adult women [24]. It has been proposed that fat deposits may have mechanical effects on ventilatory function [23]. We believe that the limited number of participants in the present study may also be another reason for the absence of detectable associations between FM and FVC, FEV1, and PEF for normal subjects. However, the DXA technique scans are performed by dual energy x-ray beams, even if they pose only a minimal risk of radiation [32], which heralds its wide application to much larger populations of healthy individuals.

We found that the prediction equations based on 4 independent variables were significantly correlated with FVC, FEV1, and PEF higher than those based on 2 independent variables for males and for females. We believe that this increase in the observed variability of lung function derives from the covariates sex and BF-LBM*Height. Although the two variables—age² and ln (height)—have been shown to significantly affect the observed variability of lung function [21], they were not included in the regression model of the present study because they did not provide additional explanatory power if BF-LBM*Height was included as a covariate. As shown in Figure 1, the increase in body muscular mass (BF-LBM*Height) resulted in linear increases for all lung-function variables (i.e., FVC, FEV1, and PEF) for both males and females.

To make comparisons with prediction equations in the literature, we developed prediction equations for FVC, FEV1, and PEF based on age and height. The *SEE* in our 2 independent variables prediction equations for FVC and FEV1 (0.56 and 0.35, respectively, for males and 0.37 and 0.29, respectively, for females) were comparable with those obtained from different sets of prediction equations based on the 2 independent variables (age and height) for Italians (0.58 and 0.48, respectively, for males and 0.39 and 0.29, respectively, for males) [26] and Spanish (0.53 and 0.45, respectively, for males and 0.40 and 0.32, respectively, for females) [29].

In conclusion, this is the first study, to the best of our knowledge, reporting mathematically the effect of detailed body weight components using an accurate measuring technique (DXA) on lung function variables. It underlines the effect of BF-LBM (in addition to sex, age, and height) on lung function prediction equations in healthy Italian adults. The results of this report indicate that the

BF-LBM, expressed independently from height, can be considered for predicting FVC, FEV1, and PEF.

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