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Critical view on diagnosing muscle wasting by single-frequency bio-electrical impedance in COPD

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Received 14 April 2009; accepted 7 July 2009

Available online 30 July 2009

KEYWORDS

Skeletal muscle;
COPD;
Wasting;
Assessment

Summary

Background: Assessment of muscle wasting in COPD is relevant as it is independently associated with metabolic and functional consequences and even survival. Muscle wasting can be approached by assessing fat free mass (FFM), but it is already demonstrated that FFM measured by bio-electrical impedance analysis (BIA) underestimates FFM measured by dual energy X-ray absorptiometry (FFM_{DEXA}) in a relatively small COPD group.

Objective: To evaluate critical points for defining muscle wasting in a large cohort of moderate to severe COPD patients and with DEXA scan as reference.

Design: FFM by BIA was compared with FFM_{DEXA} in 1087 COPD patients (641♂, FEV₁: 44.8 ± 17.5%pred). In a subgroup (n = 422), FFM_{DEXA} was predicted by multivariate analysis and a new formula to calculate FFM by BIA was developed. The new formula was compared with FFM_{DEXA} in the remaining subgroup (n = 665). Muscle wasting was defined according to the cut-offs of Schols et al. (FFM index (FFMI) < 16 kg/m² for men, 15 kg/m² for women), Vestbo et al. (FFMI < 17.1 kg/m² for men, 14.6 kg/m² for women), and Coin et al. (FFMI < 17.8 kg/m² for men, 14.6 kg/m² for women).

Results: There was an underestimation of FFM by BIA when compared to FFM_{DEXA} by the Bland Altman. Comparing the new formula with FFM_{DEXA}, the mean underestimation almost disappeared but the variation remained. The proportion of muscle wasting was largely dependent on the used cut-offs, especially in men.

Conclusion: The results of the present study emphasize the importance to accurately bare in mind the technique and cut-offs to establish muscle wasting before implementing it in the clinical practice.

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Introduction

Besides the respiratory disorder, chronic obstructive pulmonary disease (COPD) is nowadays generally accepted as a systemic disease.¹ Decreased skeletal muscle mass is one of the most investigated extra-pulmonary features in COPD. Indeed, an abnormal low muscle mass is present in about 40% of the patients with moderate to severe COPD entering pulmonary rehabilitation.² A comparable proportion of muscle wasting of about 30% was found in a large group of COPD outpatients with GOLD stages 2 and 3, independent of patients' body weight.³

Muscle wasting is negatively associated with exercise capacity⁴ and quality of life⁵ in COPD. Moreover, mortality rate is higher in COPD patients with muscle wasting than in those patients with preserved muscle mass, independent of the body weight.⁶ Therefore, an accurate diagnosis of muscle wasting in COPD is clinically relevant. Indeed, clinical experience indicates that assessment of body composition is increasingly embedded in the clinical management of patients with COPD. Nevertheless, the prevalence of muscle wasting is largely dependent on the used technique. The dual energy X-ray absorptiometry (DEXA) scan has been shown to be accurate for the measurement for the lean body mass in healthy subjects⁷ and in patients with COPD.^{8,9} However, this technique is rather expensive and therefore not easy to use in clinical routine. Single-frequency bio-electrical impedance analysis (BIA) is also recognized as a reliable and useful tool to assess fat free mass (FFM, a marker for skeletal muscle mass) in clinical practice.¹⁰ However, the FFM derived from this technique is dependent on the formula used. Various general and patient specific formulas are circulating, and some of them are age-dependent while others are not. Research has shown a standard underestimation of the FFM assessed by BIA when compared to the FFM assessed by DEXA scan in patients with COPD.^{11,12} So, the current COPD specific formula to estimate FFM using the BIA does not seem to be accurate enough when compared with DEXA measures. Moreover, the formula has been based on a group of only 117 COPD patients in total.¹¹ Therefore, there seems to be a clear rationale to evaluate the formula to estimate FFM by BIA in a large cohort of COPD patients. Finally, the prevalence of muscle wasting is dependent on the used cut offs. To date, various COPD specific cut offs are circulating,³ but a proof of principle is warranted.

In the present study, FFM is measured by the BIA and compared with the FFM measured by DEXA (FFM_{DEXA}) in a large cohort of clinically stable patients with moderate to severe COPD entering pulmonary rehabilitation. The DEXA scan is used as the reference method for assessing skeletal muscle mass. Using multivariate stepwise regression analysis, FFM_{DEXA} is predicted in a subgroup of the patients by using the impedance received from the BIA. The new formula obtained from the regression equation was evaluated in the remaining group and in various age groups. In addition, the proportion of muscle wasting was determined in our sample using the different techniques and using various cut-offs widely used to define muscle wasting in COPD³ and healthy elderly.⁷

Subjects and methods

Study population

Data were retrospectively collected in 1087 patients with COPD (641♂) during the screening for a pulmonary rehabilitation program at the Center of expertise for chronic organ failure (Ciro) in Horn, the Netherlands between January 2005 and June 2008.¹³ Screening takes always place before entering the pulmonary rehabilitation. Lung function parameters were collected using standardized spirometry (Masterlab®, Viasys, Germany). Diffusion capacity of carbon monoxide was assessed by single-breath method (Masterlab®, Jaeger, Germany). Current lung related medication use was as follows: fluticasone (41.8%), tiotropium (41.4%), acetyl cysteine (29.8%), combivent (formoterol and budesonide, 29.6%), salbutamol (23.9%), formoterol (21.8%), ipratropium (21.6%), dimethylxanthine (21.8%) and oral corticosteroids as maintenance dose (19.6%). All patients were clinically stable and those with clinically diagnosed edema were excluded from the study.

Body composition

Body height was measured to the nearest 0.1 cm. Body composition was assessed by using two different techniques in the post-absorptive state and within 2 days. For the BIA analysis (Bodystat®), body weight was assessed by using an electronic beam scale with digital readout to the nearest 0.1 kg after emptying the bladder and with the subjects standing barefoot and wearing light indoor clothing. Whole body impedance (expressed in Ω) was measured in each subject by lying on the bed and with separated legs. For the calculation of the FFM, the patient and sex-specific formula of Steiner et al. was used¹¹: $FFM_{men} = 8.383 + 0.465 \times \text{height}^2 / \text{impedance} + 0.213 \times \text{weight}$, $FFM_{women} = 7.610 + 0.474 \times \text{height}^2 / \text{impedance} + 0.184 \times \text{weight}$. The FFM derived from the BIA and calculated by Steiner's formula will be abbreviated as FFM_{Steiner}. Fat free mass index (FFMI) was calculated as FFM divided by height². A total body scan was performed by DEXA using a Lunar Prodigy system (GE Healthcare, Madison, WI, USA). For this purpose, subjects lied in supine position on a scan table for approximately 15 minutes while the DEXA scanner performed multiple fast speed transverse scans from head to toes. From the total body scan, FFM was assessed by summing up lean mass and bone mineral content. FFM derived from the DEXA will be abbreviated as FFM_{DEXA}, and is used as reference values.

Statistical analyses

Data were normally distributed and reported as mean ± standard deviation (SD). Sex-differences were tested using an unpaired Student's *t*-test. The group was randomly split into two groups with comparable general characteristics (Table 1). In the first group of 422 subjects, stepwise multiple regression analysis with FFM_{DEXA} as dependent variable and age, sex, height, weight and height²/(impedance from the BIA) as independent variables is performed. From this, a new regression formula was created (FFM_{Form}).

Table 1 Baseline characteristics of the two subgroups of the total study population.

	First group	Second group
Subjects, <i>n</i>	422	665
Male, %	59.8%	59.1%
Age, y	63.5 ± 9.8	63.1 ± 9.6
Height, m	167.8 ± 8.7	167.8 ± 8.9
Weight, kg	69.4 ± 15.1	69.0 ± 15.2
BMI, kg/m ²	24.6 ± 4.6	24.4 ± 4.8
BMC, g	2448.7 ± 978.9	2453.7 ± 747.4
FEV ₁ , %pred	42.1 ± 16.1	46.3 ± 18.9
FEV ₁ /FVC	42.4 ± 12.6	39.4 ± 12.7
DLCO, %pred	53.8 ± 38.4	51.0 ± 18.9

Data are mean ± SD.

Abbreviations: BMC: bone mineral content; FEV₁: forced expiratory volume expressed in 1 s; FEV₁/FVC: Tiffeneau index; DLCO: diffusing capacity for carbon monoxide. No significances.

Intermethod correlation between FFM_{Steiner} and FFM_{DEXA} in the whole group and between FFM_{Form} and FFM_{DEXA} in the second group (*n* = 665) was tested by calculating Pearson's correlation coefficient. The limits of agreement of the FFM_{Steiner} and FFM_{Form} with the FFM_{DEXA} were determined by plotting the mean intermethod measurement difference ± 2 standard deviations (SD) as described by Bland and Altman.¹⁴ Age dependency of the FFM_{DEXA} was tested by analysis of variance (ANOVA) test and post hoc LSD test. To test differences between FFM_{DEXA} and FFM_{Form}, and the other formulas by Dey et al.,¹⁵ Deurenberg et al.,¹⁶ Steiner et al.¹¹ and Segal et al.,¹⁷ the paired Student's *t*-test was used. Muscle wasting was defined according to the cut-offs of Schols et al. (FFMI < 16 kg/m² for men, 15 kg/m² for women), Vestbo et al. (FFMI < 17.1 kg/m² for men, 14.6 kg/m² for women)³ and Coin et al. (10th percentile in the age range 60–69: FFMI < 17.8 kg/m² for men, 14.6 kg/m² for women).⁷ The prevalence of muscle wasting between the different techniques was tested by using the χ^2 -test. Analyses were performed using Statistical Package for the Social Sciences (SPSS) version 15.01 for Windows®. A *p*-value < 0.05 was considered statistically significant.

Table 2 Baseline characteristics of the study group.

	Men	Women
Subjects, <i>n</i>	641	446
Age, y	65.4 ± 9.4	60.1 ± 9.3**
Height, m	172.5 ± 7.0	161.0 ± 6.4**
Weight, kg	73.9 ± 14.5	62.4 ± 13.5**
BMI, kg/m ²	24.8 ± 4.4	24.1 ± 5.1*
BMC, g	2713.5 ± 693.5	2075.5 ± 898.9**
FEV ₁ , %pred	44.0 ± 16.8	45.7 ± 13.4
FEV ₁ /FVC	39.6 ± 12.1	41.8 ± 13.4
DLCO, %pred	52.8 ± 20.4	49.1 ± 18.4

Data are mean ± SD.

Abbreviations: BMC: bone mineral content; FEV₁: forced expiratory volume expressed in 1 s; FEV₁/FVC: Tiffeneau index; DLCO: diffusing capacity for carbon monoxide. Significantly different compared to men: **p* < 0.05, ***p* < 0.01.

Results

Characteristics of the patients are shown in Table 2. The patients were characterized by moderate to severe COPD. The women were younger than the men and they had lower weight, BMI and bone mineral content, but the same degree of lung function impairment.

The coefficient of determination between mean FFM_{Steiner} and FFM_{DEXA} was 0.88 and comparable between men and women ($R^2 = 0.80$ vs. 0.74, respectively; both *p* < 0.01, Fig. 1A). Limits of agreement between the

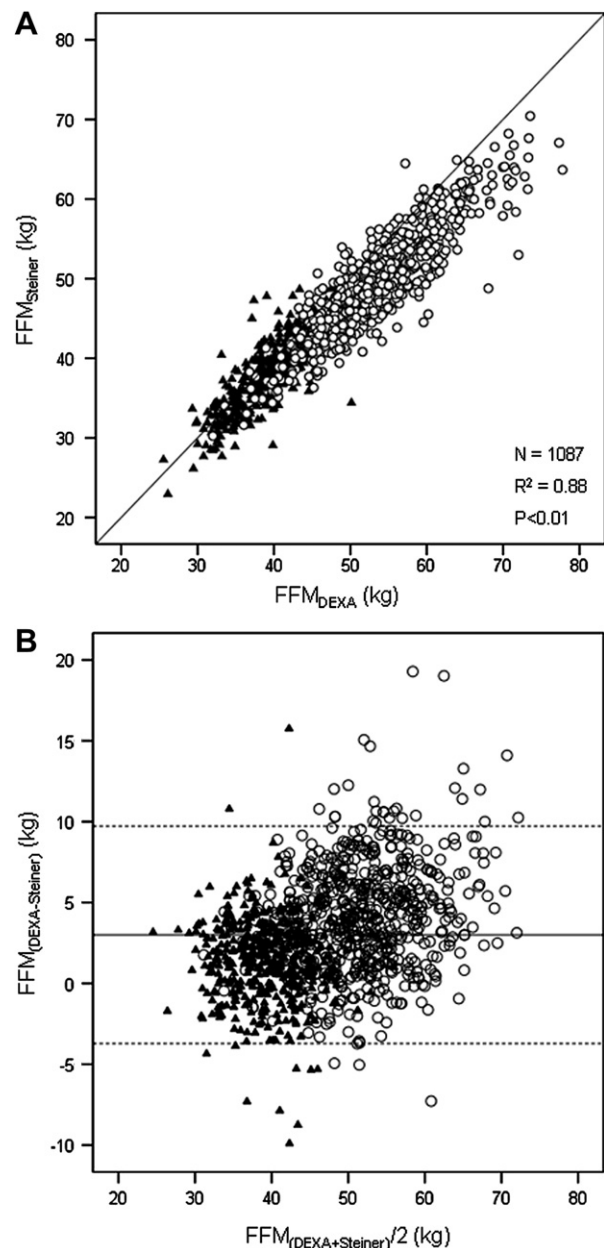


Figure 1 Correlation between FFM_{Steiner} and FFM_{DEXA} (A) and intermethod agreement of FFM measurements for DEXA and BIA (B) in male (white dots) and female (black triangles) patients with COPD. Mean differences (solid line) and limits of agreement (±2 SD, dashed line) are shown for the whole population.

measures of $FFM_{Steiner}$ compared to FFM_{DEXA} are shown in Fig. 1B. Particularly in men, $FFM_{Steiner}$ underestimated FFM when compared with FFM_{DEXA} (mean difference $FFM_{(DEXA-Steiner)}$ in men: 4.1 kg (limits of agreement -2.6 to 10.8 kg), in women: 1.4 kg (limits of agreement -5.5 to 8.3 kg)). FFM_{DEXA} was significantly correlated with age, gender, height, weight and $height^2/impedance$ (data not shown, all $p < 0.01$). Subsequently, a stepwise multiple regression analysis with FFM_{DEXA} as the dependent variable and age, gender, height, weight and $height^2/impedance$ as the independent variable was performed in the first subgroup of 422 subjects. The significant covariates gender, height, weight and $height^2/impedance$ showed a prediction of 90% (Table 3). From this, a sex-specific formula to calculate FFM by the impedance in our COPD population was created: $FFM_{Form} = -11.81 + 0.245 \times \text{weight} + 0.298 \times \text{height}^2/\text{impedance} + 0.148 \times \text{height} + 5.284 \times \text{sex}$ (1 for men, 0 for women). The coefficient of determination between mean FFM_{Form} and FFM_{DEXA} in the second group of 665 subjects was 0.91 and comparable between men and women ($R^2 = 0.82$ vs. 0.77 , respectively; both $p < 0.01$, Fig. 2A). Limits of agreement between FFM_{Form} and FFM_{DEXA} are shown in Fig. 2B (mean difference $FFM_{(DEXA-Form)}$ in men: 0.57 kg (limits of agreement -5.6 to 6.7 kg), in women: 0.68 kg (limits of agreement -4.2 to 5.5 kg)). Exploring the correlation of the FFMI between the different techniques, led to $R^2 = 0.76$ between the $FFMI_{DEXA}$ and $FFMI_{Steiner}$ and $R^2 = 0.93$ between the $FFMI_{DEXA}$ and $FFMI_{Form}$.

Fig. 3 presented the age dependency of FFM_{DEXA} , FFM_{Form} and other formulas used for patients with COPD ($FFM_{Steiner}$,¹¹ Segal et al.¹⁷) and healthy elderly (Deurenberg et al.,¹⁶ Dey et al.¹⁵). In men (Fig. 3A), FFM_{DEXA} decreased with increasing age ($p < 0.01$), while in women (Fig. 3B), FFM_{DEXA} was not age-dependent. As expected, the new formula was closely linked to the FFM_{DEXA} , as did the formula by Dey. The formulas by Deurenberg and Steiner significantly underestimated the FFM when compared to the FFM_{DEXA} ($p < 0.01$) while the formula by Segal significantly overestimated the FFM_{DEXA} ($p < 0.01$).

Table 3 Multivariate stepwise regression with FFM_{DEXA} derived from the DEXA scan as dependent variable.

Independent variable	R^2	B	P-value
Model 1	0.80		
Height ² /impedance		0.79	0.00
Model 2	0.84		
Height ² /impedance		0.59	0.00
Weight		0.19	0.00
Model 3	0.89		
Height ² /impedance		0.37	0.00
Weight		0.24	0.00
Sex		5.94	0.00
Model 4	0.90		
Height ² /impedance		0.30	0.00
Weight		0.25	0.00
Sex		5.28	0.00
Height		0.15	0.00

Newly formed formula: $-11.81 + 0.245 \times \text{weight} + 0.298 \times \text{height}^2/\text{impedance} + 0.148 \times \text{height} + 5.284 \times \text{sex}$ (sex = 1 for men, 0 for women).

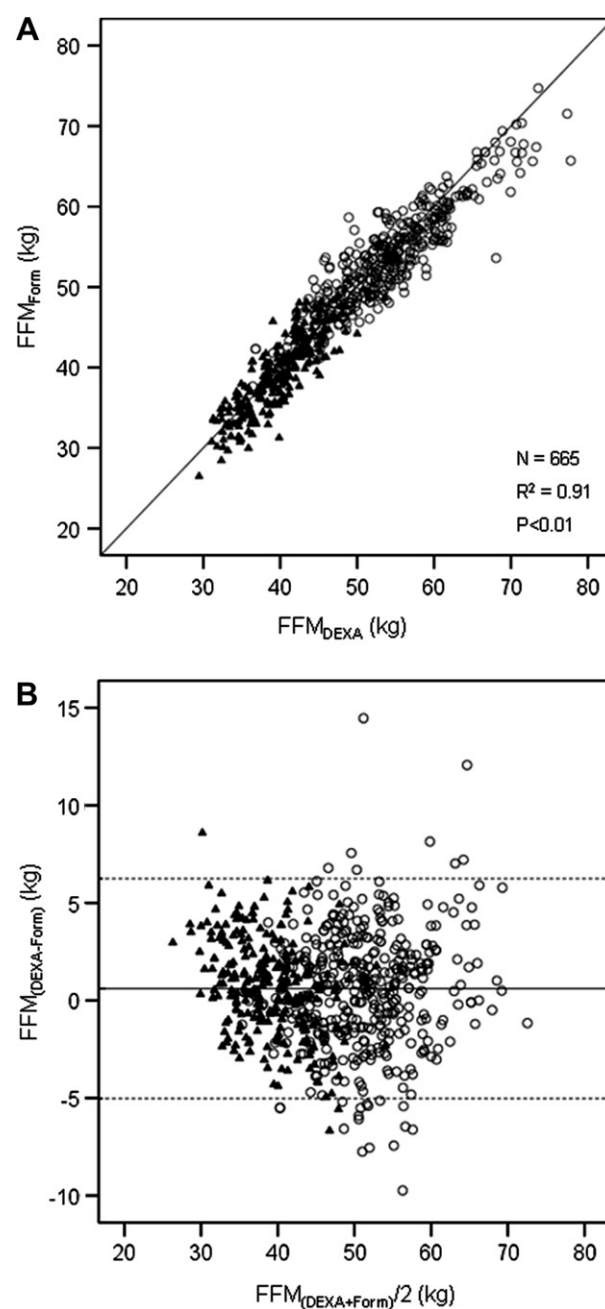


Figure 2 Correlation between FFM_{Form} and FFM_{DEXA} (A) and intermethod agreement of FFM measurements for DEXA and the calculated FFM (B) in a subgroup of male (white dots) and female (black triangles) patients with COPD ($n = 665$). Mean differences (solid line) and limits of agreement (± 2 SD, dashed line) are shown for the whole subgroup.

In Fig. 4, the percentage of patients with muscle wasting calculated by the cut offs of Schols et al.² (A), Vestbo et al.³ (B) and Coin et al.⁷ (C) is shown. FFMI is derived from DEXA scan and BIA after which FFM is calculated by the formula of Steiner et al. and the new formula. In both in men and in women, the proportion of muscle wasting was higher using the $FFM_{Steiner}$ vs. the FFM_{DEXA} and FFM_{Form} (both $p < 0.01$). Comparing the proportion muscle wasting derived from the FFM_{DEXA} with the FFM_{Form} , the difference was statistically

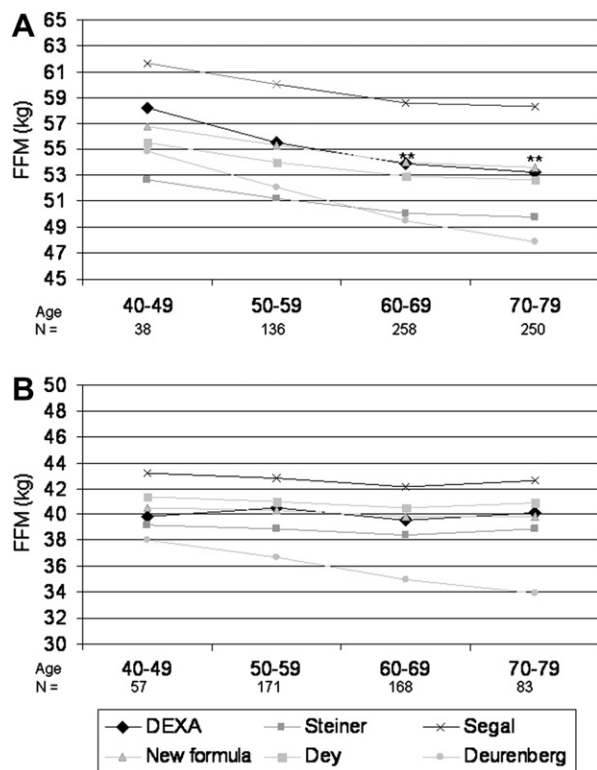


Figure 3 FFM by DEXA scan and various formulas in male (A) and female (B) COPD patients in different age categories.

significant for men ($p < 0.01$), but the absolute difference in proportion muscle wasting was only 3.9% for the criteria of Schols, 5.3% for the 10th percentile of Vestbo et al. and 3.4% for the 10th percentile of Coin et al.

Discussion

The present study evaluated critical points in the assessment of muscle wasting in a large group of moderate to severe clinically stable patients with COPD. An underestimation of the FFM measured by BIA and calculated by Steiner's formula is found when compared to the FFM measured by DEXA. As this underestimation is already previously shown,¹¹ the authors approached to create a new formula to calculate FFM by BIA by using the stepwise multivariate regression. From this, a new COPD specific formula was formed. The proportion of muscle wasting is largely dependent on the used cut-offs, especially in men. The findings of the present study emphasize the importance to accurately bare in mind these criteria to establish muscle wasting before implementing it in the clinical practice.

It has previously been shown that muscle wasting is associated with metabolic¹⁸ and functional consequences.¹⁹ Assessment of body mass index alone for screening on body composition in patients with COPD seems not accurate as there is a subgroup of patients with normal BMI and muscle wasting.² Therefore, defining muscle wasting in the screening and the treatment of COPD patients is clinically relevant. The present study shows that the accuracy of this definition depends on various factors like the technique used to measure FFM and the cut-offs on

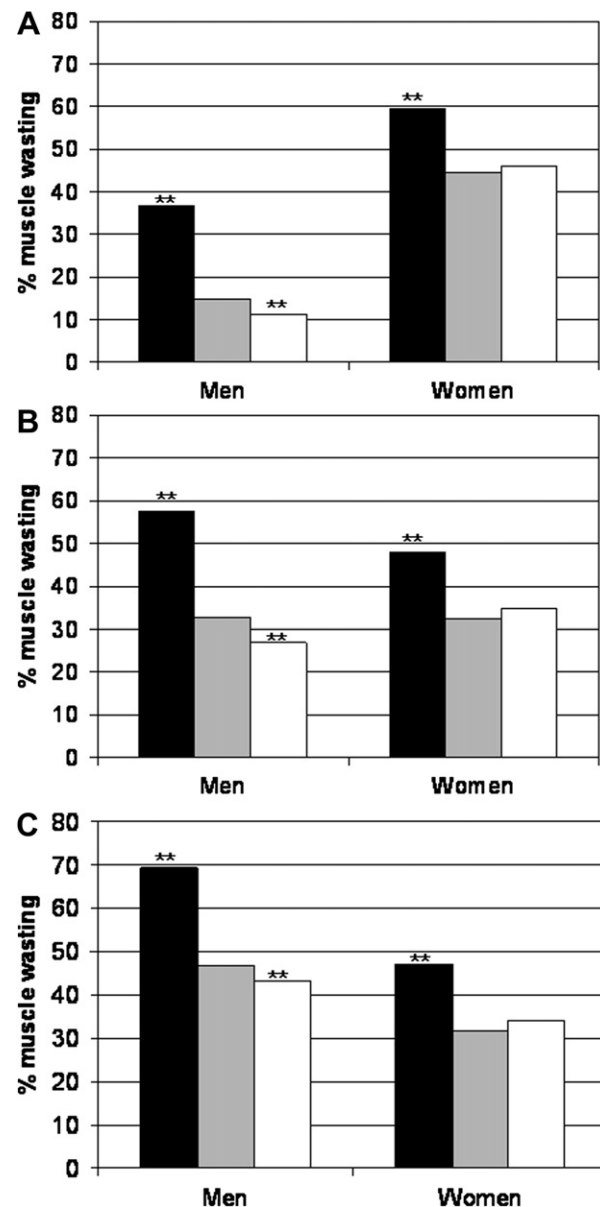


Figure 4 Percentage of muscle wasting in male and female patients with COPD by using the formula by Steiner et al. (black bars), the FFM derived from the DEXA (grey bars) and with the FFM calculated by the new formula (white bars). Muscle wasting was defined according to the cut-offs of Schols et al. (A, $\text{FFMI} < 16 \text{ kg/m}^2$ for men and 15 kg/m^2 for women), Vestbo et al. (B, $\text{FFMI} < 17.1 \text{ kg/m}^2$ for men and 14.6 kg/m^2 for women) (3) and Coin et al. (C, 10th percentile in the age range 60–69: 17.8 kg/m^2 for men and 14.6 kg/m^2 for women). Significant different from FFM_{DEXA} : ** $P < 0.01$.

which muscle wasting is based. Both factors will be discussed in the following section.

Various studies evaluated the proportion of muscle mass in patients with COPD by using different techniques and with the DEXA scan as the reference method.^{11,12} In both studies, there is great discrepancy of the limits of agreement when the BIA and the anthropometric methods were compared with the DEXA scan. Conclusive, the proportion

muscle wasting in a COPD population differs depending on the technique used. Even, besides intra-technical differences (various soft wares for DEXA scan, different BIA devices), inter-technical differences are even greater. In the study by Steiner et al.,¹¹ the prevalence of muscle wasting was 36 and 42% in men and 72 and 59% in women when respectively the DEXA and BIA was used. In the more recent study by Lerario et al.,¹² the changes between the DEXA scan and BIA were smaller, respectively 25 and 28%. In both studies, the cut-offs of Schols et al. were used to define muscle wasting.² Moreover, the proportion of muscle wasting was higher in the study by Steiner et al.¹¹ compared to the study by Lerario et al.,¹² likely partly because the patients included in the study by Steiner et al. had more severe COPD. Both studies concluded that BIA underestimated FFM when compared with DEXA. In the present study, the proportion of muscle wasting according to the cut-offs of Schols et al. was about 15 and 37% for men and about 45 and 59% for women for respectively DEXA and BIA. The discrepancy between methods may have great impact as nutritional supplements are often prescribed in clinical research,^{20,21} but also in patient's health care.²² In this view, the new formula in the present study is proficient to minimize the discrepancy of the FFM, and particularly the FFMI that existed between the DEXA and the BIA method. However, as relatively great limits of agreements remain with the new formula, the DEXA device still is more profound to screen for muscle wasting, as confirmed in a recent published paper.⁹ If the BIA method is only at hand, the new formula may give a better approach to estimate skeletal muscle mass than previous COPD specific formulas.

Recently, three studies summarized the prevalence of muscle wasting in cohorts of COPD outpatients^{3,23,24} (Table 4). In all these studies, BIA was used to calculate FFM, and the prevalence of muscle wasting was defined by the cut-offs of Schols et al. The formulas of Segal et al.^{3,23,24} and Steiner et al.^{3,23,24} were used to calculate FFM. The proportion of muscle wasting in the present study is higher when compared to the other studies. This can at least partly be explained by the fact that we studied complex COPD patients admitted for pulmonary rehabilitation. Until now, there is no study that appraises muscle wasting by using the DEXA scan in a large group of COPD patients.

The findings of the present study emphasize the importance of the cut-offs for defining muscle wasting. The cut-offs of Schols et al. ($\text{FFMI} < 16 \text{ kg/m}^2$ for men and 15 kg/m^2

for women) are based on the percentage of ideal body weight,² while the cut-offs of Vestbo et al.³ and of Coin et al.⁷ are based on the 10th percentile of a large cohort of healthy subjects in respectively Copenhagen (age range 20–93) and various parts in Italy (age range 60–69). The cut-off for women is similar for the Copenhagen and Italy cohort ($\text{FFMI} < 14.6 \text{ kg/m}^2$), and only slightly lower than the cut-off of Schols et al. A larger discrepancy exists in the cut-offs for men. The 10th percentile of the FFMI in the Copenhagen and Italy cohort for men is respectively 17.1 kg/m^2 and 17.8 kg/m^2 . The cut-off of Vestbo et al. (17.1 kg/m^2),³ is positioned between the cut-off of Schols et al. (16 kg/m^2),² and Coin et al. (17.8 kg/m^2).⁷ Together with the fact that the proportion of muscle wasting based on the cut-off of Vestbo et al. in men move toward the proportion in women (see Fig. 4), the authors conclude that the cut-offs of Vestbo et al. approach most optimal the cut-offs for defining muscle wasting. Based on these cut offs, the prevalence of muscle wasting in the present cohort of moderate to severe patients with COPD admitted for pulmonary rehabilitation is about 30% for both men and women. Nevertheless, the present authors believe that future epidemiologic research has to further evaluate the criteria for diagnosing muscle wasting in chronically ill patients.

To further evaluate the new formula, the authors compared FFM_{DEXA} and FFM_{Form} with different formulas in various age categories. In male but not in female COPD patients, FFM_{DEXA} decreased with increasing age. These findings are in line with findings in healthy elderly, where FFM assessed by BIA decreased from 35 to 55 y in men but remained stable in women.²⁵ Another study reported that the FFM decreased after 60 y in men, and to a lower extent also in women.²⁶ These data imply that, at least the pattern, of the age-dependant progress remains comparable in patients with COPD and healthy subjects. Moreover as expected, the new formula was closely linked to the FFM_{DEXA} , as did the formula by Dey et al.¹⁵

Limitations of the study

The authors would like to address various limitation of the study. Firstly, the DEXA scan was used as the reference method for the FFM. The authors are aware that the DEXA scan is not the golden standard for body compositional measurement, like double labeled water technique or magnetic resonance imaging.²⁷ There are few studies determining the accuracy of the DEXA scan for muscle mass assessment. These studies concluded that DEXA scan showed better precision compared to bedside methods like BIA.²⁸ Indeed, DEXA has been shown as a useful technique to measure FFM in patients with COPD.⁸ Furthermore, FFM_{DEXA} was assessed by summing up lean mass and bone mineral content. It has been shown that bone mineral content is lower in patients with COPD compared to healthy controls,²⁹ which could contribute to the lower FFM_{DEXA} compared to the FFM_{BIA} . Nevertheless, the contribution of the bone mineral content to the FFM is relatively small and is therefore unlikely to influence our results. Secondly, patients with clinically diagnosed edema were excluded from the study, but it cannot be concluded that all patients were free of any level of edema. Especially in patients with

Table 4 Proportion of muscle wasting in various studies.

% of patients with muscle wasting	Formula	Men	Women	References
Vermeeren et al.	Steiner	20	40	[20]
Vestbo et al.	Segal	7	36	[3]
Steuten et al.	Steiner	20	29	[4]
Present study ^a	Steiner	37	59	

In all studies, COPD outpatients were included, BIA was used to estimate fat free mass, and the prevalence of muscle wasting was defined by the criteria of Schols et al.²

^a The original BIA calculation was used.

extreme low FFM, the extracellular water compartment can be increased.⁴ In these patients with non-visual levels of edema, the body composition data are not reliable. This hassle counts for both the BIA and the DEXA technique.

To summarize, the results of the present study show that both the technique to determine FFM and the cut-offs to define an abnormal low FFMI are of importance to accurately diagnose muscle wasting in patients with COPD. The authors concluded that the formula derived in the present study can be used for the FFM assessment by using BIA in clinically stable patients with COPD.

Conflict of interest

The authors have nothing to declare.

Acknowledgment

EPAR participated in the study design, analyzed the data and wrote the manuscript. MAS participated in the study design, assist with the analyses of the data, and manuscript revision. EFMW contributed in the manuscript revision. None of the authors had any personnel or financial conflict of interest.

References

- Wouters EF. Chronic obstructive pulmonary disease. 5: systemic effects of COPD. *Thorax* 2002 Dec;**57**(12):1067–70.
- Schols AMWJ, Soeters PB, Dingemans AMC, Mostert R, Frantzen PJ, Wouters EFM. Prevalence and characteristics of nutritional depletion in patients with stable COPD eligible for pulmonary rehabilitation. *Am Rev Respir Dis* 1993;**147**:1151–6.
- Vestbo J, Prescott E, Almdal T, Dahl M, Nordestgaard BG, Andersen T, et al. Body mass, fat-free body mass, and prognosis in patients with chronic obstructive pulmonary disease from a random population sample: findings from the Copenhagen city heart study. *Am J Respir Crit Care Med* 2006 Jan 1;**173**(1):79–83.
- Baarends EM, Schols AM, Mostert R, Wouters EF. Peak exercise response in relation to tissue depletion in patients with chronic obstructive pulmonary disease. *Eur Respir J* 1997 Dec;**10**(12):2807–13.
- Mostert R, Goris A, Weling-Scheepers C, Wouters EF, Schols AM. Tissue depletion and health related quality of life in patients with chronic obstructive pulmonary disease. *Respir Med* 2000 Sep;**94**(9):859–67.
- Schols AM, Broekhuizen R, Weling-Scheepers CA, Wouters EF. Body composition and mortality in chronic obstructive pulmonary disease. *Am J Clin Nutr* 2005 Jul;**82**(1):53–9.
- Coin A, Sergi G, Minicuci N, Giannini S, Barbiero E, Manzato E, et al. Fat-free mass and fat mass reference values by dual-energy X-ray absorptiometry (DEXA) in a 20–80 year-old Italian population. *Clin Nutr* 2008 Feb;**27**(1):87–94.
- Engelen MP, Schols AM, Heidendal GA, Wouters EF. Dual-energy X-ray absorptiometry in the clinical evaluation of body composition and bone mineral density in patients with chronic obstructive pulmonary disease. *Am J Clin Nutr* 1998 Dec;**68**(6):1298–303.
- Miller A, Strauss BJ, Mol S, Kyoong A, Holmes PH, Finlay P, et al. Dual-energy X-ray absorptiometry is the method of choice to assess body composition in COPD. *Respirology* 2009 Apr;**14**(3):411–8.
- Schols AM, Wouters EF, Soeters PB, Westerterp KR. Body composition by bioelectrical-impedance analysis compared with deuterium dilution and skinfold anthropometry in patients with chronic obstructive pulmonary disease. *Am J Clin Nutr* 1991 Feb;**53**(2):421–4.
- Steiner MC, Barton RL, Singh SJ, Morgan MD. Bedside methods versus dual energy X-ray absorptiometry for body composition measurement in COPD. *Eur Respir J* 2002 Apr;**19**(4):626–31.
- Lerario MC, Sachs A, Lazaretti-Castro M, Saraiva LG, Jardim JR. Body composition in patients with chronic obstructive pulmonary disease: which method to use in clinical practice? *Br J Nutr* 2006 July;**96**(1):86–92.
- Spruit MA, Vanderhoven-Augustin I, Janssen PP, Wouters EF. Integration of pulmonary rehabilitation in COPD. *Lancet* 2008 Jan 5;**371**(9606):12–3.
- Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986 Feb 8;**1**(8476):307–10.
- Dey DK, Bosaeus I, Lissner L, Steen B. Body composition estimated by bioelectrical impedance in the Swedish elderly. Development of population-based prediction equation and reference values of fat-free mass and body fat for 70- and 75-y olds. *Eur J Clin Nutr* 2003 Aug;**57**(8):909–16.
- Deurenberg P, van der Kooy K, Leenen R, Weststrate JA, Seidell JC. Sex and age specific prediction formulas for estimating body composition from bioelectrical impedance: a cross-validation study. *Int J Obes* 1991 Jan;**15**(1):17–25.
- Segal KR, Van Loan M, Fitzgerald PI, Hodgdon JA, Van Itallie TB. Lean body mass estimation by bioelectrical impedance analysis: a four-site cross-validation study. *Am J Clin Nutr* 1988 Jan;**47**(1):7–14.
- Van Helvoort HA, Heijdra YF, Thijs HM, Vina J, Wanten GJ, Dekhuijzen PN. Exercise-induced systemic effects in muscle-wasted patients with COPD. *Med Sci Sports Exerc* 2006 Sep;**38**(9):1543–52.
- Franssen FM, Broekhuizen R, Janssen PP, Wouters EF, Schols AM. Limb muscle dysfunction in COPD: effects of muscle wasting and exercise training. *Med Sci Sports Exerc* 2005 Jan;**37**(1):2–9.
- Vermeeren MA, Wouters EF, Geraerts-Keeris AJ, Schols AM. Nutritional support in patients with chronic obstructive pulmonary disease during hospitalization for an acute exacerbation; a randomized controlled feasibility trial. *Clin Nutr* 2004 Oct;**23**(5):1184–92.
- Broekhuizen R, Creutzberg EC, Weling-Scheepers CA, Wouters EF, Schols AM. Optimizing oral nutritional drink supplementation in patients with chronic obstructive pulmonary disease. *Br J Nutr* 2005 Jun;**93**(6):965–71.
- Dieetbehandelingsrichtlijnen*. Maarssen: Elsevier; 1997.
- Steuten LM, Creutzberg EC, Vrijhoef HJ, Wouters EF. COPD as a multicomponent disease: inventory of dyspnoea, underweight, obesity and fat free mass depletion in primary care. *Prim Care Respir J* 2006 Apr;**15**(2):84–91.
- Vermeeren MA, Creutzberg EC, Schols AM, Postma DS, Pieters WR, Roldaan AC, et al. Prevalence of nutritional depletion in a large out-patient population of patients with COPD. *Respir Med* 2006 Aug;**100**(8):1349–55.
- Pichard C, Kyle UG, Bracco D, Slosman DO, Morabia A, Schutz Y. Reference values of fat-free and fat masses by bioelectrical impedance analysis in 3393 healthy subjects. *Nutrition* 2000 Apr;**16**(4):245–54.
- Kyle UG, Genton L, Hans D, Karsgaard L, Slosman DO, Pichard C. Age-related differences in fat-free mass, skeletal muscle, body cell mass and fat mass between 18 and 94 years. *Eur J Clin Nutr* 2001 Aug;**55**(8):663–72.
- Genton L, Hans D, Kyle UG, Pichard C. Dual-energy X-ray absorptiometry and body composition: differences between

- devices and comparison with reference methods. *Nutrition* 2002 Jan; **18**(1):66–70.
28. Elia M, Fuller NJ, Hardingham CR, Graves M, Screatton N, Dixon AK, et al. Modeling leg sections by bioelectrical impedance analysis, dual-energy X-ray absorptiometry, and anthropometry: assessing segmental muscle volume using magnetic resonance imaging as a reference. *Ann N Y Acad Sci* 2000 May; **904**:298–305.
29. Engelen MP, Schols AM, Lamers RJ, Wouters EF. Different patterns of chronic tissue wasting among patients with chronic obstructive pulmonary disease. *Clin Nutr* 1999 Oct; **18**(5):275–80.