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Bedside methods *versus* dual energy X-ray absorptiometry for body composition measurement in COPD

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Bedside methods versus *dual energy X-ray absorptiometry for body composition measurement in COPD. M.C. Steiner, R.L. Barton, S.J. Singh, M.D.L. Morgan. ©ERS Journals Ltd 2002.*

ABSTRACT: The measurement of body composition is of value in the nutritional assessment of patients with chronic obstructive pulmonary disease (COPD). The purpose of the present study was to compare two bedside methods for the measurement of body composition using dual energy X-ray absorptiometry (DEXA) as a reference method.

Fat-free mass (FFM) was measured using DEXA, bioelectric impedance analysis (BIA) and skinfold anthropometry (SFA) in a cohort of 85 COPD patients accepted for pulmonary rehabilitation. Patients whose body mass index was >30 were excluded.

Relative to DEXA, BIA underestimated FFM, whereas it was overestimated by SFA. There was a systematic increase in bias with mean FFM for both DEXA *versus* BIA and DEXA *versus* SFA, but this was almost eliminated when results were expressed as FFM index. Significant sex differences in the bias of BIA and SFA measurements of FFM were found. Forty-two (49.4%) patients were identified as nutritionally depleted using DEXA. Compared to DEXA, the sensitivity for detecting nutritional depletion was 86 and 74% for BIA and SFA, respectively, and the specificity 88 and 98%, respectively.

There are significant intermethod differences in the measurement of body composition in chronic obstructive pulmonary disease patients. The choice of measurement method will have implications for nutritional assessment in chronic obstructive pulmonary disease.

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Weight loss is an important clinical feature in patients with chronic obstructive pulmonary disease (COPD). Reduced body weight and muscle mass is an independant predictor of mortality [1, 2] and correlates with physical performance in this population [3].

The prevalence of nutritional depletion in COPD patients may be underestimated by simple measurements of body weight and body mass index because many patients show relative reductions in muscle mass despite being of normal overall weight [4]. For this reason, measurements of body composition are increasingly being used to assess the nutritional status of COPD patients. These measurements subdivide the body into a number of compartments depending on the method of measurement used but of most interest is the fat-free mass (FFM) compartment, which contains functional muscle mass. Increasing muscle mass is an important therapeutic goal for rehabilitation and nutritional support programmes, emphasizing the importance of the measurement of FFM.

There is no "gold standard" method for the measurement of FFM. The choice of measurement method for body composition balances accuracy with practicality and cost. Furthermore, age-specific normal ranges for FFM have not been established, making the identification of nutritionally depleted patients difficult.

Recently, dual energy X-ray absorptiometry (DEXA) has been suggested as a suitable clinical reference method for the measurement of body composition [5, 6]. Experience of its use in COPD patients, however, remains limited and, although it is safe and easy to perform, it may be inconvenient for patients and is costly. By contrast, bioelectric impedance analysis (BIA) and skinfold anthropometry (SFA) are simple bedside measurements of body composition. However, they may be subject to greater inaccuracy in the elderly and in disease because of inherent assumptions about cellular hydration and the distribution of body fat.

In the present study, FFM was measured in a cohort of COPD patients using these three methods. In a subgroup, the reproducibility of these measurements in this population was also assessed. The aim was to define the limits of agreement between these methods and determine how interchangeable they are for the measurement of FFM in COPD.

Methods

Subjects were recruited from those accepted for pulmonary rehabilitation at Glenfield Hospital, Leicester, UK. Patients who met British Thoracic

Society (BTS) clinical and spirometric criteria for COPD and were aged 40–80 yrs were included [7]. All patients were participating in a nutritional supplementation programme embedded in pulmonary rehabilitation and were therefore excluded if their body mass index was >30 kg·m^{-2}. Approval for the study was obtained from the Leicestershire Research Ethics Committee.

Spirometry was performed in the seated position to BTS/Association of Respiratory Technicians and Physiologists standards (Vitallograph, Model R; Vitallograph Ltd, Buckingham, UK). Values are expressed as a percentage of predicted values calculated from European Respiratory Society regression equations.

Body composition

Subjects underwent BIA, SFA and DEXA within a 7-day period. A subgroup of patients underwent repeat measurements after 7 weeks. This period was chosen because it represents the length of the rehabilitation and nutritional support programme at Glenfield Hospital. All measurements were taken before rehabilitation commenced. Body weight was measured in light clothing to the nearest 0.1 kg (Seca 770; Seca Vogel, Hamburg, Germany). Body height was measured using a wall-mounted stadiometer to the nearest 1 cm.

DEXA was performed in the supine position (Lunar Expert-XL Bone Densitometer; Lunar Radiation Corporation, Madison, WI, USA). This technique measures the differential attenuation of two different energy level X-rays as they pass through the body. Total soft tissue mass, bone mass, lean mass and fat mass are derived using software provided by the manufacturer. FFM (FFMDEXA) is calculated as the sum of lean mass and bone mineral mass.

BIA was performed in the semisupine position (Bodystat 1500; Bodystat Ltd, Douglas, UK). Measurements were obtained in the morning after a fast of $\geqslant$1.5 h.

Skinfold thickness was measured at four sites: biceps, triceps, subscapular and suprailiac (Harpenden Skinfold Caliper; British Indicators, West Sussex, UK). Fat mass was estimated using the tables of DURNIN and WOMERSLEY [8]. FFM (FFMSFA) was calculated by subtracting fat mass from body weight.

FFM index (FFMI) was calculated as FFM/height^2 [9]. Patients were considered nutritionally depleted if they had a body mass index of $\leqslant$21 or an FFMI of $\leqslant$15 (females) or $\leqslant$16 (males).

Statistical analysis

All data was normally distributed. The limits of agreement between measurement methods were determined by plotting the mean intermethod measurement difference (the bias of the measurement) ±2 SD (the error of the measurement) as described by BLAND and ALTMAN [10]. FFM and FFMI derived from BIA and SFA were compared in turn with DEXA, as the latter would be considered by most authorities to be the most accurate. The mean intertest differences were compared in males and females using independant samples t-tests. The sensitivity and specificity of BIA and SFA relative to DEXA for identifying nutritionally depleted patients were also calculated [11].

The reproducibility of FFM measurements for each method was determined by calculating the mean difference and the intraclass correlation coefficients for repeated measurements. Significance was accepted at $p<0.05$.

Table 1. – Baseline patient characteristics

	Males	Females
Subjects n	53	32
Age yrs	67.7±8.4	65.6±8.7
Height m	1.72±0.07	1.59±0.06
Weight kg	70.2±13.0	60.2±10.5
BMI kg·m^{-2}	23.7±3.9	23.7±3.3
FEV_1 L	0.91±0.38	0.84±0.36
FVC L	2.56±0.79	1.92±0.53
FEV_1 % pred	30.9±12.8	40.6±13.7

Data are presented as mean±SD. BMI: body mass index; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; % pred: percentage of the predicted value.

Results

Eighty-five patients were recruited to the study. The baseline characteristics of the patients are shown in table 1. Mean FFM and FFMI measurements using each method are shown in table 2.

Agreement between measurements of fat-free mass

The limits of agreement between the measures of FFM are shown in figure 1. Measurements of FFM

Table 2. – Fat-free mass (FFM) and FFM index (FFMI) by dual energy X-ray absorptiometry (DEXA), bioelectric impedance analysis (BIA) and skinfold anthropometry (SFA)

	Males	Females
DEXA		
FFM kg	50.6±7.6	36.4±5.0
FFMI kg·m^{-2}	17.0±1.9	14.4±1.4
Depletion %	36	72
BIA		
FFM kg	48.8±6.4	37.5±4.6
FFMI kg·m^{-2}	16.5±2.0	14.8±1.3
Depletion %	42	59
SFA		
FFM kg	51.7±6.9	39.1±5.0
FFMI kg·m^{-2}	17.4±1.8	15.4±1.4
Depletion %	28	53

Data are presented as mean±SD. Patients were considered nutritionally depleted if they had a body mass index of $\leqslant$21 or an FFMI of $\leqslant$15 (females) or $\leqslant$16 (males).

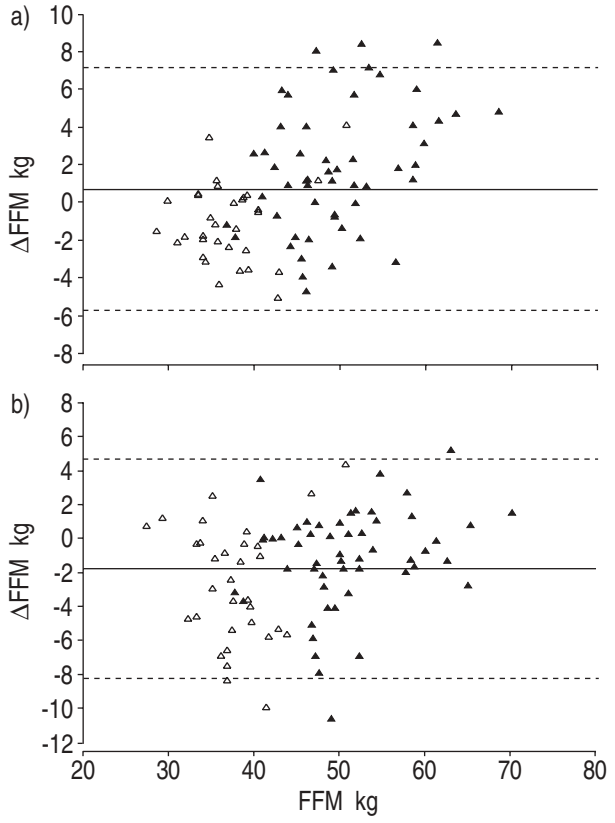

Fig. 1. – Intermethod agreement of fat-free mass (FFM) measurement for: a) dual energy X-ray absorptiometry (DEXA) and bioelectric impedance analysis (BIA) (FFMDEXA - FFMBIA); and b) DEXA and skinfold anthropometry (SFA) (FFMDEXA - FFMSFA). Bland and Altman plots of the differences (Δ) between methods of measuring FFM (△: females; ▲: males). Mean differences (solid line) and limits of agreement (±2SD; - - -) are shown for the whole population.

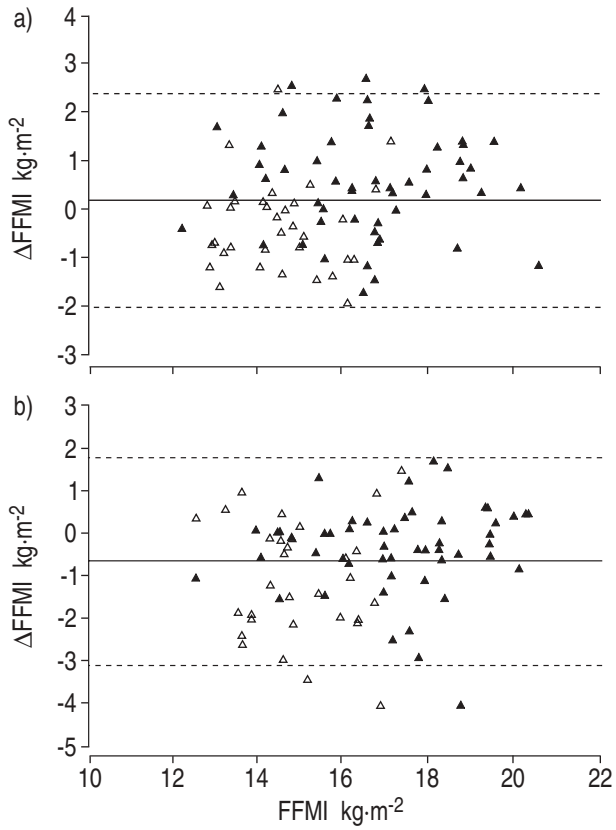

Fig. 2. – Intermethod agreement of fat-free mass index (FFMI) measurement for: a) dual energy X-ray absorptiometry (DEXA) and bioelectric impedance analysis (BIA) (FFMIDEXA - FFMIBIA); and b) DEXA and skinfold anthropometry (SFA) (FFMIDEXA - FFMISFA). Bland and Altman plots of the differences (Δ) between methods of measuring FFMI (△: females; ▲: males). Mean differences (solid line) and limits of agreement (±2SD; - - -) are shown for the whole population.

by BIA and SFA are compared with FFMDEXA. For the whole group, BIA gave rise to underestimation of FFM relative to DEXA (mean difference (FFMDEXA - FFMBIA) 0.72 kg; limits of agreement -5.68–7.20 kg). By contrast, SFA gave rise to overestimation of FFM relative to DEXA (mean difference (FFMDEXA - FFMSFA -1.70 kg; limits of agreement -8.20–4.80 kg). There was a systematic increase in bias with mean FFM for both FFMDEXA *versus* FFMBIA ($r=0.51$, $p<0.01$) and FFMDEXA *versus* FFMSFA ($r=0.27$, $p<0.05$) (fig. 1). However, when FFMI was plotted rather than FFM, these correlations were considerably weakened or eliminated (FFMIDEXA *versus* FFMIBIA $r=0.23$, $p<0.05$; FFMIDEXA *versus* FFMISFA $r=0.18$, $p=0.1$) (fig. 2).

Within this cohort, there were significant sex differences in the bias of FFM measurements for these three methods (fig. 3). In males, BIA gave rise to underestimation of FFM, whereas, in females, it was overestimated. SFA gave rise to overestimation of FFM relative to DEXA in both males and females, but this bias was significantly greater in females than in males. These differences were significant. These intermethod differences were also seen when FFMI was used.

The overall prevalence of nutritional depletion for DEXA, BIA and SFA was 49, 48 and 38%, respectively. Differences in the identification of depletion between sexes are shown in table 2. Using DEXA as the reference method, the sensitivity of BIA and SFA for detecting nutritional depletion was 86 and 74%, respectively, and the specificity 88 and 98%.

Reproducibility of body composition measurements

Twenty-five patients participated in this part of the study. Sex balance and baseline characteristics were representative of the whole group (16 males, age 68.2±1.25 yrs, FEV_1 0.96±0.07 L (mean±SEM). Mean differences and intraclass correlation coefficients between the repeat measures of body weight and FFM from different methods are shown in table 3. The difference between the body weight measurements was small but significant. Intraclass correlation coefficients for all of the measurements were >0.9, indicating good reproducibility.

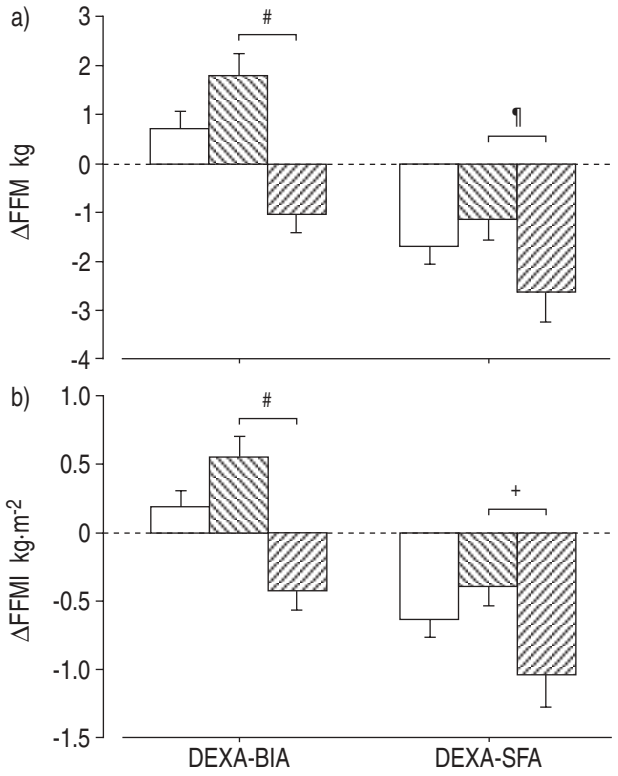

Fig. 3. – Sex differences in body composition measurements for: a) fat-free mass (FFM); and b) FFM index (FFMI) (□: total; ▨: males; ▨: females). Data are presented as mean±SEM inter-method difference (Δ). DEXA: dual energy X-ray absorptiometry; BIA: bioelectric impedance analysis; SFA: skinfold anthropometry. #: p=0.000; ¶: p=0.042; +: p=0.018.

Table 3. – Reproducibility of fat-free mass (FFM) measurements

Patient characteristics	Mean difference*	SD#	p-value	ICC
Weight kg	0.43	0.97	0.035	0.997
FFM_{DEXA} kg	-0.17	1.39	0.54	0.991
FFM_{BIA} kg	-0.20	1.37	0.48	0.987
FFM_{SFA} kg	0.02	1.29	0.93	0.99

*: calculated by subtracting the first measurement from a second taken 7 weeks later; #: of mean difference. Significance was tested using paired t-tests. ICC: intraclass correlation coefficient; DEXA: dual energy X-ray absorptiometry; BIA: bioelectric impedance analysis; SFA: skinfold anthropometry.

Discussion

In the present study, the limits of agreement for three different methods of measuring body composition in a cohort of COPD patients presenting for rehabilitation were defined. Overall, BIA caused underestimation of FFM relative to DEXA, whereas SFA caused overestimation. The mean differences between methods (bias) were small but the limits of agreement (error) were relatively large. The bias was greater for SFA relative to DEXA than BIA. There were significant sex differences in bias for both BIA and SFA relative to DEXA. The reproducibility of FFM measurements over a 7-week period for all three measurements was excellent. The small weight gain over the reference period is of doubtful clinical significance.

This study highlights the importance of the choice of method for measuring body composition in COPD patients. The intermethod differences demonstrated in this study are reflected in the lower sensitivity of BIA and SFA for detecting nutritional depletion relative to DEXA. The systematic increase in bias for FFM from both BIA and SFA with mean FFM was almost eliminated when FFMI was used, suggesting that height was a crucial factor. The effect of height on the accuracy of FFM measurements appears to apply to each method as the same effect was observed when BIA and SFA were compared independently of DEXA. The sex difference in bias between measurements was not explained by the lower height and weight of females since when FFMI was substituted the sex effect persisted, whereas the systematic bias was lost.

DEXA was used as the reference method for measuring FFM in the present study. It is recognized that this is not a measurement of true FFM; indeed, a gold standard method for measuring true FFM does not exist. However, DEXA has been proposed as a suitable reference method for the measurement of body composition and has been validated in animals, whose chemical composition is known in detail, and humans using hydrodensitometry as a reference method [12]. DEXA also has the advantage of providing a three-compartment model of body composition and allows the quantification of bone-free lean mass. Commonly used reference methods for measuring body composition such as hydrodensitometry or isotope-dilution techniques measure total body water and then calculate FFM by making the assumption that intracellular hydration is constant. This may not be true in the elderly or in disease. Although the calculation of soft tissue compartments from DEXA also requires the assumption of constant intracellular hydration, there is evidence from studies in which the hydration factor is manipulated that this method may be less prone to errors [12]. The true precision of DEXA remains uncertain, however, and significant differences arise when soft tissue mass is compared using apparatus from different manufacturers [13].

Defining nutritional depletion is difficult because there is no range of normality for FFM in the study population. The definition used in the present study is arbitrary but widely used and corresponds with earlier definitions for COPD patients using percentage of ideal body weight [4, 14]. Nutritional depletion by this definition has been shown to have significant consequences for health status and physical functioning in COPD patients [14, 15].

There are a number of possible reasons for the differences between measurement methods for body composition seen in this study. BIA relies on the estimation of total body water from measurements of whole body impedance. FFM is calculated from

total body water using a prediction equation derived from comparison with a reference method. Errors may arise from incorrect assumptions about the hydration of the lean tissue compartments in the population studied or from the population and reference method used to derive the prediction equation. In a study of patients with respiratory insufficiency, PICHARD *et al.* [16] demonstrated that the choice of prediction equation is critical to the accuracy of FFM measurements using BIA. In their study, the agreement of DEXA with BIA using a reference equation derived from COPD patients [17] was particularly poor. A more recent equation from the same institution, derived from a larger group of group of COPD patients using deuterium-dilution as a reference method (A.M.W. Schols, University of Maastricht, Maastricht, the Netherlands, personal communication), was used in the present study. By contrast to their original equation, this provides sex-specific equations for COPD patients and may explain why the agreement between BIA and DEXA is better in the present study than in that of PICHARD *et al.* [16]. More recently, a prediction equation for COPD patients using DEXA as a reference method has been published [18]. Perhaps not surprisingly (as the equation used was derived from data within the study), the limits of agreement between DEXA and BIA reported in this latter study were narrower than in the present one.

The sex differences seen in bias between BIA, SFA and DEXA in the present study may relate to differences in regional fat distribution in males and females. Impedance is inversely proportional to the circumference of the conduction system and therefore BIA may be subject to errors resulting from changes in the distribution of fat between the limbs and the trunk [19]. It is important to recognize, however, that DEXA may cause underestimation of the effect of central fat redistribution in the elderly, resulting in errors in FFM measurements when these populations are studied [20] and may result in sex differences in FFM measurements from DEXA. In the study of KYLE *et al.* [18], no sex differences were detected, but such differences were seen in the study of ENGELEN *et al.* [21], who compared FFM from DEXA with that from deuterium-dilution. The present results suggest that the effect of sex applies across each method as similar differences were found when BIA was compared with SFA independently of DEXA.

The finding of greater error in FFM from SFA relative to DEXA contrasts with those of FULLER *et al.* [5], who found SFA to be the most accurate bedside method for the measurement of body composition when compared to a range of reference methods. This is probably due to differences in the study population, which was considerably younger in the study of FULLER *et al.* [5]. Significant differences in the results obtained by SFA compared to reference methods for FFM have been found in COPD patients and other elderly groups [17]. Errors in this method in the elderly have been ascribed to changes in fat distribution with age, which may not be reflected in the depth of subcutaneous fat [22, 23]. Although skinfold measurements do not directly measure total body water, the prediction of FFM is derived from a comparison with hydrodensitometry [8] and may therefore be subject to similar errors regarding hydration status to other methods.

The choice of method for the measurement of body composition should be determined by the purpose for which the measurement is intended. In clinical practice, this is likely to be the identification of nutritionally depleted patients as there is evidence that simple measurements of body weight are inadequate in COPD patients. The present authors have demonstrated that the identification of depleted patients is crucially dependant on the method of measurement of body composition. In practice, the choice of measurement method is likely to be determined by the availability of resources and equipment. Although DEXA may be the most accurate method for measuring FFM, it may impose logistical difficulties on patients with limited mobility (in Glenfield Hospital, for example, it requires travel to a different hospital within Leicester) and has a cost implication. For these reasons, it is appealing to use a bedside method for the measurement of body composition. The present study would support the use of BIA rather than SFA if this option is chosen. Furthermore, the data support the use of FFMI for expressing body composition data.

The reproducibility of body composition measurements over the rehabilitation period of the present study was excellent. This is reassuring if FFM is to be used as an outcome measure in pulmonary rehabilitation or nutritional intervention studies. However, the responsiveness of these measurements to such interventions is unknown. Clinically significant changes may not be detected unless reflected in an alteration in total body water or water distribution.

To conclude, significant intermethod differences in the measurement of body composition in chronic obstructive pulmonary disease patients have been demonstrated, indicating that they are not interchangeable in the present study population. These differences need to be borne in mind when choosing a method for the assessment of nutritional status in clinical practice or research studies.

Appendix

Fat-free mass (FFM) was estimated from impedance measurements using sex-specific regression equations as follows:

$$\text{FFM} = 8.383 + 0.465\text{ht}^2/R + 0.213\text{wt (males)}$$

$$\text{FFM} = 7.610 + 0.474\text{ht}^2/R + 0.184\text{wt (females)}$$

where ht is height, R is resistance, wt is weight, and mass/weight is given in kilograms, height in centimetres and resistance in ohms.

These equations were derived from a population of chronic obstructive pulmonary disease patients using deuterium-dilution as a validation method (A.M.W. Schols, University of Maastricht, Maastricht, the Netherlands, personal communication) (fig. 4).

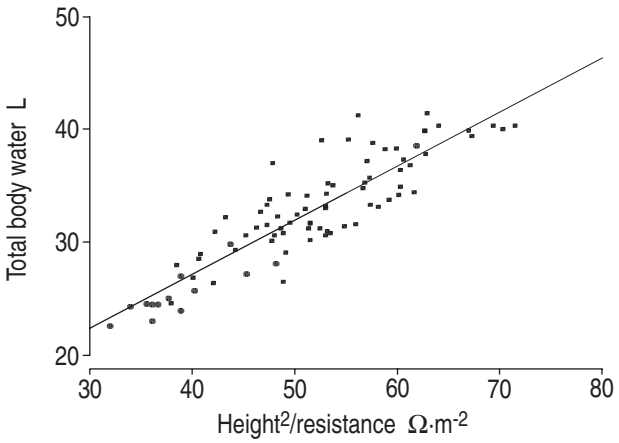

Fig. 4.–Validation of bioelectric impedance analysis as a means of measuring fat-free mass (FFM) against deuterium-dilution (total body water measurement). Data were obtained from a study of 117 chronic obstructive pulmonary disease patients (■: males; ●: females). Sex-specific regression equations for the calculation of FFM from impedance measurements were derived from this study (see Appendix). The regression line for the whole group is shown. (Reproduced with permission from A.M.W. Schols, University of Maastricht, Maastricht, the Netherlands).

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