Clinical value of anthropometric estimates of leg lean volume in nutritionally depleted and non-depleted patients with chronic obstructive pulmonary disease

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This study aimed to investigate the clinical usefulness of an anthropometrically based method for estimating leg lean volume (LLV) in patients with chronic obstructive pulmonary disease (COPD) who presented or not with nutritional depletion. We prospectively evaluated a group of fortyeight patients (thirty-eight males) with moderate to severe COPD (Global Initiative for Chronic Obstructive Lung disease stages II–IV) who underwent a 6 min walking test and knee isokinetic dynamometry. Leg lean mass (muscle mass plus bone) was determined by dual-energy X-ray absorptiometry (DEXA) with derivation of its respective volume: these values were compared with those obtained by the truncated cones method first described by Jones and Pearson in 1969. As expected, depleted patients (*n* 19) had reduced exercise capacity and impaired muscle performance as compared to non-depleted subjects (P < 0.01). The mean bias of the LLV differences between anthropometry and DEXA were 0.40 litre (95 % CI – 0.59, 1.39) and 0.50 litre (95 % CI – 1.08, 2.08) for depleted and non-depleted patients, respectively. Anthropometrically and DEXA-based estimates correlated similarly with muscle functional attributes. A ROC curve analysis revealed that leg height-corrected LLV values had acceptable sensitivity and specificity to identify depleted patients (area under the curve 0.93 (range 0.86–1.00); P < 0.001). Moreover, patients with LLV ≤ 9.2 litres/m (the best cut-off value according to the ROC curve) had significantly lower exercise capacity and muscle performance than their counterparts (P < 0.05). In conclusion, an anthropometrically based method of estimating LLV (Jones and Pearson method) was shown to present with clinically acceptable accuracy and external validity in depleted and non-depleted patients with stable COPD.

Anthropometry: DEXA: Chronic obstructive pulmonary disease: Body composition

Peripheral muscle dysfunction has been consistently related to local tissue depletion in patients with chronic obstructive pulmonary disease (COPD). Several studies have found that the preferential loss of muscle mass in the lower limbs has profound effects in patients' daily functioning⁽¹⁻⁵⁾.

A number of methods have been used to assess segmental body composition in this patient population^(1,6-8). Although some of them are highly accurate and precise, e.g. dualenergy X-ray absorptiometry (DEXA) and computed tomography, they are not widely available and require sophisticated equipment in a purpose-designed setting. For a widespread use in the clinical context, however, the 'ideal' method needs to be practical, portable and inexpensive. Moreover, it should be sensitive to detect tissue depletion and present with a high-degree of external validity, i.e. its estimates need to correlate well with independent measures of functional capacity. In this context, the anthropometrically based method of Jones & Pearson⁽⁹⁾ to estimate leg lean volume (LLV) could be valuable⁽¹⁰⁾. Despite this method being extensively used in healthy subjects^(11–13), including the elderly^(14,15), no previous study has evaluated its clinical usefulness in patients with COPD presenting with variable degrees of tissue depletion.

The present objective, therefore, was to determine the feasibility, accuracy and external validity of LLV estimates as established by the Jones & Pearson approach⁽⁹⁾ in depleted and non-depleted patients with stable COPD.

Methods

Study population

Forty-eight (ten females) patients, aged 50 or older, with stable, moderate-to-severe COPD according to the Global

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Abbreviations: COPD, chronic obstructive pulmonary disease; DEXA, dual-energy X-ray absorptiometry; DL_{CO}, carbon monoxide diffusing capacity; FEV₁, forced expiratory volume in 1 s; FFM, fat-free mass; FVC, forced vital capacity; LLV, leg lean volume.

Initiative for Chronic Obstructive Lung disease criteria⁽¹⁶⁾, were studied. They were referred from the COPD outpatients clinic of the Federal University of São Paulo (São Paulo, Brazil). All patients had forced expiratory volume in 1s (FEV₁)/forced vital capacity (FVC) ratio < 0.70 and postbronchodilator $FEV_1 < 70\%$ predicted; in addition, they were clinically stable with no disease exacerbation in the past 4 weeks and they had quit smoking for at least 6 months. Patients presenting with physical disabilities, other wasting chronic diseases (e.g. chronic renal failure, diabetes), under long-term oxygen therapy and BMI higher than 30 kg/m^2 were excluded. No patient had taken part in a pulmonary rehabilitation programme in the preceding 6 months. All patients were optimized in terms of standard medical therapy: maintenance medication included long- and short-acting β_2 -agonists, theophylline and inhaled steroids. No patient was receiving oral steroids or diuretics. The Local Ethics Committee approved the study and written informed consent was obtained from all participants.

Measurements

Pulmonary function tests. Spirometric tests were performed by using the CPF System[™] (Medical Graphics Corporation, St Paul, MN, USA) with airflow being measured by a calibrated pneumotachograph. The subjects completed at least three acceptable maximal forced expiratory manoeuvres before and after 400 µg inhaled salbutamol; in the present paper, only post-bronchodilator data are reported. FVC (litre) and FEV₁ (litre) were recorded and expressed as percentage of the predicted value⁽¹⁷⁾. A constant-volume and differential-pressure body plethysmograph (1085 Profiler & Elite, Series D; Medical Graphics Corporation) was used to measure static lung volumes (total lung capacity (litre) and residual volume (litre), respectively). Carbon monoxide diffusing capacity (DL_{CO}) was measured by the modified Krogh technique (single breath); the subjects performed three acceptable and reproducible tests, with the results being within 10% or 3 ml CO/min per mmHg. Predicted values for lung volumes and DL_{CO} were those proposed by Neder *et al.* ^(18,19) for the adult Brazilian population. Arterial blood was taken from the radial artery according to standard anaerobic conditions for pH, arterial oxygen tension (mmHg) and arterial carbon dioxide tension (mmHg) measurements.

Body composition assessment

Body anthropometry. Body height was determined to the nearest 0.1 cm with subjects standing barefoot. Body weight was assessed with the beam scale to the nearest 0.1 kg, with subjects standing barefoot and in light clothing. BMI was calculated as weight/height² (kg/m²).

Leg lean volume anthropometry. The lean (fat-free) volume of the right leg (litre) was calculated by the Jones & Pearson method⁽⁹⁾, which is based on the summation of truncated cones (Fig. 1). Briefly, with the patient standing erect and the feet slightly apart seven circumferences were taken with a metric tape at predetermined sites: the gluteal furrow (C1), one-third of the subischial height up from the tibial–femoral joint space (C2), the minimum circumference above the knee (C3), the maximum circumference around the knee

381

(C4), the minimum circumference below the knee (C5), the maximum calf circumference (C6) and the minimum ankle circumference (C7). The heights (h) above the floor level for each circumference were obtained by using a stadiometer. In addition, anterior and posterior skinfold thicknesses were measured at C2 (thigh) and C6 (calf) using a Harpenden caliper following standard techniques⁽²⁰⁾. All measurements were performed by a nutritionist or dietitian.

In order to obtain the volume of a truncated right circular cone (Vc), the following equation was used:

$$Vc = 1/3\pi h(r^2 + Rr + R^2),$$

where h is the distance between the circumferences, r is the radius of the upper plane and R is the radius of the lower plane. The volume of the foot (*Vf*) was also calculated by assuming the foot to be wedge-shaped:

$$Vf = 1/2l \times b \times h$$
,

where *l* is the foot's length and *b* is the diameter calculated from C7 (Fig. 1). LLV (litre) was then calculated by summing up the volumes of the six lean cones (i.e. by subtracting the skinfold readings from their respective diameters) plus *Vf*. In addition, LLV was expressed as a function of leg height (m) to further correct for inter-individual differences in leg dimensions. All equations have been previously entered into a widely available data sheet software for faster results (MicrosoftTM Office Excel, 2003).



Fig. 1. Schematic illustration of the sites from which the anthropometric measurements should be taken in order to obtain the six truncated cones (1-6) for leg lean volume estimation according to the Jones & Pearson technique⁽⁹⁾. *b*, diameter of ankle; *h*, height above floor level. Reproduced with the permission of Wiley-Blackwell Publishing Ltd from Jones PR & Pearson J (1969) Anthropometric determination of leg fat and muscle plus bone volumes in young male and female adults, *Journal of Physiology* **204**, 63–66.

Dual-energy X-ray absorptiometry. Total body and right leg fat-free masses (FFM; kg) were also measured by DEXA fan beam technology (QDR-4500A; Hologic Inc., Bedford, MA, USA). In this method, the subjects are scanned with photons produced by an X-ray source at two different energy levels. Bone ash (calcium hydroxyapatite) tissue and soft tissue are separated based on the degree of photon attenuation. The differential absorption with soft tissue is also measured and the ratio of absorbency of the two energy level photons has been shown to be linearly related to the percentage of fat in these tissues. In order to obtain lean (bone plus muscle) leg volumes by DEXA, we divided the mass of each compartment (fat, muscle and bone) by their mean respective densities $^{(21-23)}$. In the present study, nutritional depletion was established if $BMI \le 21 \text{ kg/m}^2$ and/or the FFM index (FFM/height²) from whole-body DEXA was $\leq 15 \text{ kg/m}^2$ for females and $\leq 16 \text{ kg/m}^2$ for males⁽²⁴⁾.

Exercise and peripheral muscle performance

Six-minute walking distance. Functional exercise capacity was measured by the 6 min walking distance test (m) in a 50 m in-hospital corridor. Technical procedures were those recommended by the American Thoracic Society⁽²⁵⁾. The tests were performed in duplicate after familiarization and the highest value was recorded.

Isokinetic dynamometry. Concentric contractions of the quadriceps femoris (knee extension) of the right leg were evaluated by using an isokinetic dynamometer (Con-TrexTM; Cybex, Chattanooga, NY, USA). All patients performed a maximum isokinetic strength test with two trials of five sequential contractions at an angular velocity of 60° per s as peak torque (N × m). After a rest period of at least 5 min, patients performed an isometric strength (N × m) test with two trials against a fixed resistance pad at 60° per s. After another resting period, patients performed two knee-extensor tests at 300° per s (thirty repetitions) to record mean total work (J/contraction)⁽²⁶⁾. The highest value was selected for analysis in all tests.

Statistical analysis

Results are presented as means and standard deviations. In order to contrast body composition and functional variables between depleted and non-depleted patients, a non-paired *t* test was used. Pearson's correlation coefficient was obtained to estimate the level of association between continuous variables. Sensitivity and specificity of LLV by anthropometry in identifying depleted patients were assessed by a ROC curve analysis. The level of statistical significance was set at P < 0.05.

The limits of agreement between LLV estimates by anthropometry and DEXA were investigated by plotting the individual differences against their respective means (Bland–Altman analysis). Heteroscedasticity was examined by plotting the absolute (i.e. ignoring any sign) differences against the individual means and calculating the Spearman's correlation coefficient⁽²⁷⁾. If the heteroscedasticity correlation was close to zero, the mean bias and the 95 % limits of agreement were calculated as mean \pm 1.96 sD of the between-estimate differences.

Results

Nineteen subjects (39%) were considered as nutritionally depleted⁽²⁴⁾. As shown in Table 1, they had more severe airflow obstruction and lower DL_{CO} than non-depleted subjects. In fact, fifteen of the nineteen depleted patients (79%) were classified as stages III–IV according to the Global Initiative for Chronic Obstructive Lung disease guidelines⁽¹⁶⁾; in contrast, twenty-five of the twenty-nine non-depleted subjects (86%) were on stages II–III. In addition, depleted subjects had significantly lower LLV, exercise capacity and peripheral muscle performance (P < 0.01; Table 1).

As described in the Methods, LLV by anthropometry was compared with the values derived from DEXA scan of the right leg (Table 2). A Bland–Altman analysis revealed that the mean bias of the LLV differences between anthropometry and DEXA were 0.40 litre (95 % CI -0.59, 1.39) and 0.50 litre (95 % CI -1.08, 2.08) for depleted and non-depleted patients, respectively (Fig. 2). There were significant correlations between all of the muscle functional attributes with LLV by anthropometry: the correlation coefficients did not differ substantially from those obtained against leg FFM by

 Table 1. Demographic, body composition and functional characteristics

 of depleted and non-depleted patients with chronic obstructive pulmonary disease

	Depleted (n 19)		Non-depleted (n 29)	
Variables	Mean	SD	Mean	SD
Demography and body compo	sition			
Sex (male/female)	13/6		25/4	
Age (years)	64.2	8.2	64.6	7.0
BMI (kg/m²)	19.3*	2.1	25.6	2.6
FFM (kg)	39.4*	5.6	50.0	8.0
FFMI (kg/m ²)	15.0*	1.1	18.3	1.5
Spirometry				
FEV ₁ (litres)	0.99*	0.39	1.38	0.48
FEV ₁ (% predicted)	39.6*	13.8	52.0	14.7
FVC (litres)	2.58	0.84	2.95	0.85
FVC (% predicted)	81.1	21.0	88.6	18.4
FEV ₁ /FVC (% predicted)	48.6*	9.4	58.5	11.7
Static lung volumes				
TLC (litres)	7.06	1.61	7.02	1.20
TLC (% predicted)	121.1	15.9	114.6	16.5
RV (litres)	4.25	1.45	3.82	0.97
RV (% predicted)	223.7	75.8	191.7	45.6
RV/TLC (% predicted)	176.5	55.0	166.6	28.3
Arterial blood gases				
PaO ₂ (mmHg)	68.5	6.3	66.6	6.8
PaCO ₂ (mmHg)	42.1	6.7	40.2	4.3
рН	7.39	0.02	7.40	0.04
Lung diffusing capacity				
DL _{CO} (% predicted)	43.0*	16.6	57.8	15.3
Exercise tolerance				
Distance walked (m)	443.5*	65.5	506.1	68.0
Muscle performance				
Peak torque (N × m)	89.3*	24.4	117.6	33.1
Isometric strength (N \times m)	105.5*	26.4	135.6	36.1
Mean work (J/contraction)	42.0*	14.8	53.0	15.0

DL_{CO}, carbon monoxide diffusing capacity; FEV₁, forced expiratory volume in 1 s; FFM, fat-free mass; FFMI, fat-free mass index; FVC, forced vital capacity; PaCO₂, arterial carbon dioxide tension; PaO₂, arterial oxygen tension; RV, residual volume; TLC, total lung capacity.

Mean values were significantly different from those of the non-depleted group (non-paired t test): *P<0.05.

	Depleted (n 19)		Non-de (n 2	pleted 29)	
Variables	Mean	SD	Mean	SD	
Leg composition					
FM (kg)	1.8*	0.8	2.7	0.7	
FM (%)	22.4	8.8	26.2	5.9	
FFM (kg)	6·1*	1.1	7.8	1.4	
FFM (%)	77.5	8.8	73.7	5.9	
Leg anthopometric measurements					
C1 (cm)	45·1*	3.9	53.1	4.0	
C2 (cm)	42.9*	3.7	50.2	3.9	
C3 (cm)	33.4*	3.2	37.8	3.2	
C4 (cm)	32.8*	2.0	37.2	3.0	
C5 (cm)	29.7*	1.6	33.0	3.1	
C6 (cm)	30.7*	2.1	34.8	2.5	
C7 (cm)	21.3*	1.8	23.0	2.0	
LF (cm)	24.8	1.6	25.0	1.4	
LLC1 (cm)	42.7*	3.2	49.9	3.5	
LLC2 (cm)	40.5*	3.0	46.9	3.5	
LLC3 (cm)	31.0*	3.0	34.6	3.2	
LLC4 cm)	30.4*	2.0	34.0	2.8	
LLC5 (cm)	28.5*	1.6	31.5	2.9	
LLC6 (cm)	29.4*	2.0	33.3	2.6	
LLC7 (cm)	20.1*	1.9	21.5	2.1	
TLV (litres)	6.84*	1.11	8.91	1.48	
LLV (litres)	6.24*	1.04	7.97	1.31	

C1 to C7, circumferences 1 to 7; FFM, fat-free mass; FM, fat mass; LF, length of the foot; LLC1 to LLC7, leg lean circumferences 1 to 7; LLV, lean leg volume; TLV, total leg volume.

Mean values were significantly different from those of the non-depleted group (nonpaired *t* test): **P*<0.05.

DEXA. Interestingly, however, only in non-depleted patients was there a significant correlation between distance walked and leg volume and mass (Table 3).

We also sought to investigate whether the leg height-corrected LLV estimates would be sensitive enough to differentiate depleted from non-depleted patients. As depicted in Fig. 3, the area under the ROC curve showed high sensitivity and



Fig. 2. The limits of agreement (Bland–Altman plot) between anthropometry (ANTHRO) and dual-energy X-ray absorptiometry (DEXA) in estimating the leg lean volume (litre) in depleted (●) and non-depleted (○) patients with chronic obstructive pulmonary disease.

specificity in identifying depleted patients. Therefore, a leg height-corrected LLV ≤ 9.2 litres/m was 95% sensitive and 80% specific to indicate nutritional depletion. Moreover, patients with reduced height-corrected LLV had significantly lower exercise capacity and muscle performance than their counterparts who presented with higher values (Table 4; P < 0.05).

Discussion

The present study has shown that LLV estimates, as determined by the anthropometric technique of Jones & Pearson⁽⁹⁾, were comparable with those derived from DEXA and they correlated as well as lean (bone plus muscle) DEXA readings with measures of peripheral muscle function in depleted and non-depleted patients with COPD. The present data indicate that this method presented with acceptable accuracy and external validity in this patient population. Moreover, LLV showed high specificity and sensitivity to identify patients with wholebody FFM depletion. This technique, therefore, might prove to be useful in clinical settings where more advanced and expensive techniques for segmental body composition assessment are not accessible.

There is a long-standing interest in developing anthropometry-based methods for segmental body composition evaluation in different clinical populations. More recently, it has been shown that many patients with COPD may develop important functional abnormalities on the peripheral muscle, which seem to be related, at least partially, to local FFM depletion^(2,5,28,29). There is also evidence demonstrating that leg FFM depletion is a strong predictor of morbidity and mortality in these patients⁽⁴⁾. However, several investigators have found that appendicular muscle depletion correlates variably with whole-body measurements and direct evaluation of limb tissue depletion is $advisable^{(10,30)}$. Unfortunately, most studies involving segmental body composition assessment in patients with COPD used sophisticated and expensive methods (e.g. computed tomography and DEXA) which hampered their practical application in clinical settings.

In the present study, we investigated the feasibility, accuracy and external validity of an alternative, anthropometry-based technique that was proposed almost four decades ago⁽⁹⁾. The Jones & Pearson approach⁽⁹⁾ uses standard geometric principles to model the human leg as a series of truncated cones from the gluteal furrow down to the foot (Fig. 1). By obtaining the thickness of anterior and posterior subcutaneous fat deposition on the thigh and on the mid-calf, the inner (lean) leg volume can be estimated. The main advantage of this method relies on its low cost and the lack of a need for technologically advanced equipment. However, it should be recognized that it requires a reasonable amount of manual labour (approximately 20 min/patient) and careful standardization of the places to measure the circumferences and their heights from the floor. As cited, the method also assumes that anterior and posterior skinfold thickness remains invariable across the thigh and leg cones which can introduce a source of error in the estimation of lean volume. In addition, it is advisable that the recorded values be entered into a previously designed computing program for quicker and more precise results.

We found that the limits of agreement between LLV measured by this technique and by DEXA have a small

D. S. Villaça et al.

Table 3. Correlation between leg lean mass by dual-energy X-ray absorptiometry and leg lean volume by anthropometry with selected indexes of functional capacity and peripheral muscle strength in depleted and non-depleted patients with chronic obstructive pulmonary disease

Variable	Leg lean mass (kg)		Leg lean volume (litres)		
	Depleted	Non-depleted	Depleted	Non-depleted	
Distance walked (m)	0.022	0.475*	-0.104	0.500*	
Peak torque (N × m)	0.756*	0.549*	0.667*	0.567*	
Isometric strength $(N \times m)$	0.814*	0.599*	0.763*	0.611*	
Mean work (J/contraction)	0.724*	0.515*	0.676*	0.543*	

Pearson's *R* correlation coefficients: **P*<0.05.

mean bias (within 0.5 litre or 7%) with a symmetrical distribution of the residuals, either in depleted and non-depleted patients. Therefore, as there was no evidence of heteroscedasticity on data distribution (i.e. error proportional to the mean) and the mean inter-method difference was within 20% for most subjects, the estimates seem to provide an acceptable accuracy for estimating LLV in these patients (see later). In this regard, however, a note of caution should be made: it is likely that a small error has been introduced in the betweenmethod comparison of the thigh volume, as a diagonal line delimits the upper limit of the thigh by DEXA but the top plane of cone 1 is horizontal (Fig. 1).

We also showed that LLV estimated by anthropometry and FFM readings by DEXA correlate similarly with selected indexes of skeletal muscle functioning, which indicated a comparable degree of external validity. Interestingly, however, neither LLV nor FFM were significantly related to 6 min walking distance in depleted patients. Although the exact reason for this finding is not clear, it should be noted that depleted patients had significantly lower maximal ventilatory capacity than non-depleted subjects (Table 1).



Fig. 3. A ROC curve analysis of the diagnostic performance of anthropometric estimates (leg lean volume/leg height, l/m) in identifying patients with nutritional depletion. Note that a threshold value of 9.2 litres/m presented with the best combination of sensitivity and specificity (95 and 80 %, respectively). Depletion was defined according to the following criteria⁽²⁴⁾: BMI \leq 21 kg/m² and/or fat-free mass index \leq 15 kg/m² in females and \leq 16 kg/m² in males. AUC, area under the curve.

Therefore, it is conceivable that pulmonary-ventilatory mechanisms, as opposed to peripheral muscles factors, played a greater role to limit whole-body exercise capacity in depleted patients.

Another interesting finding of the present study was the high specificity and sensitivity of the technique in identifying depleted patients with COPD (Fig. 3). In fact, patients with leg-height corrected LLV \leq 9·2 litres/m, the best cut-off to indicate nutritional depletion on a ROC curve analysis, had significantly worse lung function and physical performance than patients with higher LLV values (Table 4). To the authors' knowledge, this is the first study to look at the practical value of segmental anthropometry in distinguishing

Table 4. Resting and exercise characteristics of chronic obstructive pul-
monary disease patients presenting (Group A) or not (Group B) with leg
lean volume/leg height \leq 9·2 litres/m

	Group A (<i>n</i> 22)		Group B (<i>n</i> 26)	
Variable	Mean	SD	Mean	SD
Demographic				
Sex (male/female)	14/8		24/2	
Age (years)	66.0	8.6	63-1	6.0
BMI (kg/m ²)	19.9*	2.3	25.8	2.7
FFM (kg)	38.7*	4.7	51.9	6.6
FFMI (kg/m ²)	15.2*	1.2	18.5	1.5
Spirometry				
FEV1 (litres)	0.98*	0.29	1.44	0.52
FEV1 (% predicted)	41.5*	12.5	51.8	16.3
FEV1/FVC (% predicted)	49.3*	10.3	59.0	11.3
Static lung volumes				
TLC (% predicted)	126.9*	16.0	109.4	12.5
RV (% predicted)	235.6*	66.7	183.1	41.6
RV/TLC (% predicted)	183.5	35.8	166.9	31.4
Arterial blood gases				
PaO ₂ (mmHg)	65.9	6.2	68.4	6.9
Lung diffusing capacity				
DL _{CO} (% predicted)	44.5*	16.2	57.5	16.0
Exercise tolerance				
Distance walked (m)	437.9*	61.3	517.4	63.0
Muscle performance				
Peak torque (N \times m)	85·1*	22.1	124.4	29.6
Isometric strength (N \times m)	97.8*	14.7	145.3	33.4
Mean work (J/contraction)	38.1*	11.1	57.5	13.6

DL_{CO}, carbon monoxide diffusing capacity; FEV₁, forced expiratory volume in 1 s; FFM, fat-free mass; FFMI, fat-free mass index; FVC, forced vital capacity; PaCO₂, arterial carbon dioxide tension; PaO₂, arterial oxygen tension; RV, residual volume; TLC, total lung capacity.

Mean values were significantly different from those of Group B (non-paired t test): *P<0.05.

depleted from non-depleted patients with COPD. However, this threshold value should be further validated in larger and more heterogeneous samples (see later).

The present study has some relevant limitations. Firstly, the method inter- and intra-subject variabilities remain to be determined; however, they are expected to be similar to other anthropometric techniques as only a few skinfold measurements are needed and the limb circumferences are not especially difficult for trained subjects to obtain. Secondly, it was not our objective to establish the responsiveness of the technique to nutritional or ergogenic interventions and future studies should address this issue. Thirdly, we did not use more direct techniques for LLV determination in order to compare them with anthropometry: the DEXA estimates, therefore, cannot be assumed as the 'true' values. Fourthly, it remains to be determined whether this method compares favourably against other similarly simple, albeit costlier, techniques for the evaluation of segmental body composition, such as appendicular bioimpedance $^{(31,32)}$. Finally, the present results should not be extrapolated to other sub-populations of patients with COPD, including those who are obese $(BMI > 30 \text{ kg/m}^2)$, hypoxaemic, clinically unstable and dehydrated.

In conclusion, a simple and inexpensive technique to estimate the LLV by anthropometry⁽⁹⁾ was shown to present with acceptable accuracy and external validity in depleted and nondepleted patients with stable COPD. This approach seems to be of practical value when more complex and costlier techniques for segmental body composition assessment are not available.

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References

 Bernard S, LeBlanc P, Whittom F, Carrier G, Jobin J, Belleau R & Maltais F (1998) Peripheral muscle weakness in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 158, 629–634.

- Serres I, Hayot M, Prefaut C & Mercier J (1998) Skeletal muscle abnormalities in patients with COPD: contribution to exercise intolerance. *Med Sci Sports Exerc* 30, 1019–1027.
- Yoshikawa M, Yoneda T, Takenaka H, Fukuoka A, Okamoto Y, Narita N & Nezu K (2001) Distribution of muscle mass and maximal exercise performance in patients with COPD. *Chest* 119, 93–98.
- Marquis K, Debigare R, Lacasse Y, LeBlanc P, Jobin J, Carrier G & Maltais F (2002) Midthigh muscle cross-sectional area is a better predictor of mortality than body mass index in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 166, 809–813.
- Franssen FME, Broekhuizen R, Janssen PP, Wouters EFM & Schols AMW (2005) Limb muscle dysfunction in COPD: effects of muscle wasting and exercise training. *Med Sci Sports Exerc* 37, 2–9.
- Steiner MC, Barton RL, Singh SJ & Morgan MDL (2002) Bedside methods versus dual energy X-ray absorptiometry for body composition measurement in COPD. *Eur Respir J* 19, 626–631.
- Engelen MPKJ, Schols AMWJ, Heidendal GAK & Wouters EFM (1998) 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* 68, 1298–1303.
- Kilduff LP, Fuld JP, Neder JA, Pitsiladis YP, Carter R, Stevenson R & Ward SA (2003) Clinical relevance of inter-method differences in fat-free mass estimation in chronic obstructive pulmonary disease. *Respiration* **70**, 585–593.
- Jones PR & Pearson J (1969) Anthropometric determination of leg fat and muscle plus bone volumes in young male and female adults. J Physiol 204, 63–66.
- Degens H, Sanchez-Horneros JM, Heijdra YF, Dekhuijzen PNR & Hopman MTE (2005) Skeletal muscle contractility is preserved in COPD patients with normal fat-free mass. *Acta Physiol Scand* 184, 235–242.
- Doré E, Bedu M, França NM & Van Praagh M (2001) Anaerobic cycling performance characteristics in prepubescent, adolescent and young adult females. *Eur J Appl Physiol* 84, 476–481.
- Howden R, Lightfoot JT, Brown SJ & Swaine IL (2002) The effects of isometric exercise training on resting blood pressure and orthostatic tolerance in humans. *Exp Physiol* 87, 507–515.
- 13. Tothill P & Stewart AD (2002) Estimation of thigh muscle and adipose tissue volume using magnetic resonance imaging and anthropometry. *J Sports Sci* **20**, 563–576.
- Marsh GD, Paterson DH, Govindasamy D & Cunningham DA (1999) Anaerobic power of the arms and legs of young and older men. *Exp Physiol* 84, 589–597.
- Pearson S, Cabbold M, Orrell RW & Harridge SDR (2006) Power output and muscle myosin heavy chain composition in young and elderly men. *Med Sci Sports Exerc* 38, 1601–1607.
- Pauwels RA, Buist AS, Calverley PM, Jenkins CR & Hurd SS (2001) Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/ WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) workshop summary. *Am J Respir Crit Care Med* 163, 1256–1276.
- Pereira CAC, Barreto SP, Simões JG, Pereira FWJ, Gerstler JG & Nakatani J (1992) Valores de referência para a espirometria em uma amostra da população brasileira adulta. *J Pneumol* 18, 10–22.
- Neder JA, Andreoni S, Castelo-Filho A & Nery LE (1999) Reference values for lung function tests. I. Static volumes. *Braz J Med Biol Res* 32, 703–717.
- Neder JA, Andreoni S, Peres C & Nery LE (1999) Reference values for lung function tests. III. Carbon monoxide diffusing capacity (transfer factor). *Braz J Med Biol Res* 32, 729–737.

385

D. S. Villaça et al.

- Harrison GG, Buskirk ER, Carter JEL, Johnston FE, Lohman TG, Pollock ML, Roche AF & Wilmore J (1988) Skinfold thicknesses and measurement technique. In *Anthropometric Standardization Reference Manual*, pp. 55–70 [TG Lohman, AF Roche and R Martorell, editors]. Champaign, IL: Human Kinetics Publishers.
- 21. Cheng X, Li J, Lu Y, Keyak J & Lang T (2007) Proximal femoral density and geometry measurements by quantitative computed tomography: association with hip fracture. *Bone* **40**, 169–174.
- Prior BM, Modlesky CM, Evans EM, Sloninges MA, Sauders MJ, Lewis RD & Cureton KJ (2001) Muscularity and the density of the fat-free mass in athletes. *J Appl Physiol* 90, 1523–1531.
- Wang MC, Bachrach LK, Van Loan M, Hudes M, Flegal KM & Crawford PB (2005) The relative contributions of lean tissue mass and fat mass to bone density in young women. *Bone* 37, 474–481.
- Vermeeren M, Creutzberg E, Schols A, Postma D, Pieters W, Roldaan A, Wouters E & on behalf of the COSMIC study group (2006) Prevalence of nutritional depletion in a large out-patient population of patients with COPD. *Respir Med* 100, 349–1355.
- American Thoracic Society Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories (2002) ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 166, 111–117.

- Neder JA, Nery LE, Shinzato GT, Andrade MS, Peres C & Silva AC (1999) Reference values for concentric knee isokinetic strength and power in nonathletic men and women from 20 to 80 years old. J Orthop Sports Phys Ther 29, 116–126.
- 27. Bland JM & Altman DG (1986) Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* **1**, 307–310.
- Baarends EM, Schols AMWJ, Mostert R & Wouters EFM (1997) Peak exercise response in relation to tissue depletion in patients with chronic obstructive pulmonary disease. *Eur Repir J* 10, 2807–2813.
- Malaguti C, Nery LE, Dal Corso S, Nápolis L, De Fuccio MB, Lerario MC, Castro M & Neder JA (2006) Scaling skeletal muscle function to mass in patients with moderate-to-severe COPD. *Eur J Appl Physiol* **98**, 482–488.
- Couillard A, Maltais F, Saey D, Debigaré R, Michaud A, Koechlin C, LerBlanc P & Préfaut C (2003) Exercise-induced quadriceps oxidative stress and peripheral muscle dysfunction in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 167, 1664–1669.
- Loenzo AD & Andredi A (2003) Segmental bioelectrical impedance analysis. *Curr Opin Nutr Metab care* 6, 551–555.
- Salinari S (2003) Bioimpedance analysis: a useful technique for assessing appendicular lean soft tissue mass and distribution. *J Appl Physiol* 94, 1552–1556.