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# Searching for a relevant definition of sarcopenia: results from the cross-sectional EPIDOS study

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## Abstract

**Background** The diversity of definitions proposed for sarcopenia has been rarely tested in the same population, and so far, their clinical utilities for predicting physical difficulties could not be clearly understood. Our objective is to report the prevalence of sarcopenia and the characteristics of sarcopenic community-dwelling older women according to the different definitions of sarcopenia currently proposed. We also assessed these definitions for their incremental predictive value over currently standard predictors for some self-reported difficulties in physical function and knee extension strength.

**Methods** Cross-sectional analysis included data from 3025 non-disabled women aged 75 years or older without previous history of hip fracture from the inclusion visit of the EPIDémiologie de l'Ostéoporose study. A total body composition evaluation was available for 2725 women. Sarcopenia was defined using six different definitions of sarcopenia based on different muscle mass, gait speed, and grip strength cut-offs. Self-reported difficulties in physical function and knee extension strength were collected. Logistic regression and multiple linear regression models were built for each physical dysfunction, and the predictive capacity of sarcopenia (one model for each definition) was studied using the C-statistic, the net reclassification index, or adjusted  $R^2$ .

**Results** The estimated prevalence of sarcopenia ranged from 3.3–20.0%. Only 85 participants (3.1%) were identified having sarcopenia according to all definitions. All definitions were, to some degree, associated with self-reported difficulties in physical function and knee extension strength, but none improved the predictive ability of the self-reported difficulties in physical function. Conversely, all definitions accounted for a small but significant amount of explained variation for predicting knee extension strength.

**Conclusions** Prevalence of sarcopenia varies widely depending on the definition adopted. Based on this research, the current definitions for sarcopenia does not substantially increment the predictive value of clinical characteristics of patients to predict self-reported physical difficulties and knee extension strength.

**Keywords** Sarcopenia; Muscle mass; Definition; Physical function

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## Introduction

Sarcopenia is a growing area of research and a great opportunity for the development of new drugs because it is an important determinant of physical function in older people<sup>1</sup> and a potential pharmaceutical target in the prevention of mobility disability in older people. Researchers agree that sarcopenia

is defined by a loss of muscle mass, muscle strength, and muscle quality, but a unique consensual operational definition of sarcopenia is lacking. In fact, no less than six clinical approaches have been proposed since 1998 to establish the diagnosis of sarcopenia in practice.<sup>2–7</sup> To our knowledge, no definition has clearly proven its superiority over previous definitions. The first approach<sup>2</sup> to define sarcopenia has been

used by a number of investigators and relies on an arbitrary cut-off of appendicular muscle mass assessed by dual X-ray absorptiometry (DXA). A different statistical approach<sup>4</sup> and a different cut-off of muscle mass have also been proposed few years later to reduce the limitation of this first approach in obese and thin subjects and to improve the rationale of the cut-point.<sup>5</sup> However, these first proposals are not completely satisfactory because the influence of muscle mass on mobility is complex. Muscle mass is definitely not the only determinant of mobility, and physical performances measures have appeared as prominent determinants of lower functional capacities. Then, the last three definitions of sarcopenia<sup>3,6,7</sup> are characterized by different easy-to-measure functional tool (gait speed and/or handgrip strength with a different cut-off) in addition to muscle mass (with a different cut-off).

This controversy in the definition of sarcopenia results in inconsistent conclusions across cohorts and impossible comparison and represents an important limitation for drug agencies such as the Federal Drug Administration or the European Medicines Agency to consider sarcopenia as a treatable condition. A cohesive view of sarcopenia is urgently needed.

The aims of this study were to report the prevalence of sarcopenia and the characteristics of the sarcopenic older people according to six current different definitions in a large cohort study and also to quantify the improvement in self-reported difficulties in physical function and knee extension strength (KES) prediction offered by these definitions.

## Materials and methods

### *EPIDémiologie de l'OStéoporose cohort*

We studied data from the Epidemiologie de l'Osteoporose (EPIDOS) study, a prospective cohort study whose primary purpose was to evaluate risk factors for hip fracture in a healthy community-dwelling population of elderly women. The sampling and data collection procedures have been previously described in detail.<sup>8</sup> Briefly, between January 1992 and January 1994, 7598 women recruited from the electoral lists, in five French cities, volunteered to participate. Women disabled for walking (walking aids allowed), with a history of femoral neck fracture, hip replacement or institutionalization, or subjects unable to understand or answer the questionnaire were excluded. The present study was limited to the 1563 participant included in Lyon and the 1462 participant included in Toulouse. These participants completed a total body composition assessment [bone mineral density, lean mass (LM), and fat mass (FM)] by DXA and a physical exam including anthropometric measures (height, weight, and calf circumference). A total body composition assessment was available for 2725 women. Cognition was evaluated using the short portable mental

status questionnaire (SPMSQ, 10). The SPMSQ, a 10-item questionnaire, was developed to detect the presence of cognitive decline in community-dwelling older adults. The validated cut-off value for normal cognitive functioning is a score of 8 or above.<sup>9</sup> The local ethics committee of the participating centres approved the study, and each woman signed informed consent.

### *Sarcopenia definitions*

Six different definitions were used to define sarcopenia (coded I to VI). Three of them rely on muscle mass only (2, 4, and 5), two rely on muscle mass and gait speed,<sup>6,7</sup> and one on muscle mass, gait speed, and/or handgrip strength.<sup>3</sup>

#### *Assessment of body composition*

The body composition of all participants was measured using DXA. The DXA apparatus (Hologic QDR 4500 W, Hologic, Waltham, MA, USA) was regularly calibrated, and the DXA protocol was performed by a trained technician. We used an accurate method to quantify appendicular skeletal muscle mass (ASM),<sup>10,11</sup> which corresponds to the sum of the muscle mass (in kilogrammes) of the four limbs.

#### *Assessment of gait speed*

A standardized assessment of gait speed was performed at baseline. Participants were asked to perform a 6 m walk at their usual pace; walking aids were allowed.<sup>12,13</sup> Timing began when the command was given, and time in seconds needed to complete the 6 m walk was recorded. The faster of two walks was retained for the present analysis. Gait speed was calculated in metres (m) per second (s).

#### *Assessment of handgrip strength*

Handgrip strength was measured for the dominant hand with a hydraulic hand dynamometer (Martin Vigorimeter, Medizin Technik, Tuttlingen, Germany). The size of the grip was adjusted so that the participant felt comfortable. The participant stood upright with the arm vertical and the dynamometer close to the body. The maximal peak pressure expressed in Newton per square metre ( $\text{Nm}^{-2}$ ) was recorded for a set of three contractions and was used for the present analyses. Handgrip strength was analysed in quartiles. This following overview summarizes chronologically the six diagnostic criteria used in this study. They have been previously described in detail<sup>2-6,14</sup>.

#### *Definition I*

Sarcopenia definition proposed by Baumgartner *et al.*<sup>2</sup> Baumgartner defined sarcopenia using the ASM/height<sup>2</sup> ratio establishing the threshold at two standard deviations lower than the average of a young reference population defined sarcopenia. The cut-off that defines sarcopenia in women is  $\text{ASM/height}^2 \leq 5.45 \text{ kg/m}^2$ .

#### Definition II

Sarcopenia definition using the residuals method proposed by Newman *et al.*<sup>4</sup> A measure of relative LM (LM, kilogrammes, kg) was derived by adjusting for fat mass (FM, kg) in addition to height (metres, m). The residuals of the regression were used to identify those whose LM was much lower or higher than the predicted value. A positive residual would indicate a relatively muscular individual, whereas negative values would indicate relatively sarcopenic individuals. The 20th percentile of the distribution of residuals was used as the cut-off for sarcopenia.

#### Definition III

Sarcopenia definition using the ASM cut-off proposed by Delmonico *et al.*<sup>5</sup> Instead of comparing ASM/height<sup>2</sup> with a cut-off from younger population, participants were classified as sarcopenic if their ASM/height<sup>2</sup> fell into the sex-specific lowest 20% of the health ageing and body composition study distribution of the index (ASM/height<sup>2</sup> ≤ 5.67 kg/m<sup>2</sup>).

#### Definition IV

Sarcopenia definition proposed by the European Working Group on Sarcopenia in Older People<sup>3</sup> This definition is based on the presence of a low ASM using the Baumgartner's criteria (ASM/height<sup>2</sup> ≤ 5.45 kg/m<sup>2</sup>) combined with a low gait speed with a threshold established at ≤ 0.8 m/s (s) or the presence of low handgrip strength with a cut-off of 20 kg using the dynamometer. In our population, as handgrip strength was measured in Newton per square metre, a pressure unit that cannot be translated into kilogramme, we used an approximation of this definition with a cut-off based on the lower quartile of the distribution as was done in the cardiovascular health study.

#### Definition V

Sarcopenia using the ASM and gait speed defined by Muscaretoli *et al.*<sup>14</sup> This definition used Baumgartner's cut-off (ASM/height<sup>2</sup> ≤ 5.45 kg/m<sup>2</sup>) and a gait speed ≤ 0.8 m/s.

#### Definition VI

Sarcopenia definition proposed by the International Working Group on Sarcopenia<sup>6,7</sup> The definition combined Delmonico's definition (ASM/h<sup>2</sup> ≤ 5.67 kg/m<sup>2</sup>) with a poor performance at the gait speed test. The threshold of gait speed was established at ≤ 1 m/s.

In our study, we used gait speed only because a 6 m walk test was not assessed. This definition is quite similar than the Definition V, but the cut-off of ASM and gait speed is different.

### Self-reported difficulty in physical function

Participants were asked by a trained nurse whether they had difficulties (no/some/serious difficulty) performing various physical movements such as walking, climbing stairs,

descending stairs, rising from a chair, picking up an object from the floor, and lifting heavy objects. The categories some and serious difficulties were grouped all together. Women with three or more difficulties (labelled as 'moving difficulties') were grouped together.<sup>15,16</sup>

### Assessment of knee extension strength

To measure maximum isometric KES, participants were seated in an adjustable straight back chair with the pelvis fixed by a strap and a strength gauge attached by a strap just above the ankle [ADCRO (Association pour le Développement de la Chirurgie Réparatrice et Orthopédique) electronic statometers, Valenton, France].<sup>17</sup> For analysis, we used the mean of the highest score of three attempts of each leg, recorded in Newton (N). Each time, verbal encouragement was given to obtain the maximal score.

### Assessment of health and disability

Trained nurses performed the assessment of health and disability.

A physical examination and a health status questionnaire were used to record age and co-morbid disease [hypertension, diabetes, dyslipidemia, coronary heart disease, peripheral vascular disease, cancer, stroke, Parkinson's disease, depression, and pain (pain of the back, hip, knee, ankle, or feet)]. Obesity was defined as a body mass index (weight/height<sup>2</sup>) above 30. Impaired vision was assessed using a visual acuity test. It was measured at a distance of 5 m with a Snellen letter test chart. Smoking (previous or current) and alcohol intake were noted. Monthly income was classified into three groups. Educational level was assessed as a dichotomous variable indicating receipt of the French certificate of elementary school education. Participants were also asked whether they had had a previous job. Dressing, toileting, and mobility were items assessed for basic activities of daily living and categorized as a dichotomous variable, independent or not, for all of the three items. Participants were considered disabled if they had limitation in at least one of the three items.<sup>18</sup> Women were also asked whether they had taken hormone replacement therapy or corticosteroids during the last 3 months. Participants reported in a structured questionnaire whether they practised recreational activities such as walking, gymnastics, cycling, swimming, or gardening. Type, frequency, and duration of each activity were recorded. As the previous paper, the 'physically active' variable was constructed to obtain the fittest 20% of the study sample; this was equivalent to a participant practising at least one activity for at least 1 h a week for the past month or more. This approach has been used previously.<sup>19</sup>

### Statistical analysis

The prevalence of sarcopenia was calculated according to the six different definitions. Characteristics of the sarcopenic participants were expressed as means and standard deviations or median and inter quartile range for quantitative variables and as frequencies and percentage for qualitative variables.

A reference model was built for each of the five specific self-reported difficulties in physical function including relevant predictive factors (age, obesity, income, previous job, education, physical activity, cognitive status, hypertension, diabetes mellitus, dyslipidemia, coronary heart disease, peripheral vascular disease, cancer, stroke, Parkinson's disease, depression, pain, anger, visual impairment, hormone replacement therapy, corticosteroid treatment, smoking, alcohol intake, and living alone). The goodness-of-fit of each model was estimated using Akaike's information criteria (AIC). These criteria help for identifying an optimal model from a class of competing models taking model complexity into account. The chosen model is the one that minimizes the AIC. The concordance (C)-statistic was calculated to evaluate the discriminatory ability of the reference models. This statistic represents the capacity to distinguish high from low risk subjects and is analogous to the area under the receiver-operating characteristic curve. We performed an internal validation of the model using a bootstrapping method (5000 random bootstrap samplings) for correcting the C-statistic for optimism.<sup>20</sup> To assess the calibration of our models, the Hosmer–Lemeshow statistic was calculated.<sup>21</sup> To test the relevance of sarcopenia as a predictive factor, we inserted into the reference model sarcopenia using the six published definitions. First order interaction between sarcopenia and the other predictors was tested. In these final models, the value of the AIC, the C-statistic, and the calibration were re-estimated. Finally, we assessed the incremental value of the variable defining sarcopenia calculating the net reclassification index (NRI, 95% confidence interval, CI). The NRI is the net fraction of reclassifications in the right direction by making decisions based on predictions with the model including sarcopenia compared with a decision without this information.<sup>22</sup>

The same approach was performed for KES. A reference model was built for, except that the analysis was performed using multiple linear regression models and that gain in prediction was measured comparing adjusted  $R^2$ , a measure of the proportion of the total variability explained by the model, using bootstrapping.

Tests were two-sided, and  $P$ -values lower than 0.05 were considered significant. Data analysis was performed using STATA 11.2 software (Stata Corporation, College Station, TX, USA).

## Results

Baseline characteristics and prevalence of sarcopenia according to the six different definitions are presented in *Table 1*.

The prevalence extended from 3.3(95% CI, 2.6–4, Definition V)–20.0% (95% CI, 17.3–20.3, Definition III).

*Figure 1* (a Venn diagram build by STATA) shows the respective distribution of participants identified as sarcopenic according to the different definitions. A large overlapping exists between the six definitions but only 85 participants (3.1%) matched with all six definitions of sarcopenia.

*Table 2* shows the goodness of fit and the discriminatory ability for each reference model that include all clinically relevant predictors for the different self-reported difficulties in physical function. For each reference model of relevant predictors for the difficulties in physical function, we added a different definition of sarcopenia. Concerning the different self-reported difficulties in physical function, 3.7% have walking difficulties, 40.9% have climbing stairs difficulties, 51.2% have descending stairs difficulties, 39.5% have rising a chair difficulties, and 48.5% have more than three difficulties. The predictive power of each reference model varied between 68% and 81%.

All the definitions of sarcopenia were significantly associated with these items 'descending stairs' and 'moving difficulties'. They provided a better fit for the data than the reference model with AIC systematically lower in models including sarcopenia definition. Regarding the item 'moving difficulties', the adjusted odd ratio ranged from (ORa)=1.5 (95% CI, 1.2 and 1.9, Definition III) to 2.7 (95% CI, 1.6 and 4.6, Definition V).

But in spite of significant association and improvement of model fit, no definitions significantly improved the predictive capacity of the reference model. In fact, the area under curve remained unchanged in the different models explored. Moreover, for all definitions, the NRIs were zero or almost nil. By looking at physical difficulties one by one, Definition I added complexity to the reference model without improving model fit (except for descending stairs and moving difficulties) without any improvement of predictive power.

Definitions III and VI were the only ones that clearly improved the modelling of all self-reported difficulties in physical function but, once more, without improvement of predictive power.<sup>21</sup> The conclusions are the same for models picking and lifting an object from the floor (data not shown).

*Table 3* shows the adjusted mean difference in KES between sarcopenic and non-sarcopenic women and the proportion of the total variability explained using the six definitions of sarcopenia. Whatever the definitions used, all sarcopenic women had a significantly lower KES than non-sarcopenic women. The initial model fit was always improved by adding one of the definitions of sarcopenia and all definitions accounted for a small but significant amount of explained variation (compared with the initial model, difference in adjusted  $R^2$  varied between 1 and 2%).



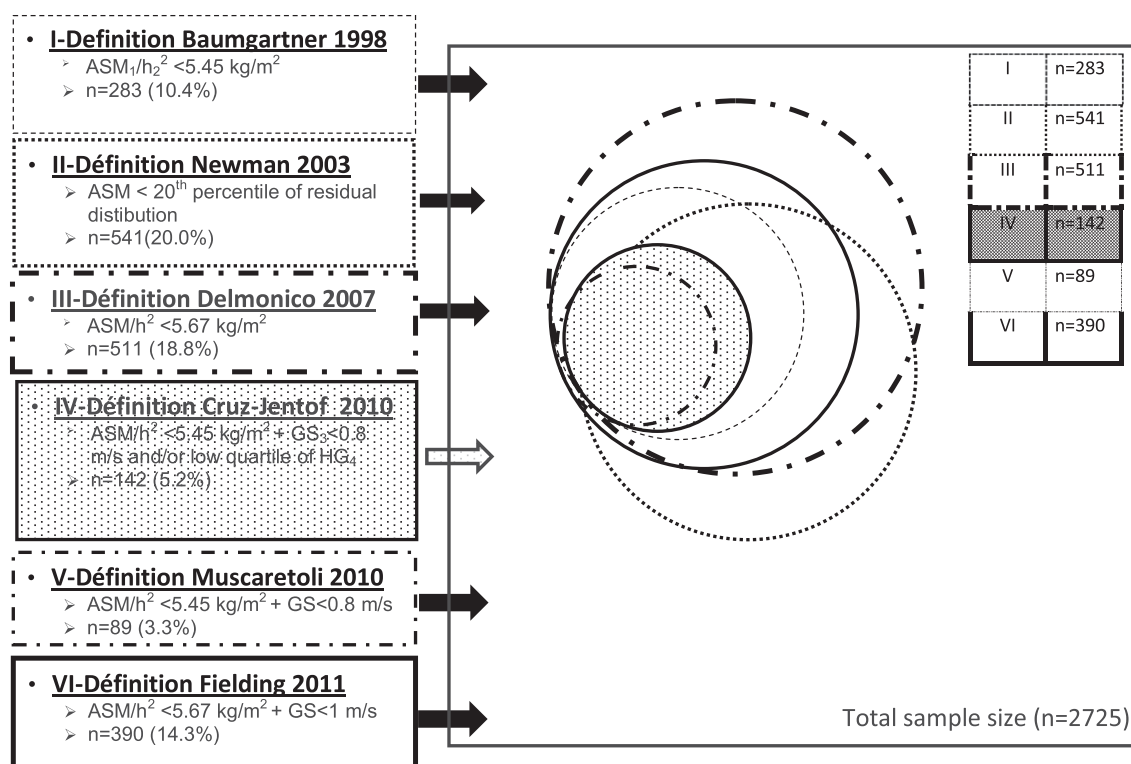
Table 1 Sample characteristics by sarcopenia definitions

Entire population		Sarcopenic patients					
Baseline characteristics		Definition I Baumgartner 1998	Definition II Newman 2003	Definition III Delmonico 2007	Definition IV Cruz-Jentoft 2010 EWGSOP	Definition V Muscaretoli 2010	Definition VI Fielding 2011 IWGS Morley 2011
Variables, <i>n</i> (%)		ASM/h <sup>2b</sup> ≤5.45 kg/m <sup>2</sup>	ASM <20th percentile of residual distribution	ASM/h <sup>2</sup> ≤5.67 kg/m <sup>2</sup>	ASM/h <sup>2</sup> ≤5.45 kg/m <sup>2</sup> + GS <sup>c</sup> ≤0.8 m/s and/or lowest quartile HG <sup>d</sup>	ASM/h <sup>2</sup> ≤5.45 kg/m <sup>2</sup> + GS ≤0.8 m/s	ASM/h <sup>2</sup> ≤5.67 kg/m <sup>2</sup> + GS ≤1 m/s
	<i>n</i> = 3025	<i>n</i> = 283 (10.4%) <sup>e</sup>	<i>n</i> = 541 (20.0%) <sup>e</sup>	<i>n</i> = 511 (18.8%) <sup>e</sup>	<i>n</i> = 142 (5.2%) <sup>e</sup>	<i>n</i> = 89 (3.3%) <sup>e</sup>	<i>n</i> = 390 (14.3%) <sup>e</sup>
Age (years), mean ± SD	80.5 ± 3.9	80.3 ± 3.9	80.1 ± 3.0	80.4 ± 3.8	81.4 ± 4.1	81.9 ± 4.0	80.8 ± 3.9
Living alone, <i>n</i> (%)	1684 (55.7)	150 (53.0)	291 (53.4)	277 (54.2)	73 (51.4)	42 (47.2)	206 (52.8)
Certificate of elementary education, <i>n</i> (%)	2430 (80.4)	244 (86.2)	482 (83.7)	442 (86.7)	115 (81.0)	70 (78.6)	335 (86.1)
Disability, <i>n</i> (%)	844 (27.9)	88 (31.9)	161 (30.5)	149 (29.7)	43 (31.6)	23 (27.1)	111 (29.1)
Physically active, <i>n</i> (%)	825 (27.3)	101 (35.7)	1254 (28.5)	156 (30.5)	34 (23.9)	19 (21.4)	99 (25.4)
SPMSQ, <i>n</i> (%)	2533 (83.7)	240 (84.8)	459 (84.8)	438 (85.7)	114 (80.3)	67 (75.3)	326 (83.6)
	492 (16.3)	43 (15.2)	82 (15.2)	73 (14.3)	28 (19.7)	22 (24.7)	64 (16.4)
Cancer, <i>n</i> (%)	398 (14.8)	41 (10.3)	89 (22.4)	85 (16.9)	17 (4.3)	11 (2.8)	64 (16.1)
Depression, <i>n</i> (%)	445 (16.5)	49 (17.4)	98 (18.2)	96 (19.0)	31 (21.8)	22 (24.7)	83 (21.3)
Hypertension, <i>n</i> (%)	1280 (47.5)	122 (9.5)	262 (20.5)	219 (17.1)	64 (5.0)	46 (3.6)	174 (13.6)
Pain, <i>n</i> (%)	2063 (76.4)	205 (9.9)	411 (19.9)	374 (18.1)	98 (4.8)	65 (3.2)	288 (14.0)
Visual impairment, <i>n</i> (%)	1583 (58.9)	168 (10.6)	323 (20.4)	303 (60.2)	92 (65.7)	61 (3.9)	242 (15.3)
Fat mass (kg), mean ± SD	31.5 ± 7.4	17.1 ± 5.7	21.5 ± 6.4	18.18 ± 6.2	16.8 ± 5.8	17.3 ± 5.7	18.4 ± 6.5
Lean mass (kg), mean ± SD	34.7 ± 2.6	30.6 ± 2.8	31.0 ± 2.8	31.1 ± 2.7	30.2 ± 2.3	30.4 ± 2.2	31.0 ± 2.6
Bone mineral density (g/cm <sup>2</sup> ), mean ± SD	1.0 ± 0.1	0.9 ± 0.1	1.0 ± 0.1	1.0 ± 0.0	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1
Calf circumference (cm), mean ± SD	34.6 ± 3.1	31.6 ± 2.3	33.0 ± 2.7	32.2 ± 2.4	31.3 ± 2.3	31.3 ± 2.4	32.1 ± 2.5
Gait speed (m/s), mean ± SD	0.8 ± 0.2	0.9 ± 0.2	0.9 ± 0.2	0.9 ± 0.2	0.8 ± 0.2	0.7 ± 0.2	0.8 ± 0.2
ASM/h <sup>2</sup> (kg/m <sup>2</sup> ), mean ± SD	6.3 ± 0.7	5.2 ± 0.2	5.5 ± 0.3	5.4 ± 0.2	5.2 ± 0.2	5.2 ± 0.2	5.4 ± 0.3
Handgrip strength, <i>n</i> (%)							
Lowest quartile	758 (25.1)	98 (34.9)	160 (29.5)	159 (31.4)	98 (69.5)	45 (51.1)	133 (34.5)
Highest quartile	738 (2.4)	37 (13.2)	92 (17.0)	79 (15.6)	6 (4.3)	6 (6.8)	50 (13.0)
Knee extension strength (N), mean ± SD	161.7 ± 48.9	141.8 ± 43.1	149.2 ± 43.6	144.9 ± 42.7	131.8 ± 39.6	126.3 ± 37.5	139.6 ± 41.4

SD, standard deviation; EWGOP, European Working Group on Sarcopenia in Older People, IWGS, International Working Group on Sarcopenia

<sup>a</sup>ASM, appendicular skeletal muscle mass.<sup>b</sup>h, height.<sup>c</sup>GS, gait speed in metre per seconds.<sup>d</sup>HG, handgrip strength.<sup>e</sup>Prevalence of sarcopenia calculated on 2725 available data of total body composition evaluation.<sup>f</sup>Disability in dressing and toileting and mobility.<sup>g</sup>SPMSQ, short portable mental status questionnaire, a 10-item questionnaire, to detect the presence of cognitive decline in community-dwelling older adults. The validated cut-off value for normal cognitive functioning is a score of 8 or above.

**Figure 1** Distribution of a participant identified as sarcopenic according to the different definitions. ASM, appendicular skeletal muscle mass; h, height; GS, gait speed, HG, handgrip strength.



## Discussion

This study examines different aspects of six definitions of sarcopenia in the same and large cohort of elderly women. Five of these definitions were exactly the same than the ones previously described; one was approximated using a different cut-off for handgrip strength than the one initially used because there is no possible unit conversion between Newton per square metre and kilogramme. Our study confirms the large range of prevalence (3.3–20.0%) depending on the definition adopted. These results have been highlighted by previous reviews of different cohorts.<sup>23</sup> A tiny difference in the cut-off of the muscle mass ratio (i.e.  $0.22 \text{ kg/m}^2$  between the cut-offs) or gait speed (i.e.  $0.2 \text{ m/s}$  between the cut-offs) results in large differences in the prevalence.

It should be noted that a clear overlapping exists between these different definitions of sarcopenia (Figure 1).

Based on our statistical approach, none of the definitions clearly added predictive value comparatively to the other clinical predictors may be because clinical factors included in the reference model were sufficient to reach the threshold of 70% required for a useful predictive model.<sup>21</sup>

Definitions that combine mass and physical performance measures seem not more relevant than the definition based on muscle mass only in predicting physical difficulties. None

of the six definitions of sarcopenia explored seemed superior to the other. In other words, sarcopenia, whatever the definition used, did not significantly improve the prediction for the self-reported physical difficulties. However, Definitions I and IV clearly added complexity in the different statistical modelling. A tiny statistical advantage can be reported for Definitions III and VI, probably because its large thresholds select more participants with the poorer muscle mass index and the slower gait speed compared with the other definitions. However, assessment of different physical tasks could have resulted in different trends. Definition V results in the smallest prevalence of sarcopenia (only 3.3%). This definition may exclude participants who could benefit from intervention against sarcopenia.

In this work, the different definitions of sarcopenia did not improve the predictive capacity to report the self-reported difficulties in physical function. No significant improvement of predictive value was found with any of the six definitions, compared to the model based only on the clinical characteristics of the participants. The different definitions of sarcopenia were significantly associated with some of the reported difficulties in physical function, but the clinical characteristics of the participant provided statistically similar predictive values. The six definitions of sarcopenia explored in this work were statistically and significantly inversely associated with maximum KES.

Table 2 Association between self-reported physical dysfunction and each sarcopenia definitions

	n (%) <sup>a</sup>	Difficulty for physical function					Moving difficulties <sup>f</sup> (≥3 difficulties) <sup>g</sup> 1301 (48.5)/2680
		Walking difficulties <sup>b</sup> 95 (3.7)/2661	Climbing stairs <sup>c</sup> 1100 (40.9)/2688	Descending stairs <sup>d</sup> 1371 (51.2)/2677	Rising from a chair <sup>e</sup> 1061 (39.5)/2685		
Initial model	AIC AUC % <sup>g</sup>	792 68	2896 79	3156 76	3029 77	2879 81	
Definition I (n = 283) Baumgartner 1998, sarcopenia defined by ASM/h <sup>2</sup> <5.45 kg/m <sup>2</sup>	ORa 95% CI AIC AUC % <sup>f</sup>	1.5 0.8, 2.7 793 68	1.1 0.8–1.6 2897 80	1.4 1.0, 1.8 3153 76	1.3 0.9, 1.1 3029 77	1.6 1.2, 2.2 2871 81	
Definition II (n = 541) Newman 2003, sarcopenia defined by linear regression	ORa 95% CI AIC AUC % <sup>f</sup>	1.6 0.9, 2.6 792 67	1.3 1.0, 1.7 2893 80	1.5 1.2, 1.9 3148 76	1.4 1.1, 1.7 3025 77	1.5 1.2, 1.9 2862 81	
Definition III (n = 511) Delmonico 2007, sarcopenia defined by ASM/h <sup>2</sup> <5.67 kg/m <sup>2</sup>	ORa 95% CI AIC AUC % <sup>f</sup>	1.8 1.1, 2.9 787 68	1.3 1.0, 1.7 2894 80	1.4 1.1, 1.7 3151 76	1.3 1.0, 1.6 3028 77	1.5 1.2, 1.9 2870 81	
Definition IV (n = 142) Cruz-Jentoft 2010, sarcopenia defined by ASM/h <sup>2</sup> <5.45 kg/m <sup>2</sup> + GS <0.8 m/s or lowest quartile HG	ORa 95% CI AIC AUC % <sup>f</sup>	1.7 0.7, 3.7 793 67	1.5 1.0, 2.2 2895 80	2.2 1.5, 3.2 3142 76	1.4 1.0, 2.2 3028 77	2.1 1.4, 3.2 2867 81	
Definition V (n = 89) Muscaretoli 2010, sarcopenia defined by ASM/h <sup>2</sup> <5.45 kg/m <sup>2</sup> + GS <0.8 m/s	ORa 95% CI AIC AUC % <sup>f</sup>	1.4 0.5, 3.8 794 67	2.3 1.4, 3.9 2887 80	2.2 1.3, 3.6 3148 76	2.4 1.5, 3.9 3018 77	2.7 1.6, 4.6 2860 81	
Definition VI (n = 390) Fielding and Morley 2011, sarcopenia defined by ASM/h <sup>2</sup> <5.67 kg/m <sup>2</sup> + GS <1 m/s	ORa 95% CI AIC AUC % <sup>f</sup>	2.0 1.2, 3.3 787 68	1.6 1.2, 2.1 2886 80	1.6 1.2, 2.0 3145 76	1.4 1.1, 1.8 3024 77	1.6 1.3, 2.1 2867 81	

AIC, Akaike information criteria; ASM, appendicular skeletal muscle mass; AUC, area under curve; CI, confidence interval; GS, gait speed in metre per second (m/s); h, height; HG, hand-grip strength; ORa, adjusted odds ratio.

<sup>a</sup>Number and percentage of patients reporting the specified physical difficulty/number of patients in each model.

<sup>b</sup>Adjusted for age, hypertension, pain, visual impairment, and previous job.

<sup>c</sup>Adjusted for age, obesity, peripheral vascular disease, cancer, depression, pain, visual impairment, physical activity, and cognitive status.

<sup>d</sup>Adjusted for age, obesity, hypertension, cancer, depression, pain, visual impairment, coronary heart disease, and physical activity.

<sup>e</sup>Adjusted for age, obesity, peripheral vascular disease, depression, pain, visual impairment, and physical activity.

<sup>f</sup>Moving difficulties: walking, climbing stairs, rising from a chair or bed, picking an object from the floor, lifting heavy objects, and reaching an object.

<sup>g</sup>Adjusted for age, obesity, cancer, depression, pain, visual impairment, coronary heart disease, physical activity, and cognitive status.

<sup>h</sup>Optimist was corrected by bootstrap procedure.



**Table 3** Association between maximum knee extension strength and each sarcopenia definitions

<i>n</i> = 2419		Maximum knee extension strength (Newton)
Initial model <sup>a</sup>	AIC Adjusted <i>R</i> <sup>2</sup> %	25 469 8.3
Definition I ( <i>n</i> = 283)	Coef 95% CI	−19.7 −26.0, −13.2
Baumgartner 1998, sarcopenia defined by ASM/h <sup>2</sup> <5.45 kg/m <sup>2</sup>	AIC Adjusted <i>R</i> <sup>2</sup> %	25 434 9.6 <sup>b</sup>
Definition II ( <i>n</i> = 541)	Coef 95% CI	−14.1 −18.8, −9.4
Newman 2003, sarcopenia defined by linear regression	AIC Adjusted <i>R</i> <sup>2</sup> %	25 436 9.5 <sup>b</sup>
Definition III ( <i>n</i> = 511)	Coef 95% CI	−18.4 −23.5, −13.3
Delmonico 2007, sarcopenia defined by ASM/h <sup>2</sup> <5.67 kg/m <sup>2</sup>	AIC Adjusted <i>R</i> <sup>2</sup> %	25 420 10.1 <sup>b</sup>
Definition IV ( <i>n</i> = 142)	Coef 95% CI	−26.5 −32.5, −17.8
Cruz-Jentoft 2010, sarcopenia defined by ASM/h <sup>2</sup> <5.45 kg/m <sup>2</sup> + GS <0.8 m/s or lowest quartile HG	AIC Adjusted <i>R</i> <sup>2</sup> %	25 435 9.6
Definition V ( <i>n</i> = 89)	Coef 95% CI	−29.4 −40.4, −18.3
Muscaretoli 2010, sarcopenia defined by ASM/h <sup>2</sup> <5.45 kg/m <sup>2</sup> + GS <0.8 m/s	AIC Adjusted <i>R</i> <sup>2</sup> %	25 443 9.3 <sup>b</sup>
Definition VI ( <i>n</i> = 390)	Coef 95% CI	−21.3 −26.8, −15.7
Fielding and Morley 2011, sarcopenia defined by ASM/h <sup>2</sup> <5.67 kg/m <sup>2</sup> + GS <1 m/s	AIC Adjusted <i>R</i> <sup>2</sup> %	25 414 10.4 <sup>b</sup>

AIC, Akaike information criteria; ASM, appendicular skeletal muscle mass; CI, confidence interval; GS, gait speed; h, height; HG, handgrip strength; Coef, mean difference in kes between sarcoepnic and non sarcoepnic.

<sup>a</sup>Adjusted for age, obesity, depression, visual impairment, pain, physical activity, corticosteroid treatment, and income.

<sup>b</sup>Significant difference between adjusted *R*<sup>2</sup> in the model with sarcopenia and the initial model (tested by bootstrap).

Compared to the initial model that only includes patients' clinical characteristics, all definitions slightly improved KES prediction. However, additional information provided by these definitions was small and not clinically relevant.

Our results support that the cut-offs used in the different definitions of sarcopenia were not appropriate. This hypothesis is supported by several studies showing no or tiny significant relationship between muscle mass and incidence of clinical adverse outcomes.<sup>24–26</sup> Currently, the relationship between muscle mass, physical performances, and physical function remains unclear. However, growing evidence suggests that muscle quality, a marker of muscle strength developed by the amount of muscle mass, should be investigated.<sup>27</sup> Muscle power, the strength multiplied by speed, is a key component of

muscle quality. These domains involved large number of component of mobility (the peripheral nervous system, muscle metabolism, balance, and cognitive function) other than muscle mass. The loss of muscle mass that includes the kinetic of the muscle lost may also be more predictive of future functional decline than the punctual muscle mass. In the field of nutrition in geriatrics, the predictive value of weight loss is stronger than the weight at one time.<sup>28</sup>

Low muscle strength and poor physical performance measures have been repeatedly reported to predict functional decline, while conflicting results are reported for the predicting value of low muscle mass.<sup>29–31</sup> While physical performance measures can capture an overall neuromuscular function, they are nevertheless not specific to the muscle function.<sup>30</sup> Whether physical performance measures alone would have results in a similar association with difficulties in physical function as the composite definitions of sarcopenia are off topic in this study, as no definition of sarcopenia relies on physical performances measures alone. Some functional difficulties are more or less sensitive to loss of lean body mass.<sup>32–36</sup> The assessment of other physical tasks may also have result in other results. These results seem to be related to the different cut-offs chosen; therefore, we think continuous measures of the muscle mass and handgrip have probable other benefits. Dichotomization is artificial and often unnecessary. Further, it discards potentially important quantitative information, thus reducing the power to detect a real association.<sup>37</sup> To our knowledge, this is one of the few studies that examine the current definitions of sarcopenia in the same population.<sup>38,39</sup> One study<sup>38</sup> recently explores the degree of agreement between different diagnostic criteria for sarcopenia, but this study involved 329 women and 325 men older than 60 years, body composition assessment by bio-impedance analysis, and gait speed was not assessed. Another recent studies<sup>39</sup> are attempting to identify existing associations between sarcopenia and the risk of falling. Indeed, Scott *et al.*<sup>39</sup> noted a positive association with the increases in fall risks over 5 years in community-dwelling middle-age and older adults. However, they also supported that the significant associations could not be explained by muscle strength only and suggested that other physiological criteria that contributed to falls. This finding may be reflective of our study and may indicate that the criteria of definition of sarcopenia should be use with differential weightings for muscle mass and functional performance. Indeed, in this study, gait speed was not assessed; therefore, they would not be able to use the latest consensual definitions of sarcopenia (European Working Group on Sarcopenia in Older People or International Working Group on Sarcopenia). Using respectively eight and two different definitions of sarcopenia, Batsis *et al.*<sup>40</sup> and Dam *et al.*<sup>41</sup> previously reported the large range of prevalence of sarcopenia depending on the research definitions adopted. Our study confirms these works and reinforced the need for consensus reliable criteria.

Our study is however a cross-sectional analysis and does not allow conclusion about cause and effect relationships. Our population was composed only of elderly women; consequently, our conclusions cannot be extrapolated to men, and we must the possibility that our results may not be valid for younger groups in whom sarcopenia could help to predict functional limitation occurring in later years. Another important limitation of our study is that the difficulties in physical function were self-reported. Self-reported measures are known to be affected by environmental,<sup>42,43</sup> cultural, and socio-economic differences.<sup>44,45</sup> However, reliability of self-reported physical function in older adults is about 85%,<sup>46</sup> and it has been shown that self-reported measures may complement performance measures in providing useful information about functional status and health outcome.<sup>47,48</sup> Moreover, our results on self-reported difficulties in physical function were concordant with our results on KES, which are an objective measure of functional limitation. Lastly, some potential confounding variables were not addressed in this study such as low motivation and environmental factor.

The originality of this work was being supported by the use of different definitions of sarcopenia into one cohort.

Deciding the most appropriated criteria and cut-off to define sarcopenia has been a complicated work during the past 20 years because sarcopenia escapes from the traditional definitions of diseases. What constitutes an indication for a treatment remains unclear. At this stage, and for this newly described condition, our point of view is that a first consensual start, inevitably open to criticism, is needed. In future studies, thresholds will have to be determined on the basis of the probability that an intervention can avoid adverse outcomes such as fracture, difficulty for major mobility tasks, or disability that risks occurring in the coming years (i.e. 10 years). In this highly prevalent condition, cost-effectiveness considerations will be warranted. The same process can be observed in the field of osteoporosis. The National Osteoporosis Foundation currently warrants a cost-effective treatment intervention threshold<sup>49</sup> after years of definition based on arbitrary bone mineral density cut-point. However, important differences exist between sarcopenia and osteoporosis. In

osteoporosis, a clear and unique clinical outcome is defined as the optimal combination of sensitivity and specificity to determine the risk of fractures.<sup>50,51</sup>

In conclusion, the different definitions explored were, to some degree, associated with the self-reported difficulty in physical function and with the KES. Based on our results, the never-ending discussion on the criteria to define sarcopenia remains open. Prevalence of sarcopenia varies widely depending on the definition adopted. The clinical and pathological characteristics of patients have sufficient ability to predict self-reported physical difficulties.

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## Conflict of interest

None declared.

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