### LOW MUSCLE MASS AND AGING

# PREVALENCE OF SARCOPENIA IN THE FRENCH SENIOR POPULATION

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Abstract: IntroductionA muscle mass normalized for height<sup>2</sup> (MMI) or for body weight (SMI) below 2SD under the mean for a young population defines sarcopenia. This study aimed at setting the cutoffs and the prevalence of sarcopenia in the French elderly population. Another objective was to compare the results obtained with SMI and MMI. *Methods*: Muscle mass was assessed by bioelectrical impedance analysis in 782 healthy adults (<40 years) to determine skeletal mass index (SMI, muscle mass\*100/weight) and muscle mass index (MMI, muscle mass/height<sup>2</sup>). Prevalence was estimated in 888 middle aged (40-59 years) and 218 seniors (60-78 years). All were healthy people. *Results*: For women mean-2SD were 6.2 kg/m<sup>2</sup> (MMI) and 26.6% (SMI); for men limits were 8.6 kg/m<sup>2</sup> (MMI) and 34.4% (SMI). In middle aged persons a small number of them were identified as sarcopenic. In healthy seniors, 2.8% of women and 3.6% of men were sarcopenic (MMI). The prevalence was 23.6% in women and 12.5% in men with SMI. MMI and SMI identified different sarcopenic populations, leaner subjects for MMI while fatter subjects for SMI. *Conclusion*: Cutoff values for the French population were defined. Prevalence of sarcopenia was different from that in the US population.

Key word: Sarcopenia, muscle mass, aging, frail elderly, bioelectrical impedance analysis.

#### Introduction

Sarcopenia is one of the most important threats to an aging population. It is defined as the decline in muscle mass and function associated with aging (1). Muscle mass decreases approximately 3-8% per decade after the age of 30 years, and the rate of decline is even higher after 60 years (2-4). The prevalence of severe sarcopenia in the older US population may be as high as 10-17% (5). This involuntary loss of muscle mass, strength and function is a significant contributor to disability in older people (5-6).

Although it has been known for many years that muscle mass decreases with age, it is only recently that large epidemiological data have been obtained (5, 7). This was made possible by the development and validation of easy to use and portable devices able to measure muscle mass. Firstly DEXA and MRI have been established as standards to measure muscle mass in both healthy and diseased sarcopenic (HIV positive) persons (8). Then, BIA at 50 kHz proved to be an accurate and precise tool of estimating muscle mass (9). Based on these validations, BIA wad used on large epidemiological datasets, such as the more than 14,000 adults NHANES III cohort (2-3). Two indicators have then been developed: muscle mass index (MMI) which standardizes muscle mass for height alike BMI (3) and skeletal mass index (SMI) which expresses muscle mass as a percent of body weight (2). Severe sarcopenia is defined as a value of MMI or SMI below the mean minus 2 SD of the values of a young population. With SMI, Janssen et al (2) have separated class I sarcopenia (SMI 31-37% of weight in men, 22-28% in women) and severe or class II sarcopenia (SMI <31% of weight in men, <22% in women).

Sarcopenia is associated with functional disabilities. A MMI lower than  $6.75 \text{ kg/m}^2$  in women was associated with increased *Received June 15*, 2006

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odds for moderate disabilities (2). In cross-sectional studies (reviewed in 5), the likelihood of physical disabilities is 2-5 times greater in class II sarcopenia patients than in people with normal SMI. For example, there is an increased risk of walking with a stick (OR 2.3), falling (OR 2.6), suffering from disequilibrium (OR 3.2) and autonomy loss (OR 3.7) (6). However, the association between sarcopenia and functional impairment is weaker and much more variable in longitudinal studies (5, 7). Both indicators of sarcopenia are associated with disability.

These epidemiological data have been obtained in North-American relatively healthy people. Two epidemiological data sets are available from the French population. The EPIDOS cohort, (10), shows that sarcopenia concerns 9.4% of the group. However, data were acquired on women only, 84% of whom were above 75 years. The MINOS cohort (11) shows that appendicular skeletal mass decreases with age. However, data were acquired on men only, aged above 75 years, preventing from a meaningful value for prevalence. Furthermore, sarcopenia was defined from the lowest quartile in each age group (11), in contrast to other studies that defined sarcopenia from the comparison to young adults. We do not know if the 2 indicators (SMI and MMI) identify the same patients. The aim of the present study was to evaluate the criteria for sarcopenia in a large French elderly group.

## Patients and methods

# Protocol

Seventy thousands persons per year attend health care centers of IRSA in the west France for a prevention medical check-up in two stages. Systematically, anthropometrical parameters and a blood sample are realized during first visit.

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They then come for a second visit to be examined by a medical doctor, while their biological and clinical results are discussed. All are volunteers for this free of charge medical check-up provided by the French Health Care System. The medical and socio-economical characteristics of this population are close to those of the general French population except diseased people who are weakly represented.

For the purpose of this study healthy volunteers were recruited in the health care centers of Angers, Cholet and Le Mans (France) when they agreed to have a BIA measurement during their second visit. Approval was granted by the local medical school ethical committee. Seven hundred and eighty two subjects (388 women, and 394 men) aged less than 40 years constituted the reference healthy and young group (this was the age range used by Janssen 2002). Similar measurements were made on 888 subjects aged 40 to 59 years (420 women, 468 men), and 218 subjects aged 60 to 78 years (106 women, 112 men). People were not proposed the study if they were suffering from known heart, renal or liver failure, from cancer, if they had diabetes, adrenal insufficiency, were pregnant, had thyroid disorders (hyper or hypothyroidism), or were taking drugs such as glucocorticoids, anorexigens, antidepressants, neuroleptics or diuretics.

None of the subjects of the three groups was included if BIA was impossible (a missing limb, a pace maker...) or if they refused to consent.

#### Anthropometric parameters

Body weight was measured in light clothing to the nearest 0.1 kg with SECA scales (SECA, Les Mureaux, France). Height was measured to the nearest 0.1cm with a height gauge.

BIA measurements were performed with an Impedimed multifrequency analyser (Impedimed, Brisbane, Australia). All the investigators had been equipped with analyzers from the same series and had attended a course where the complete procedure was taught. Measurements were performed after a 30 minutes rest in a temperature controlled room. Four surface electrodes were placed in a cleaned degreased skin at the limb ends in a standardized manner. The current injecting electrodes were located in the distal end of the third metacarpal bone and of the second metatarsal bone. The current detector electrodes were located between the styloid processes of the radius and ulna and between the two malleoli of the ankle. Measurements were performed on the right side of the body, at 50 kHz and a current of 400  $\mu$ Amp. Reproducibility is better than 2  $\Omega$ .

### Skeletal muscle mass estimates

Muscle mass was estimated from the resistance measured at 50 kHz according to the equation of Janssen et al (2):

Muscle mass = 0.401 height<sup>2</sup>/R50 + 3.825 gender - 0.071 age + 5.102

Height is in cm, R50 is in ohms, age is in years, and gender is 0 for women and 1 for men.

#### Sarcopenia classification

Sarcopenia was defined from the distribution of values in the group of healthy subjects aged less than 40 years. Both skeletal muscle index (SMI in %= muscle mass \* 100/ weight) and muscle mass index (MMI in kg/m<sup>2</sup>= muscle mass / height<sup>2</sup>) were computed. Sarcopenia was defined as a value below the mean minus 2 standard deviations of the SMI or MMI distributions. Sarcopenia cutoffs defined by Janssen were 22% for women and 31% for men. Because muscle mass varies with gender, both indexes were computed separately for men and women.

#### Statistical methods

Values were expressed as mean  $\pm$  SD. Pearson correlation was calculated between muscle mass and age. Normality of the distributions was verified with Kolmogorov-Smirnov test. Means were compared with analysis of variance or of covariance as appropriate. Statview software (Abacus Concept, California, USA) was used for statistical analyses.

### Results

Muscle mass was related to age (r=-0.101), BMI (r=+0.322), weight (r=+0.735), and height (r=+0.817), and was higher in men than in women (computations performed on the 1888 healthy subjects). In a multivariate model age and BMI were negatively and weight was positively related to muscle mass. Gender remained an independent determinant. With these variables 89% of the variance of muscle mass was explained.

### Young healthy subjects

Table 1 displays the physical characteristics of the young and healthy group. Muscle mass made 39.7% of body weight; i.e.  $26.7 \pm 6.3$  kg ranging from 15.3 to 49.2 kg. Both muscle mass, MMI and SMI were normally distributed. For women cutoff values to define sarcopenia were 6.2 kg/m<sup>2</sup> (MMI) and 26.6% of body weight (SMI). For men corresponding limits were 8.6 kg/m<sup>2</sup> (MMI) and 34.4% of body weight (SMI).

### Healthy middle aged (40-59 years) persons

Table 1 displays the physical characteristics of the middleaged group (48.7  $\pm$  5.3 years), with slightly higher BMI, marginally lower muscle mass and related indexes. A small number of persons were defined as sarcopenic (Table 2; 5 women and 6 men according to MMI and 29 women and 21 men according to SMI). When Janssen's SMI cutoff values for severe sarcopenia were used 1 woman and 4 men were considered sarcopenic (2).

### Healthy elderly persons

Table 1 displays the physical characteristics of the healthy elderly group ( $64.4 \pm 3.7$  years), with a higher BMI, lower muscle mass and related indexes. A small number of persons were defined as sarcopenic (Table 2; 3 women and 4 men according to MMI and 25 women and 14 men according to SMI). When Janssen's SMI cutoff values for severe sarcopenia were used no women and no men were considered sarcopenic (2).

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Table 1

Mean (SD) of physical characteristics of the healthy volunteers according to age

age (years)									
	18-39		40-59		60-78				
	Women	Men	Women	Men	Women	Men			
n	388	394	420	468	106	112			
Body weight (kg)	60.2 (9.5)	74.0 (10.5)	61.5 (10.4)	77.9 (10.7)	62.7 (9.5)	76.2 (10.3)			
BMI (kg/m <sup>2</sup> )	22.5 (3.4)	23.9 (3.0)	23.9 (4.0)	25.8 (3.1)	25.3 (3.9)	26.2 (3.1)			
Height (m)	1.634 (0.058)	1.760 (0.062)	1.603 (0.056)	1.738 (0.066)	1.574 (0.052)	1.704 (0.064)			
Age (years)	29.2 (6.3)	30.2 (6.1)	48.6 (5.3)	48.9 (5.2)	64.7 (3.6)	64.1 (3.8)			
Muscle mass (kg)	21.0 (2.5)	32.2 (3.3)	19.8 (2.5)	31.7 (3.5)	18.5 (2.2)	29.4 (3.8)			
MMI (kg/m <sup>2</sup> )	7.8 (0.8)	10.4 (0.9)	7.7 (0.8)	10.5 (0.9)	7.5 (0.8)	10.1 (1.1)			
SMI (%)	35.3 (4.3)	44.1 (4.9)	32.7 (4.3)	41.0 (4.2)	30.0 (4.1)	38.8 (3.8)			

Muscle mass by BIA from the resistance at 50 kHz according to the equation of Janssen (13); MMI: muscle mass index i.e. muscle mass/height<sup>2</sup>: SMI skeletal mass index i.e. muscle mass/weight

Table 2 Cutoff values and prevalence of sarcopenia in healthy and diseased subjects

	MMI		SMI	
	Women	Men	Women	Men
Cutoff value	6.2 kg/m <sup>2</sup>	8.6 kg/m <sup>2</sup>	26.6 %	34.4%
Healthy middle aged (40-59 yrs)				
n	420	468	420	468
Sarcopenia (%)	1.2%	1.3%	6.9%	4.5%
Healthy elderly subjects (60-78 yrs)				
n	106	112	106	112
Sarcopenia (%)	2.8%	3.6%	23.6%	12.5%

Muscle mass by BIA from the resistance at 50 kHz according to the equation of Janssen (9) MMI: muscle mass index i.e. muscle mass/height2; SMI skeletal mass index i.e. muscle mass/weight

### Comparison of the indicators

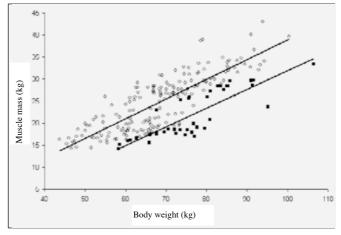
Cutoffs values and prevalence of sarcopenia according to sex were represented in table 2. There was an apparent discrepancy between the prevalence estimated by SMI (standardized for weight) and MMI (standardized for height squared). Moreover these indicators selected different populations. Middle-aged subjects identified as sarcopenic with MMI were of similar age and height, but were leaner (significantly lower weight and BMI in both males and females) than their non sarcopenic pairs. Those identified as sarcopenic with SMI had a similar age and height but were significantly heavier and fatter. The same observation could be made in healthy elderly people. In 40-59 yrs subjects men (women) 438 (387) were not sarcopenic with both indicators, 1 (0) was sarcopenic with both. Nineteen (28) were sarcopenic with MMI but not with SMI. Five (5) were sarcopenic with SMI but not with MMI.

Healthy elderly persons considered sarcopenic with SMI only (versus those identified with MMI only) were heavier (76.2 vs 49.7 kg), taller (160.5 vs 156.1 cm), fatter (BMI 29.5 vs 20.4 kg/m<sup>2</sup>), younger (65.4 vs 68.5 yrs), and with a higher muscle mass (21.3 vs 17.8 kg).

### Figure 1

Relationship between muscle mass and body weight in sarcopenic (filled squares) and non-sarcopenic (open circles) healthy elderly. Sarcopenia is defined with a SMI value below the mean minus 2SD of the young population. The two slopes do not differ (t=0.5, P=NS). Adjusted muscle mass is lower in sarcopenic persons irrespective of weight (P<0.0001)





### Discussion

The present study describes the cutoff points to define sarcopenia in a European population, which turn out to be different from those in the North American population (2, 3). It appears that the two indicators do not identify the same kind of sarcopenic people.

Severe sarcopenia can be defined as a muscle mass lower than 2SD below the mean for healthy subjects aged 18-39 years (such as those of NHANES III). Two indicators are used, either muscle mass index (MMI= muscle mass/ height<sup>2</sup>, in kg/m<sup>2</sup>, 2) or skeletal muscle index (SMI=muscle mass/weight, in %, 3). Based on SMI it is estimated that 10% of US women and 7% of US men aged more than 60 years in NHANES III are severely sarcopenic (4). There are at least twice as many people suffering from sarcopenia above an age of 80, than below 70 years. About 29% of healthy men and 16% of healthy women above 80 yrs are sarcopenic (6). Sarcopenia incidence varies according to the sex being 12.3% in Chinese men and 7.6% in Chinese women (12). It also varies according to race; the prevalence is greater in the Hispanic population in comparison with that of the non-Hispanic white subjects (6). In the French EPIDOS cohort (10) prevalence in women older than 75 years is low (9.7%).

In the present study, although muscle mass was shown to decrease with age, very few healthy middle aged volunteers could be considered sarcopenic based on MMI (about 1%) or SMI (4-7%) cutoffs. In older people (mean age 64.3 years) a small number of respectively women and men were sarcopenic according to MMI (2.8-3.6%) but a larger number was found with SMI (23.6%-12.5%). This latter prevalence was higher than in Janssen's dataset (2). MMI in the present population was 7.8  $\pm$  0.8 kg/m<sup>2</sup> in women and 10.4  $\pm$  0.9 kg/m<sup>2</sup> in men. This was similar to figures described by Janssen (3) in men  $(9.86 \pm 1.18 \text{ kg/m}^2)$ ; the two groups being very similar, in weight and BMI. Present values were slightly higher in women than in Janssen's study (3; 7.04  $\pm$  1.11 kg/m<sup>2</sup>). The present women were slightly leaner (BMI 25.3 vs. 27.0 kg/m<sup>2</sup>) with a slightly higher muscle mass (18.5 vs 17.9 kg). The values of SMI to define severe sarcopenia are quite different in the two studies (26.6 vs. 22% in women; 34.4 vs. 31% in men Janssen's (2). When Janssen's cutoff values were used a dramatic decrease in the prevalence of sarcopenia was observed. This suggests that there were very few people in this French cohort with severe sarcopenia, highlighting that very few were diseased. Indeed, severe diseases with a possible cachectic component were excluded, such as organ failures or diabetes. We recruited volunteers from the general population for a free of charge medical check-up. Sick people are weakly represented. The mean age was also lower than in Janssen's studies (2-3), which also included diseased persons. This may explain the difference between prevalences.

The present prevalence is lower than in the French EPIDOS cohort (10) where it was 9.7%. That study only involved women, most of whom (84%) were between 75 and 85 years of age. Because muscle mass decreases with age, we did not expect to find a similar prevalence as in the EPIDOS cohort. The indicators were different although both were normalized for height<sup>2</sup>. In the EPIDOS study, appendicular skeletal muscle mass was obtained with DEXA, and it has been shown that age related muscle mass decline affects more limb than other muscles (4). It is possible that BIA measures more than the appendicular mass, and therefore BIA cut offs slightly underestimate the true rate of limb decline as compared to DEXA. However, DEXA is only available in research facilities, and data obtained with BIA are of interest. The tool has been validated and limits of this study are discussed below. The other French cohort (MINOS, 11) shows that appendicular skeletal mass decreases with age. However, data were from only men aged above 75 years. Furthermore, sarcopenia was defined from the lowest quartile in each age group (11) in

contrast to other studies, that defined sarcopenia from the comparison to young adults. It prevents from a meaningful comparison.

Prevalence of sarcopenia varies depending on the chosen criteria. A lower prevalence is observed with MMI (standardized for height), with only 2.8% of the women and 3.6% of men age above 60 years considered sarcopenic. Our data suggest that SMI identifies sarcopenic patients that are heavier and fatter than those identified as non sarcopenic. Therefore, SMI identifies sarcopenic obese people, not only because of a higher weight (which could artificially decrease the ratio of muscle mass to weight) but also because of a lower muscle mass (see figure 1). Analysis of covariance shows that both regression lines are parallel (t=0.5; P=NS), but adjusted muscle mass of sarcopenic people 21.7±5.4 kg is significantly lower than that of non-sarcopenic subjects (24.7±6.3 kg; P< 0.0001). These subjects display a dual disorder: decreased muscle mass and increased fat mass. The reasons for this dual disorder have been discussed by Baumgartner (13).

Prevalence of sarcopenic obesity (the association of a high BMI and low muscle mass) increases with age (13.5% in men before 70 years compared to 17.5% in those above 70 yrs. Corresponding figures in women are 3.5% (<70 yrs) and 8.4% (>70 years) (14). Here, 13 out of 228 elderly patients were sarcopenic obese while 28 were sarcopenic but non obese. These subjects are more prone to disability and metabolic diseases than lean sarcopenic individuals. Whether lean and sarcopenic individuals (identified by MMI) are prone to malnutrition remains to be established. More studies are necessary to delineate the respective interest of each indicator of sarcopenia.

Therefore, since SMI is associated with functional disabilities that are more likely in sarcopenic obese people (5, 13), and MMI defines severe sarcopenia in lean people, specific European cutoffs are justified. MMI, which does not vary much, and SMI are alike Z and T score for osteoporosis.

The strength of this study is the large number of subjects recruited from health care centers. All are volunteers for this free of charge medical check-up provided by the French Health Care System. The medical and socio-economical characteristics of this population are close to those of the general French population except diseased people who are weakly represented. The interest of this study is that it complements French data (10-11) about middle aged and young seniors (age range 60-78). One limitation is that muscle mass was estimated by means of bioelectrical impedance analysis (BIA). BIA has been shown to provide valid estimates of muscle mass in a similar population, and measurements have been cross-validated against state of the art techniques such as DEXA and MRI (2). The BIA equation used here has been extensively used by Janssen (2-5). Nonetheless, because BIA is not very precise the results are likely to be biased towards an underestimation of the prevalence of severe sarcopenia.

In conclusion, the present study shows that the prevalence of sarcopenia is low in Europe when the MMI is used. Cutoffs

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values for SMI are slightly different than those in the US and justify the use of specific European values. It appears that MMI and SMI identify two different sarcopenic populations: MMI for leaner subjects while SMI for the fatter ones.

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