

Appendicular Skeletal Muscle Mass Reference Values and the Peak Muscle Mass to Identify Sarcopenia among Iranian Healthy Population

Abstract

Background: Sarcopenia is a common problem in elderly with the adverse outcomes. The objective of this study was to estimate the peak appendicular skeletal muscle mass (ASM) and age of its attainment by sex among the Iranian population. **Methods:** A total of 691 men and women aged 18–94 years participated in this cross-sectional, population-based study in Bushehr, Iran. ASM was measured by dual X-ray absorptiometry. Cutoff points for men and women were established considering two standard deviations (SDs) below the mean values of the skeletal muscle index (SMI) for young reference groups. The relationship between ASM and age was described by the second-degree regression models. Two SDs below the mean SMIs of reference groups were as cutoff values of low muscle mass in Iranian population. **Results:** The peak ASM values were 21.35 ± 0.12 Kg and 13.68 ± 0.10 Kg, and the age at peak ASM were 26 (24–28) years and 34 (33–35) years for men and women, respectively. Mean and SD of SMI in those ages were 7.01 ± 0.02 Kg/m² and 5.44 ± 0.02 Kg/m² among men and women, respectively. Calculated cutoff values of low muscle mass among the Iranian population were 7.0 Kg/m² and 5.4 Kg/m² among men and women, respectively. **Conclusions:** Iranian reference values of SMI for both genders were similar to Asia Working Group for Sarcopenia recommendation and lower than the United States and European values. Further studies from different nations and the Middle East countries are needed to obtain reference values for populations, enabling the researchers for comparison and also more valid reports on sarcopenia prevalence.

Keywords: Iran, peak muscle mass, reference values, sarcopenia

Introduction

The skeletal muscle mass plays an important role in functions such as movement and metabolism and loss of muscle mass is a common problem in the elderly.^[1] The age-related loss of muscle mass along with muscle functions is called sarcopenia.^[2] Sarcopenia is now recognized as a major public health problem in the world with adverse outcomes such as physical disability, poor quality of life, falling, related skeletal fracture, and even death.^[3-5]

Researches in Europe and Asia have developed a consensus set of diagnostic criteria for sarcopenia based on its parameters.^[2,6] Determining the most appropriate reference value of muscle mass for the purpose of establishing a sarcopenic diagnosis is still an important issue in different populations in the world. To establish low muscle mass,

some studies have assessed the total or appendicular skeletal muscle in young adults as the reference value.^[7,8] For a clinically applicable definition, correction factors such as height, body mass index, and body fat have been used.^[4,8,9] To calculate skeletal muscle index (SMI), the sum of muscle masses of the four limbs is defined as appendicular skeletal muscle mass (ASM) (SMI; ASM/height²). Several cut points based on SMI have been derived; however, some factors, such as measurement techniques, age, gender, and ethnicity affect these cutoffs.^[10] Some studies have used the cut points based on SMI from the European Working Group on Sarcopenia in Older People (EWGSOP) or Asia Working Group for Sarcopenia (AWGS) guidelines.^[11-13] Furthermore, researchers have shown significant differences and a strong bias in the prevalence of sarcopenia when different cut points of the distinct

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populations are used instead of the original sex-specific group of subjects.^[14] Therefore, the recommendation is that SMI would ideally refer to sex-specific ethnic group populations. For the Iranian population, no reference value of ASM exists and few studies on sarcopenia have used a cutoff point derived from EWGSOP.

For this reason, the aim of this study was to determine cut points of SMI for Iranian subjects, which can lead to reference values in Iran and other Middle East countries.

Methods

Study population

The study was performed in 2016 among healthy Iranian subjects who live in urban areas of Bushehr city, the capital of Bushehr province in southwestern Iran. The participants in this study were selected through a multistage, age and sex stratified, and cluster-random sampling. Equal size clusters were selected based on a systematic random approach among unique postal codes for each household with the cooperation of the post office. As shown in Figure 1, among 920 individuals who were invited, a total of 818 attended the clinic (response rate: 88.9%). In each cluster, individuals were invited to participate in the study among 46 age-sex groups. Age groups have been defined in 3-year-old increments between 18 and 94 years old. All individuals were evaluated for the eligibility criteria. We selected subjects free from metabolic diseases (cardiovascular disease, diabetes, and hypertension), any kind of cancer and they were not taking any medications that may affect muscle functions or weight (corticosteroids, bisphosphonates, parathyroid hormone, calcium, and vitamin D). In addition, we included subjects with body mass index BMI between 18 and 30 Kg/m².

The study was approved by the National Institute for Medical Research Development. A written informed consent was signed by all the participants.

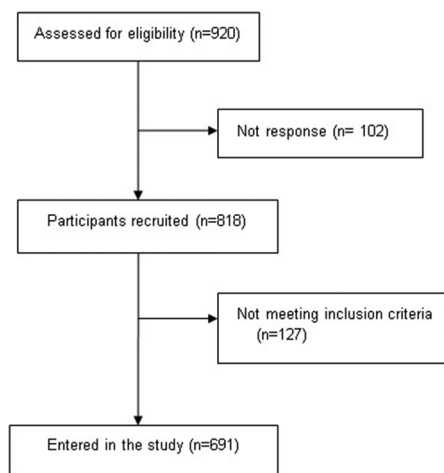


Figure 1: Flow chart of enrollments the study

Measurements

Anthropometric measurements were taken with shoes removed and with the participants wearing light clothing. The height and weight were measured with a fixed stadiometer and a digital scale according to the standard protocol. BMI was calculated as weight (Kg) divided by height (m²). A flexible circumference measuring tape was used to measure waist circumference; at a point midway between the iliac crest and the lowest rib in the standing position, and the hip circumference was measured at the widest part of the hip. All measurements were read to the nearest 0.1 cm.

Body composition for each participant was measured using dual X-ray absorptiometry (DXA) (DXA, Discovery WI, Hologic Inc., USA; CV = 1% for whole body values). The device could measure bone mineral density, fat mass as well as muscle mass of the head, trunk, and extremities separately with minimal radiation exposure. According to DXA results, we calculated the ASM for each participant as the sum of the upper and lower limb muscle mass without fat and bone tissue. The time required for the evaluation of each person was 20 min.

The participants were also interviewed by trained nurses and then completed a questionnaire regarding sociodemographic data, lifestyle factors, medical, and drug use history.

Skeletal muscle mass indices and cutoff points

The SMI was defined as ASM/height² (Kg/m²). According to EWGSOP, the International Working Group on Sarcopenia IWGS, and AWGS definitions, cutoff points for men and women were established considering two SDs below the mean values of indices for young reference groups.^[2,6,15]

Statistical analysis

The normality of variables was assessed using visual inspection of histograms and the measures of skewness and kurtosis as well as Kolmogorov–Smirnov and Shapiro–Wilk tests. The square root transformation was applied to ASM and SMI values to fit the normal distribution assumption.

To estimate the relationship between the ASM and age in both genders, three regression models (up to the third degree) were fitted to the scatter diagrams of the two variables. To find the best-fitted model, we used a hierarchical approach. In this model, the cubic model was first considered as the “saturated” model and was compared with the quadratic model as the “reduced” model using adjusted *r*² and root MSE. Rejection of the null hypothesis in this test meant that the “saturated” model is the appropriate model for the calculation of the Peak ASM, and the inability to reject the null hypothesis indicated an acceptance of the “reduced” model. In the second case, this process was repeated for the comparison

of the quadratic and linear models. After fitting the best models, the corresponding equations for the fitted curves or lines were constructed and the age point of peak ASM was identified. Participants within the nearest 5-year-age group, calculated as peak ASM age point ± 2 years for models, were considered as a reference group.

The analysis was performed using SPSS (version 16; SPSS Inc., Chicago, IL, USA) and STATA (Release 12. Statistical software. STATA Corp., LP, College Station, Texas, USA).

Results

In total, 691 participants aged 18–94 years (381 men and 310 women) were selected for the study [Figure 1]. As expected, ASM in men was higher than in women ($P < 0.001$). In addition, there was a significant difference in waist circumference between men and women ($P = 0.003$).

The distribution of the ASM according to age was presented as scatter plots in both genders in Figure 2 and Table 1. As expected, the ASM increased during younger ages and then gradually declined with increasing of the age in both genders.

The relationship between ASM and age was best described by the second-degree regression models in both genders. Based on these equations [Table 2], age points with highest ASM values were estimated and these points were used for determining a 5-year age interval with the peak ASM. The peak ASM value for men was 21.35 ± 0.12 Kg and the age at the peak ASM was around 26 (24–28 years). The corresponding value for the peak ASM among women was 13.68 ± 0.10 Kg but the age at this peak was between 33 and 37. These values were used for calculating SMI in both sexes. The mean and standard deviation (SD) of SMI in those ages were calculated 7.01 ± 0.02 Kg/m² and 5.44 ± 0.02 Kg/m² in men and women, respectively. Two SDs below the mean SMIs of the reference groups were 7.0 Kg/m² in men and 5.4 Kg/m² in women and were considered as cutoff values of low muscle mass in the Iranian population.

Table 3 shows cutoff points of SMI that have been provided by EWGSOP, AWGS, other studies, and our results.

Discussion

The present study is the first population-based investigation that characterizes reference values of muscle mass among healthy subjects in Iran. We found that men aged 24–28 and women aged 33–37 had a peak ASM, and the mean \pm SD of SMI in those ages were 7.01 ± 0.02 kg/m² for men and 5.44 ± 0.02 kg/m² for women. Cut-off points for SMIs were 7.0 kg/m² and 5.4 kg/m² in Iranian men and women respectively.

To assess sarcopenia, a common problem in the elderly, it is essential to establish an appropriate measure for the

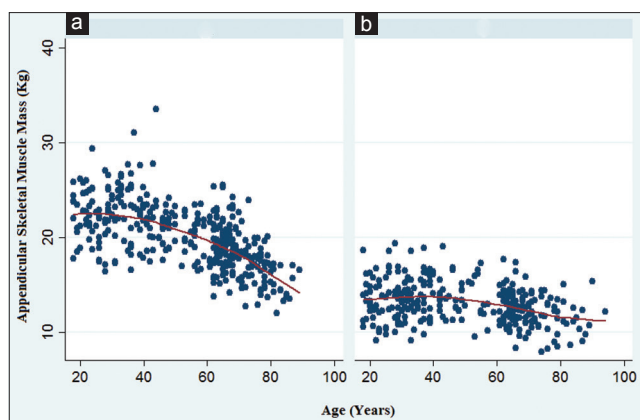


Figure 2: Scatter plots for age-related changes in the appendicular skeletal muscle mass in men (a) and women (b)

Table 1: General characteristics of study subjects

Variable	Men (n=381)	Women (n=310)	P
Age (years)	53.76 \pm 19.06	50.11 \pm 19.83	0.010
Weight (kg)	71.98 \pm 10.55	61.35 \pm 9.63	<0.001
Height (cm)	168.64 \pm 7.47	156.06 \pm 8.10	0.000
WC (cm)	92.07 \pm 8.82	89.81 \pm 10.60	0.003
Hip circumference (cm)	98.69 \pm 7.19	99.64 \pm 6.97	0.080
BMI (kg/m ²)	25.24 \pm 2.79	25.12 \pm 3.05	0.600
ASM (kg)	19.92 \pm 0.13	13.04 \pm 0.08	0.000

Data shown are mean \pm SD. WC=Waist circumference, BMI=Body mass index, ASM=Appendicular skeletal muscle mass, SD=Standard deviation

diagnosis of this disease. In recent years, some research groups in the world have been trying to make a consensus definition, diagnosis and management of sarcopenia.^[2]

Based on different definitions, skeletal muscle mass is evaluated by magnetic resonance imaging (MRI), computed tomography (CT), dual energy absorptiometry (DXA) and bio-impedance analysis (BIA). However, CT and MRI are the gold standards of assessing muscle mass; there are many limitations in terms of cost and radiation exposure. BIA is also a noninvasive and inexpensive method for measuring fat and muscle mass, but it may overestimate muscle mass.^[2,16] Therefore, DXA is an appropriate alternative to evaluate body composition and EWGSOP, IWGS and AWGS have accepted the determination of cut-off points for low muscle mass by DXA as a parameter for sarcopenia.^[2,6,15]

Some studies have used fat free mass^[17,18], the total skeletal muscle mass^[7,9,19], and ASM^[8,20], as the parameters for muscle mass. There are some different methods used to define cut-off points for muscle mass. Some use two standard deviations below the mean values of indices for young adults from the same population under study^[21,22]; while some others use the sex specific lowest quintile of the older study participants.^[9,19]

Other studies use the cut-off values that were recommended by EWGSOP or AWGS.^[11,23] Studies have shown that

Table 2: Maximum appendicular skeletal muscle mass values and related age groups for men and women

Gender	Age of peak ASM (age group) ^a	Peak ASM (kg)	SMI (kg/m ²)	Regression equation ^b
Men	26 (24-28)	21.35±0.12	7.01±0.02	Y=4.5754+0.012926X-0.000248X ²
Women	35 (33-37)	13.68±0.10	5.44±0.02	Y=3.52619+0.010135X-0.00014569X ²

Data shown are mean±SD. ^a5-year age groups are characterized by age point estimate for peak ASM ±2 years for men and women,

^bIn the regression equations, “Y” and “X” stand for ASM and age for both genders, respectively. ASM=Appendicular skeletal muscle mass, SMI=Skeletal muscle mass index, SD=Standard deviation

Table 3: Comparison of cutoff for skeletal muscle mass index in different studies

Definition	Cutoff for SMI (kg/m ²)	
	Men	Women
EWGSOP ^[2]	7.26	5.54
The society for sarcopenia, cachexia, and wasting disorders ^[21]	6.81	5.18
China ^[22]	6.08	4.79
Japan ^[23]	6.87	5.46
KNHNES-Korea ^[24]	6.58	4.59
AWGS ^[6]	7.0	5.4
Present study from Middle East	7.0	5.4

EWGSOP=European Working Group on Sarcopenia in Older People, KNHNES=The Korea National Health and Nutrition Examination Survey, AWGS=Asia Working Group for Sarcopenia, SMI=Skeletal muscle mass index

the prevalence of sarcopenia may not be accurate when reference values of the selfsame population are unavailable.^[16,24] Therefore, EWGSOP and AWGS have encouraged the use of healthy young adults' data of the same population to obtain valid cut-off points for the world population in order to improve the diagnosis of low muscle mass and sarcopenia in an elderly population.

Muscle mass decreases approximately 3–8% per decade after the age of 30 and this rate of decline is even greater after the age of 60.^[25] The age-related skeletal muscle mass decline is associated with gender and ethnic differences.^[26] The ASM in our study reached a peak at the age of 35 in women, which was later than that of the studied women from China^[20] but comparable with their Italian, Korean and Indian counterparts.^[27-29] Also, the peak ASM occurred among the 24 to 28-year-old Iranian men, which was similar to data gathered in Italy and China.^[20,27] It seems that the peak ASM occurs about one decade later among women than men. This should be discussed and studied more to discover its determinants and underlying factors.

Table 3 compares our cut- offs for SMI, measured by using DXA, with other populations. According to EWGSOP, based on a definition proposed by Cruz-Jentoft *et al* in 2010^[2], individuals whose SMI is 2 or more than the standard deviations below sex-specific means of the Rosetta study^[26] reference data set are defined as having low muscle mass. Cut-offs for this definition are 7.26 kg/m² for men and 5.54 kg/m² for women. Another definition was

proposed by Morley *et al.* for the Society for Sarcopenia, Cachexia, and Wasting Disorders in 2011.^[30] Low SMI is defined as 2 SD below the mean of healthy individuals aged 20 -30, with NHANES IV study^[31] as the reference population. Cut-offs for this definition are 6.81 kg/m² and 5.18 kg/m² for men and women respectively. In recent years, many studies were conducted in Asian countries. In one study in china,^[20] the cut- off values for sarcopenia were defined as 6.08 Kg/m² for men and 4.79 Kg/m² for women. However, other studies among the Japanese^[32] and Koreans^[33,34] indicated that the cut- off values SMI are relatively higher among Chinese people, but generally, the peak ASM value is lower in the Asian population than the western countries.^[6] These results show that even within the same race, there is a significant variation in peak muscle mass, which may reflect the impact of other factors on the occurrence of sarcopenia. Overall, AWGS recommended using height- adjusted ASM, and suggested cut- offs be 7.0 Kg/m² in men and 5.4 Kg/m² in women by using DXA.^[6] In our study, Iranian reference values for both genders are similar to the AWGS recommendation and lower than the United States and European values. As our study results reveal, it seems that the cut- off points for sarcopenia in the Middle East are similar to Eastern Asian countries and lower than western countries.

However, ethnic differences may be the main reason for this difference; other factors such as lifestyle habits, body size and cultural backgrounds should be considered. Therefore, comparing the prevalence of sarcopenia in different races in various countries is difficult, mostly because of practical difficulties in measurement techniques of muscle mass, reference data, differences in the age of the study population and the selection bias.

The present results have to be interpreted within the context of strengths and potential limitations. Firstly, the study represents one of the studies of sarcopenia in the Middle East, and as such, it increases the reliability of estimates of peak ASM, SMI and prevalence of sarcopenia in this region. Secondly, the participants were randomly selected, which confirms the representativeness of our population. Thirdly, the technique of measurement of ASM with DXA is considered the “gold standard” after CT and MRI for the assessment of muscle mass.

Nevertheless, the study also has a number of potential limitations. The participants in this study were sampled

from an urban population; as a result, the study's finding may not be generalisable to the rural population. Also, the peak ASM should be estimated from a longitudinal study in which a large number of men and women are followed, but such a study is not practically possible. On the other hand, estimating the peak ASM in a cross-sectional study such as the present study can be biased by unmeasured confounders.

Conclusions

Our study suggests cut-off values for SMI in an Iranian population by using DXA. Further studies from different nations along with Middle Eastern countries are needed to obtain reference values for populations, enabling the researchers to compare and also produce more valid reports on sarcopenia prevalence.

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Conflicts of interest

There are no conflicts of interest.

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