

# The differences of sarcopenia-related phenotypes: effects of gender and population

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**Abstract** Sarcopenia is a serious condition especially in the elderly population mainly characterized by the loss of skeletal muscle mass and strength with aging. Extremity skeletal muscle mass index (EMMI) (sum of skeletal muscle mass in arms and legs/height<sup>2</sup>) is gaining popularity in sarcopenia definition (less than two standard deviations below the mean of a young adult reference group), but little is known about the gender- and population-specific differences of EMMI. This study aimed at investigating the differences of EMMI, arm muscle mass index (AMMI), and leg muscle mass index (LMMI) between gender groups and populations (Chinese vs. Caucasians). The participants included 1,809 Chinese and 362 Caucasians with normal weight aged from 19 to 45 years old. Extremity muscle mass, arm muscle mass, and leg muscle mass were measured by using dual energy x-ray absorptiometry. Independent sample *t* tests were used to analyze the differences in muscle mass indexes between the studied groups. All the study parameters

including EMMIs, AMMIs, and LMMIs were significantly higher ( $P \leq 0.0003$ ) in the Caucasian group than in the Chinese group and also higher in the male group than in the female group, and these significant differences ( $P \leq 0.0005$ ) remained after adjusting for age by simple regressions. The detected differences of muscle mass indexes between different gender and ethnic groups may provide important implications in their different risk of future sarcopenia.

**Keywords** Sarcopenia · Extremity muscle mass · Gender · Population

## Introduction

Sarcopenia is a serious condition mainly characterized by the loss of skeletal muscle mass (MM) and strength with aging [13], which is becoming recognized as a major cause of disability and morbidity in the elderly population [25, 44]. In addition, it imposes a heavy economic burden in the USA. In 2000, the estimated direct health care cost attributable to sarcopenia in the USA was \$18.5 billion, which represented about 1.5% of annual total health care expenditures [23].

Several parameters were used in measuring MM and were compared to investigate the effects of gender and population. Previous studies found that men had significantly higher MM in comparison with women in both absolute terms and relative to body mass [1, 6, 15, 16, 18, 22, 50]. Caucasians had significantly higher total body potassium, a measure of MM, than Asians [18]. American Caucasian women had significantly larger fat free weight and muscle thickness than Japanese women [21]. Europeans' MM was significantly larger than that of the Chinese [28]. However, these parameters (e.g., total body potassium) have more or less

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limitations in accurately evaluating sarcopenia due to the limited accuracy of measuring MM and no adjustment for body size.

Currently available techniques (such as dual energy x-ray absorptiometry, DXA) make accurate measurement of extremity muscle mass (EMM sum of skeletal muscle mass in arms and legs) easy and cheap. Extremity skeletal muscle mass index (EMMI) ( $\text{EMM}/\text{height}^2$ ), a new parameter considering body size, is gaining popularity in sarcopenia definition (less than two standard deviations below the mean of a young adult reference group) [2, 9], but little is known if there are gender- and population-specific differences of EMMI. This study aimed at investigating the differences in muscle mass indexes (MMIs) including EMMI, arm muscle mass index (AMMI), and leg muscle mass index (LMMI), in Chinese vs. Caucasians and in males vs. females.

## Materials and methods

### Subjects

The study was approved by the Creighton University Institutional Review Board and the Research Administration Department, Hunan Normal University. All the study subjects signed informed consent documents before entering the project. The study subjects came from a database that is created for studies to search for genes underlying the risk of osteoporosis and obesity. Only “healthy” people (defined by the following exclusion criteria) were included in the analysis. The exclusion criteria for the study subjects were histories of (1) serious residual effects of cerebral vascular disease; (2) diabetes mellitus, except for easily controlled, non-insulin-dependent diabetes mellitus (defined as adult asymptomatic hyperglycemia controlled by diet or oral agents); (3) chronic renal disease manifested by serum creatinine  $>1.9$  mg/dl; (4) chronic liver disease or alcoholism; (5) significant chronic lung disease; (6)  $>6$  months of corticosteroid therapy at pharmacologic levels; (7)  $>6$  months of treatment with

anticonvulsant therapy; (8) evidence of other metabolic or inherited bone disease, such as hyper- or hypoparathyroidism, Paget's disease, osteomalacia, or osteogenesis imperfecta; (9) rheumatoid arthritis or collagen disease; (10) recent (within the past year) major gastrointestinal disease, such as peptic ulcer, malabsorption, chronic ulcerative colitis, regional enteritis, or any significant chronic diarrhea state; (11) significant disease of any endocrine organ that would affect bone mass; (12) hyperthyroidism; (13) any neurologic or musculoskeletal condition that would be a non-genetic cause of low bone mass; and (14) any disease, treatment, or condition that would be a nongenetic cause of low bone mass. To minimize the confounding effect of overweight, we excluded the subjects with body mass index (BMI)  $\geq 25$   $\text{kg}/\text{m}^2$ .

### The Chinese sample

A total of 1,809 unrelated subjects aged 19–45 years, who belong to the Chinese Han ethnic group, were recruited in Changsha City and its surrounding areas of central south of China.

### The Caucasian sample

The sample contains a total of 362 unrelated Caucasian subjects aged from 19 to 45 years who were selected from more than 4,000 participants from 451 pedigrees recruited from Omaha, NE, USA. Individuals without consanguineous relationships are considered unrelated and selected for the present study. For example, if an individual was selected, his/her children, cousins, siblings, parents, parents' siblings, and parents' siblings' children were not chosen, but the person who married the one in the pedigree was selected. The basic characteristics of the study subjects were listed in Table 1.

### Measurements

The MM of the Chinese was measured by a Hologic 4500 DXA scanner (Hologic Corp., Waltham, MA, USA) at Hunan

**Table 1** Basic characteristics of the studied subjects

	Women		Men	
	Chinese	Caucasians	Chinese	Caucasians
<i>N</i>	851	232	958	130
Age (years)	27.1 $\pm$ 4.7	34.0 $\pm$ 7.1	26.9 $\pm$ 4.0	32.4 $\pm$ 8.0
Weight (kg)	50.4 $\pm$ 5.7	59.8 $\pm$ 6.9	60.5 $\pm$ 6.7	74.3 $\pm$ 7.1
Height (cm)	158.3 $\pm$ 5.1	165.5 $\pm$ 6.2	169.5 $\pm$ 5.2	180.9 $\pm$ 6.5
Body mass index ( $\text{kg}/\text{m}^2$ )	20.1 $\pm$ 1.9	21.8 $\pm$ 2.0	21.0 $\pm$ 2.0	22.7 $\pm$ 1.7
Percentage body fat (%)	27.7 $\pm$ 4.9	29.9 $\pm$ 6.0	15.0 $\pm$ 5.3	17.4 $\pm$ 5.0

Values are means  $\pm$  SD

*N* no. of subjects

Normal University. The coefficient of variability (CV) value for whole body muscle mass (WMM), the combination of EMM and trunk muscle mass, which was obtained from 30 subjects repeatedly measured two times, was 0.21% [53]. The MM of Caucasians was measured by Hologic 2000+ or 4500 DXA scanners (Hologic, Bedford, MA, USA) in the Osteoporosis Research Center at Creighton University. The CV for WMM obtained on the Hologic 2000+ and 4500 DXA scanners was 1.0% and 0.7%, respectively [10]. The calculation of MM has been previously described in detail elsewhere [51].

EMM was calculated as the combined sum of arm muscle mass and leg muscle mass. All scanners are calibrated daily, and long-term precision is monitored with external phantoms. Technicians maintain scan-by-scan surveillance for quality control in both America and China, and all of them were trained and certified by the International Society for Clinical Densitometry as Clinical Densitometrist. Therefore, MM measurements by different scanners and technicians in the study are highly compatible with one another and are well within the precision limits.

Body height and weight of all subjects were measured routinely in typical indoor clothing without shoes with a stadiometer and a standardized balance-beam scale at the time of DXA scan. MMIs were calculated as muscle mass/height<sup>2</sup> (kilograms per meter squared).

#### Statistical analysis

Data were analyzed by using the Statistical Analysis System (SAS Institute, Cary, NC). The compared group data were normally distributed. Independent sample *t* tests were used to analyze the effects of population (Chinese vs. Caucasians) and gender (women vs. men) on sarcopenia-related indexes. Since age is also correlated with MMI (Table 4), the effects of population and gender were also tested after adjustment by regressions for age. All statistical tests were two sided with statistical significance set at  $P \leq 0.05$ .

## Results

#### Basic characteristics

The basic characteristics of the studied subjects were summarized in Table 1. The Caucasians were taller and weighed more, and had a higher BMI ( $P < 0.0001$ ), compared with the Chinese within the same gender group, respectively, while males were higher and weighed more, and had a lower BMI ( $P < 0.0001$ ), compared with the females within the same ethnic group, respectively. As shown in Table 4, age is significantly correlated with most of MMIs.

#### Differences between Chinese and Caucasian groups

The differences of MMIs between the Chinese and Caucasian groups are presented in Table 2. Within the same gender groups, the Caucasians were significantly ( $P \leq 0.0003$ ) higher than the Chinese for EMMI with a difference of 0.6 kg/m<sup>2</sup> (female) and 0.7 kg/m<sup>2</sup> (male), for LMMI with a difference of 0.3 kg/m<sup>2</sup> (female) and 0.2 kg/m<sup>2</sup> (male), and for AMMI with a difference of 0.3 kg/m<sup>2</sup> (female) and 0.5 kg/m<sup>2</sup> (male), respectively. After adjustment for age (Table 2), all these differences remain significant ( $P \leq 0.0005$ ).

#### Differences between female and male groups

The differences of MMIs between female and male groups are presented in Table 3. Within the same ethnic group, females were significantly ( $P < 0.0001$ ) lower than males for EMMI with 1.9 kg/m<sup>2</sup> (Chinese) and 1.9 kg/m<sup>2</sup> (Caucasian), for LMMI with a difference of 1.2 kg/m<sup>2</sup> (Chinese) and 1.1 kg/m<sup>2</sup> (Caucasian), and for AMMI with a difference of 0.6 kg/m<sup>2</sup> (Chinese) and 0.8 kg/m<sup>2</sup> (Caucasian), respectively. After adjustment for age (Table 3), all these differences remain significant ( $P < 0.0001$ ).

## Discussion

The present results represented our first effort of investigating the differences in MMIs between Caucasian and Chinese groups, as well as female and male groups, and the results show there are consistently significant differences in MMIs between the pairs of study groups.

The Chinese group had lower MMIs than the Caucasian group, before and after adjustment for age (Table 4). Two possible mechanisms underline the observed population difference of MMIs between the Chinese and Caucasian groups: (1) lower testosterone concentration (TC) in the native Chinese than in Caucasians. Native Chinese men's levels of testosterone production and plasma testosterone were lower than those of Caucasian men from the USA [41]. Testosterone plays a key role in muscle hypertrophy [19, 26]. (2) higher insulin resistance (IR) in the Chinese than in Caucasians. The Chinese had higher IR [12, 45], which characterized lower insulin sensitivity (IS), than Caucasians. IR can accelerate muscle protein degradation in numerous studies [29, 35, 43, 52].

Females had lower MMI than males, before and after adjustment for age. Likewise, the lower MMI in females is probably due to their lower serum TC [7] and IS [14, 17, 34]. In fact, numerous previous studies have constantly reported that TC is significantly positively associated with IS in vivo [24, 38, 40, 46, 54], and both of them can be improved with

**Table 2** Differences of MMIs in the Chinese vs. Caucasians

	MMIs (kg/m <sup>2</sup> )		Independent-samples <i>t</i> tests					
	Male		Before adjustment for age		After adjustment for age			
	Caucasians	Chinese	Caucasians	Chinese	Male	Female		
Legs	6.1±0.6	5.9±0.5	5.0±0.5	4.7±0.4	<i>t</i> (154)=-3.72, <i>P</i> =0.0003	<i>t</i> (316)=-8.6, <i>P</i> <0.0001	<i>t</i> (154)=-3.6, <i>P</i> =0.0005	<i>t</i> (312)=-6.3, <i>P</i> <0.0001
Arms	2.4±0.3	1.9±0.2	1.6±0.2	1.3±0.1	<i>t</i> (144)=-16.9, <i>P</i> <0.0001	<i>t</i> (302)=-21.8, <i>P</i> <0.0001	<i>t</i> (141)=-12.6, <i>P</i> <0.0001	<i>t</i> (286)=-13.2, <i>P</i> <0.0001
Extremities	8.5±0.9	7.8±0.7	6.6±0.7	6.0±0.5	<i>t</i> (151)=-8.6, <i>P</i> <0.0001	<i>t</i> (310)=-13.0, <i>P</i> <0.0001	<i>t</i> (150)=-7.2, <i>P</i> <0.0001	<i>t</i> (303)=-8.8, <i>P</i> <0.0001

MMIs, muscle mass indexes, were expressed as mean ± SD

**Table 3** Differences of MMIs in females vs. males

	MMIs (kg/m <sup>2</sup> )		Independent-samples <i>t</i> tests					
	Caucasians		Before adjustment for age		After adjustment for age			
	Female	Male	Female	Chinese	Caucasians	Chinese		
Legs	6.1±0.6	5.0±0.5	5.9±0.5	4.7±0.4	<i>t</i> (360)=-17.6, <i>P</i> <0.0001	<i>t</i> (1,792)=-54.6, <i>P</i> <0.0001	<i>t</i> (360)=-17.3, <i>P</i> <0.0001	<i>t</i> (1,792)=-54.5, <i>P</i> <0.0001
Arms	2.4±0.3	1.6±0.2	1.9±0.2	1.3±0.1	<i>t</i> (192)=-27.5, <i>P</i> <0.0001	<i>t</i> (1,746)=-81.2, <i>P</i> <0.0001	<i>t</i> (193)=-27.0, <i>P</i> <0.0001	<i>t</i> (1,729)=-83.9, <i>P</i> <0.0001
Extremities	8.5±0.9	6.6±0.7	7.8±0.7	6.0±0.5	<i>t</i> (224)=-21.9, <i>P</i> <0.0001	<i>t</i> (1,776)=-66.6, <i>P</i> <0.0001	<i>t</i> (226)=-21.5, <i>P</i> <0.0001	<i>t</i> (1,774)=-66.9, <i>P</i> <0.0001

MMIs, muscle mass indexes, were expressed as mean ± SD

**Table 4** Simple linear regression models for the adjustment of age's effects on MMIs

	Caucasians			Chinese			Males			Females		
	AMMI	LMMI	EMMI	AMMI	LMMI	EMMI	AMMI	LMMI	EMMI	AMMI	LMMI	EMMI
Age	-0.0035	-0.0128	-0.0163	0.0084	-0.0005	0.0076	0.0165	0.0015	0.0177	0.0149	0.0123	0.0271
<i>t(df)</i>	-1.08 (1)	-2.33 (1)	-1.95 (1)	4.24 (1)	-0.12 (1)	1.24 (1)	11.14 (1)	0.45 (1)	4.03 (1)	16.65 (1)	5.11 (1)	8.86 (1)
<i>P</i>	0.2789	0.0206	0.0518	<0.0001	0.9023	0.2164	<0.0001	0.6521	<0.0001	<0.0001	<0.0001	<0.0001

AMMI arms muscle mass index, LMMI legs muscle mass index, EMMI extremity muscle mass index

exercise [3, 5, 11, 20, 36, 37, 42, 48]. The increased plasma TC in male rats during exercise is at least partially a result of lactate's effect on the secretion of testosterone [30, 31], and testosterone may suppress the expression of proinflammatory cytokines such as tumor necrosis factor-alpha and interleukin-1 [8, 32]. In experimental models, these proinflammatory cytokines disrupt normal insulin action in fat and muscle cells, and this may be the major factor in causing the whole body IR observed in patients with visceral adiposity [47]. In addition, cholesterol, a precursor of testosterone, comes for about one third from the dietary intake and for about two thirds from endogenous synthesis from unburned food metabolites [27]; thus, different cholesterol intake from food may also impose a significant impact on plasma TC and consequently the IS in skeletal muscle. However, due to the lack of data of physical activity/exercise and nutrition/food in the current study, it is impossible to investigate their effects on the differences in MMIs.

Several approaches, e.g., DXA, total body potassium, isotope dilution for total body water, total body electrical conductivity, bioelectrical impedance analysis, and bioelectrical impedance spectroscopy, vary in their accuracy, complexity, cost, and availability, are available for MM measurement. DXA is gaining popularity in MM measurement because it is relatively quick and accurate to measure MM especially for EMM [39] with low radiation dose [33].

Currently, EMM is gaining popularity in sarcopenia definition [2, 9]. WMM is a previous important measure for sarcopenia [49]; however, current available methods are difficult to accurately measure the WMM in vivo because internal organs such as the brain, heart, and liver have relatively similar physical characteristics (e.g., density) compared with muscles and thus have confounding effects to evaluate MM. However, the extremities largely consist of fat mass, bone mass, and muscles, and DXA can accurately measure these three components [4]. So in this study, we focused on investigating the difference of EMMI, as well as AMMI and LMMI, which only takes skeletal MM into consideration, between different gender and ethnic groups.

The development of sarcopenia is determined by the peak MM attained early in young adults and subsequent rate of muscle loss with aging later in life. At the current relatively early stage, due to easy recruitment of subjects with peak MM and relative difficulty in recruiting samples for tracking MM loss, most of the studies for sarcopenia focused on peak MM. This study also focused on peak MM, as evidenced by the sample age span (19–45 years) when the peak MM is maintained. Investigating the difference in peak MMI between different ethnic and gender groups may shed some light on explaining the differences of sarcopenia risk. It would be highly beneficial for future studies to increase efforts to study MM loss for eventually elucidating the pathology of sarcopenia.



In conclusion, the present results demonstrate that before and even after adjustment for age, the Caucasian and male groups had significantly higher MMIs in comparison with the Chinese and female groups, respectively, and these findings may provide important implications in the gender- and population-specific risks of future sarcopenia among different gender and ethnic groups.

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