

low muscle mass plus low muscle strength and/or low physical performance, and we also recommend outcome indicators for further researches, as well as the conditions that sarcopenia should be assessed. In addition to sarcopenia screening for community-dwelling older people, AWGS recommends sarcopenia assessment in certain clinical conditions and healthcare settings to facilitate implementing sarcopenia in clinical practice. Moreover, we also recommend cutoff values for muscle mass measurements (7.0 kg/m^2 for men and 5.4 kg/m^2 for women by using dual X-ray absorptiometry, and 7.0 kg/m^2 for men and 5.7 kg/m^2 for women by using bioimpedance analysis), handgrip strength ($<26 \text{ kg}$ for men and $<18 \text{ kg}$ for women), and usual gait speed ($<0.8 \text{ m/s}$). However, a number of challenges remained to be solved in the future. Asia is made up of a great number of ethnicities. The majority of currently available studies have been published from eastern Asia, therefore, more studies of sarcopenia in south, south-eastern, and western Asia should be promoted. On the other hand, most Asian studies have been conducted in a cross-sectional design and few longitudinal studies have not necessarily collected the commonly used outcome indicators as other reports from Western countries. Nevertheless, the AWGS consensus report is believed to promote more Asian sarcopenia research, and most important of all, to focus on sarcopenia intervention studies and the implementation of sarcopenia in clinical practice to improve health care outcomes of older people in the communities and the healthcare settings in Asia.

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Sarcopenia has been accepted as a new geriatric syndrome,¹ and the knowledge related to sarcopenia is growing rapidly worldwide. Over the past 20 years of sarcopenia research after the first introduction by Rosenberg et al,² the etiology, pathophysiology, risk factors, and consequences of sarcopenia have gradually become clearer.³ Moreover, a number of therapeutic approaches and clinical trials have been developed and are still evolving.^{4–7} Most importantly, the association of sarcopenia with poorer health status and adverse outcomes had triggered a new approach for health promotion and health care of older people. The escalation of elderly population worldwide further strengthened the clinical importance of sarcopenia, which is even more significant in Asia because of the rapid demographic transition in this highly populated continent.^{8–10}

Sarcopenia has been described as an age-related decline in skeletal muscle mass as well as muscle function (defined by muscle strength or physical performance),¹¹ which may result in reduced physical capability,^{12–14} poorer quality of life, impaired cardiopulmonary performance,^{15,16} unfavorable metabolic effects,¹⁷ falls,¹⁸ disability, and mortality in older people,^{19,20} as well as high health care expenditure.²¹ Furthermore, sarcopenia is also associated with multimorbidity,^{22,23} cigarette smoking,^{22,24} low body mass index,²⁵ underweight,²⁶ physical inactivity,¹² and low serum levels of testosterone in men.^{27,28} In general, the association between sarcopenia and functional decline is more significant in men than in women,^{29,30} which deserves further research for therapeutic consideration. Since Asia is the most populated and fastest aging region in the world, sarcopenia will pose great impacts to Asian populations in the near future.^{31,32} Therefore, experts and researchers of sarcopenia from China, Hong Kong, Japan, South Korea, Malaysia, Taiwan, and Thailand organized the Asian Working Group for Sarcopenia (AWGS) and had several meetings in Taipei, Seoul, and Kyoto to promote further research development of sarcopenia in Asia since March 2013. This article will focus on the epidemiology of sarcopenia in Asian countries and to propose a diagnostic algorithm based on currently available evidence in Asia.

Diagnosis of Sarcopenia and Its Impact to Asia

Asia is a huge and densely populated continent with a wide range of ethnicities, cultural, social, religious backgrounds, and lifestyles. Because of the rapid population aging and the population size, the impact of sarcopenia in Asia may be stronger than in other continents. However, the status of population aging and economic development varies extensively in different Asian countries. Therefore, developing a consensus for sarcopenia diagnosis and clinical

approaches based on available evidence is of great importance for sarcopenia research in the future.

In 2010, European Working Group on Sarcopenia in Older People (EWGSOP) proposed an operational definition and diagnostic strategy for sarcopenia that had become the most widely used in the world.³³ The EWGSOP definition required measurements of muscle mass, muscle strength, and physical performance for the diagnosis of sarcopenia, which is compatible with current understanding about sarcopenia. Based on the discussion of the AWGS meetings, we decided to take similar approaches for sarcopenia diagnosis, but unlike EWGSOP, we recommended measuring both muscle strength (handgrip strength) and physical performance (usual gait speed) as the screening test (Figure 1). Although the recommended approaches for measurements of muscle mass, muscle strength, and physical performance by AWGS were similar to the EWGSOP definition, the cutoff values of these measurements in Asian populations may differ from those in Caucasians because of ethnicities, body size, lifestyles, and cultural backgrounds. Therefore, developing an Asian consensus in sarcopenia diagnosis based on the evidence derived from Asian populations is essential for research and therapeutic approaches to sarcopenia in Asia.

Strategy for Sarcopenia Screening and Assessment

In principle, AWGS followed the diagnostic approach of EWGSOP, and we added some Asian perspectives in sarcopenia diagnosis and research. In the previous studies from Western countries, the prevalence of sarcopenia in older people was around 20% among people aged 65 years and older and may reach 50%–60% in octogenarians.³⁴ EWGSOP recommends routine screening for sarcopenia among community-dwelling people aged 65 years and older. On the other hand, the International Working Group on Sarcopenia (IWGS) specifies certain conditions for sarcopenia assessment, including (1) noted decline in function, strength, “health” status, (2) self-reported mobility-related difficulty, (3) history of recurrent falls, (4) recent unintentional weight loss ($>5\%$), (5) post-hospitalization, and (6) other chronic conditions (eg, type 2 diabetes, chronic heart failure, chronic obstructive pulmonary disease, chronic kidney disease, rheumatoid arthritis, and cancer).³⁵ Moreover, IWGS recommends assessing patients with reduced physical functioning (or weakness) or patients with habitual gait speed $<1.0 \text{ m/s}$ (by 4-m course) to assess body composition by dual x-ray absorptiometry (DXA). Non-ambulatory patients or those who cannot rise from a chair unassisted should be considered to be sarcopenic without DXA measurements. Since sarcopenia is defined as an age-related condition, assessment of sarcopenia is limited to people aged 65 years and older only in the

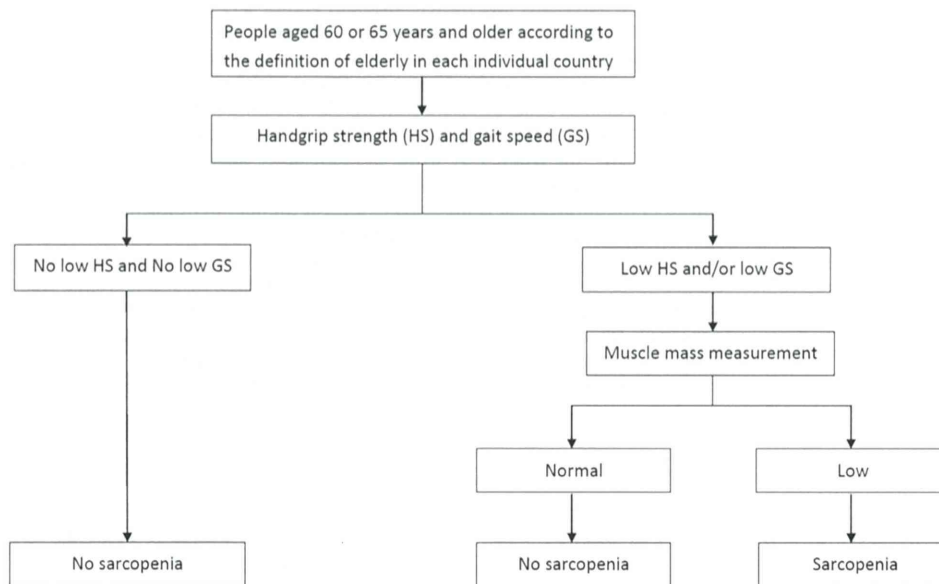


Fig. 1. Recommended diagnostic algorithm of Asian Working Group for Sarcopenia.

EWGSOP criteria, but IWGS does not specify the age for sarcopenia diagnosis.

In Asia, because of the different states of aging, not all countries use the same age cutoff to define elderly populations. Therefore, AWGS recommends using 60 or 65 years as the age for sarcopenia diagnosis according to the definitions of elderly in each country. Although muscle aging is a continuous process, most previous studies supported the idea that loss of muscle mass and muscle strength becomes pronounced around the age of 50,³⁶ progresses faster after the age of 60,³⁷ and accelerates even faster after the age of 75.³⁸ The overall benefits of sarcopenia screening or assessment programs are dependent on the outcomes of effective intervention programs. AWGS emphasizes the benefits of intervention programs in addition to sarcopenia screening and assessment; therefore, we recommend screening for sarcopenia among community-dwelling older people as well as older people with certain clinical conditions in all healthcare settings. Table 1 summarized the recommended strategy for sarcopenia screening and assessment of AWGS by dividing cases into 2 categories (ie, community settings and specific chronic conditions in all healthcare settings). From the perspective of public health, sarcopenia screening for community-dwelling older people would facilitate health promotion and disability prevention in their communities, and the assessment of sarcopenia in clinical settings would

facilitate strategies for the intervention in clinical practice. AWGS would like to emphasize the prognostic significance of sarcopenia in clinical practice through assessment under certain clinical conditions. However, the benefits of identification of and interventions for sarcopenia remain to be determined.

Suggested Outcome Indicators in Sarcopenia Research

The EWGSOP definition suggests using physical performance, muscle strength, and muscle mass as the primary treatment outcome indicators for sarcopenia intervention trials, whereas activities of daily living, quality of life, metabolic and biochemical markers, inflammatory markers, global impression of change by subject or physician, falls, admission to nursing home or hospital, social support, and mortality as secondary outcome indicators.³³ While most epidemiologic studies in sarcopenia research to date have taken a static approach, the state of sarcopenia may change over time and this dynamic approach may provide different considerations in developing sarcopenia intervention programs. Therefore, AWGS also recommends a dynamic approach for sarcopenia research by measuring changes in (1) muscle mass, strength, and function, (2) physical performance, (3) frailty status, (4) instrumental activities of daily living, and (5) basic activities of daily living over a given period of time as outcome indicators for sarcopenia research. In addition to the above-mentioned outcome indicators, AWGS also recommends using fear of falling and incontinence as outcome indicators for sarcopenia research (Table 2).

Table 1

Strategy of Sarcopenia Screening and Assessment for Older People (60 or 65 Years of Age and Older) in Asia

Community Settings
People aged 60 or 65 years and older (according to the definitions of elderly in each individual country) living in communities
Specific Clinical Conditions in All Healthcare Settings
Presence of recent functional decline or functional impairment
Unintentional body weight loss for over 5% in a month
Depressive mood or cognitive impairment
Repeated falls
Undernutrition
Chronic conditions (eg, chronic heart failure, chronic obstructive pulmonary disease, diabetes mellitus, chronic kidney disease, connective tissue disease, tuberculosis infection, and other chronic wasting conditions)

Assessment Techniques and Suggested Cutoff Values

Assessment of sarcopenia in Asian populations presents a great challenge because of the lack of outcome-based studies. However, determining appropriate cutoff values for sarcopenia diagnosis in Asia is critical to promote further sarcopenia research and treatment in Asia. Consequently, AWGS focused on the best available evidence to determine cutoff values for the diagnosis of sarcopenia in Asia. If, however, no outcome-based data are available, AWGS would recommend standardized approaches for cutoff value determination.

Table 2
Outcome Indicators for Sarcopenia Research Recommended by AWGS

Static Approach
Activities of daily living
Quality of life
Inflammatory markers
Falls
Frailty status
Mobility disorders
Admission to hospitals
Admission to long term care facilities
Mortality
Dynamic Approach
Changes in muscle mass
Changes in muscle strength
Changes in physical performance
Changes in frailty status
Changes in instrumental activities of daily living
Changes in activities of daily living

AWGS, Asian Working Group for Sarcopenia.

Muscle Mass

EWGSOP recommends DXA, computed tomography (CT), magnetic resonance imaging (MRI), and bioimpedance analysis (BIA) for sarcopenia research. Currently, the precision of DXA, CT, and MRI has been well recognized, but the precision of BIA in measuring muscle mass is controversial. BIA was developed to estimate the volume of body fat and lean body mass, but not appendicular muscle mass. Although the accuracy of BIA in sarcopenia diagnosis has been validated,^{39–41} it is heavily dependent on the accuracy of the equation of the equipment and the conditions of assessments, eg, temperature, humidity, skin condition, etc.⁴² Nevertheless, the high cost, CT-generated radiation exposure, and inconvenience for community screening have limited the applications of CT and MRI despite both CT and MRI have both been considered gold standards for evaluation of body composition. On the other hand, DXA is also considered an appropriate alternative approach to distinguish between fat, bone mineral, and lean tissues. Currently, DXA may be the most widely used method for muscle mass measurement in sarcopenia research. Despite the minimal radiation exposure from DXA, using DXA in community screening of sarcopenia is still difficult. Newly developed models of BIA equipment may obtain measurements of appendicular muscle mass with precision.^{43,44} Portability, reasonable cost, fast processing, noninvasiveness, radiation-free functions, and convenience of use made BIA suitable for community sarcopenia assessment. Results of multiple segment fat-free mass estimation using BIA are highly associated with that measured using DXA among elderly Taiwanese.⁴⁵ Although using BIA equipment with validated equations is recommended for sarcopenia research in EWGSOP criteria, the equations of BIA equipment in Western countries are not derived from Asian populations. Strasser et al⁴⁶ proposed measurement of muscle thickness, especially of musculus vastus medialis, by musculoskeletal ultrasound to be a reliable method for the estimation of sarcopenia, which deserves further research for applications in Asian studies. In current Asian studies, the most commonly used BIA machines were manufactured by only 2 companies, and the results were quite consistent. Because of its portability and reasonable cost, BIA may be considered the main approach in sarcopenia assessment in community-based screening programs. Therefore, AWGS supports using BIA for sarcopenia diagnosis and evaluation of the effect of intervention programs, but AWGS suggests researchers to provide coefficient of variance, inter- and intra-examiner reliability whenever possible to facilitate subsequent international comparisons.

In terms of cutoff value determination, most current Asian studies have adopted the classical approach for muscle mass measurement (ie, below 2 standard deviations of the mean muscle mass of young adults). However, Asian studies reported an extremely low prevalence of sarcopenia through this approach, especially in older women.^{26,47,48} Lau et al²⁶ also found that the relative total skeletal muscle of Hong Kong Chinese (total skeletal muscle/height²) was 17% lower among young Chinese men than that of Caucasian men.²⁶ A potential cohort effect may exist in this approach since younger people in Asia today leading a westernized or more urbanized lifestyle while older Asian people have carried out a traditional lifestyle since adulthood. This cohort effect may be derived from the economic development, urbanization, and development of public transportation in Asia in recent decades. Older Asian people today may have walked and performed more physical activities because of the underdevelopment of public transportation and living conditions since their early adulthood, so their muscle mass may be maintained better than that of the younger generation. On the other hand, because of the relatively higher adiposity of Asian people in comparison with Caucasians, appendicular muscle mass may be overestimated by DXA. Overall, AWGS recommends using 2 standard deviations below the mean muscle mass of young reference group or the lower quintile as the cutoff value determination. Moreover, AWGS recommends using height-adjusted skeletal muscle mass instead of weight-adjusted skeletal muscle mass, and the suggested cutoff values were 7.0 kg/m² in men and 5.4 kg/m² in women by using DXA. By using BIA, the suggested cutoff values were 7.0 kg/m² in men and 5.7 kg/m² in women, defined by appendicular skeletal muscle mass/height².

Muscle Strength

Measuring handgrip strength is considered a feasible and convenient measure of muscle strength because of cost, availability, ease of use, and its association with leg strength. Wu et al⁴⁹ presented the norm of handgrip strength in Taiwan, which disclosed that the mean grip strength of the study sample in Taiwan was significantly lower (male 25%, female 27%) than consolidated norms derived from largely Caucasian populations. Although some papers published in Taiwan using this adjusted cutoff value based on EWGSOP definition for sarcopenia research,⁵⁰ some unpublished papers from Japan, Hong Kong, and China recommended using 25 kg for men and 18 or 16 kg for women as the cutoff values for handgrip strength. Currently, handgrip strength is the most widely used measure for muscle strength in Asian sarcopenia research (Table 3), and AWGS also recommends using it for the measurement of muscle strength. Although knee flexion/extension and peak expiratory flow are also recommended for sarcopenia research in EWGSOP criteria, they are less commonly used. In Thailand, the cutoff points of quadriceps strength had been defined based on the outcome of mobility decline. The cutoff points of <18 kg in men and <16 kg in women can discriminate those had normal and abnormal various sarcopenia-related variables. Because of the lack of outcome-based cutoff values, AWGS recommends using the lower 20th percentile of handgrip strength of the study population as the cutoff value for low muscle strength before outcome-based data is available. Low handgrip strength is suggested to be defined as <26 kg for men and <18kg for women by AWGS.

Physical Performance

A wide range of tests for physical performance are recommended in EWGSOP criteria, including the Short Physical Performance Battery (SPPB), usual gait speed, the 6-minute walk test, the stair climb power test, and the timed-up-and-go test (TUG).⁵¹ Timed usual gait is highly predictive for the onset of disability,⁵² and other adverse health

Table 3
Measurable Variables and Cutoff Points in Asian Populations

Criterion	Measurement Method	Cutoff Points by Sex	Reference Group Definition	Prevalence of Sarcopenia	Country/Ethnicity	Reference	
Muscle mass	DXA	ASM/height ² Class 1 and class 2 sarcopenia Men: 7.77 and 6.87 kg/m ² Women: 6.12 and 5.46 kg/m ²	Based on values 1 and 2 SD below the sex-specific means of the study reference data (n = 529)	Class 1 and class 2 sarcopenia in subjects 70–85 years of age: Men: 6.7%, 56.7% Women: 6.3%, 33.6%	Japan	69	
		ASM/height ² Men <5.72 kg/m ² Women <4.82 kg/m ²	Based on 2 SD below the mean of young Asians in study (n = 111)	In older Chinese ≥70 years of age Men: 12.3% Women: 7.6%	Chinese	26	
		ASM/height ² Men: 7.40 kg/m ² Women: 5.14 kg/m ²	Based on 2 SD below the sex-specific mean of a younger population (n = 145)	In older subjects ≥ 60 years of age Men: 6.3% Women: 4.1%	Korea	70	
		SMI (%) ¹ Men: 35.71% Women: 30.70%	Based on 2 SD below the sex-specific mean of a younger population (n = 145)	Men: 5.1% Women: 14.2%			
		Using the residuals method		Men: 15.4% Women: 22.3%			
		ASM/height ² Class I and class II sarcopenia Men: 7.50 and 6.58 kg/m ² Women: 5.38 and 4.59 kg/m ²	Based on 1 and 2 SD below the mean of young adults in study (n = 2513)	Class I and class II sarcopenia Men: 30.8% and 12.4% Women: 10.2% and 0.1%	Korea	48	
		ASM/body weight (%) Class I and class II sarcopenia Men: 32.2% and 29.1% Women: 25.6% and 23.0%	Based on 1 and 2 SD below the mean of young adults in study	Men: 29.5% and 9.7% Women: 30.3% and 11.8%	Korea	48	
		ASM/body weight (%) ¹ Men: 29.53% Women: 23.20%	Based on 2 SD of sex-specific young normal people		Korea	71	
		Use SMI (% of skeletal muscle index) but not mentioned the cutoff points in the manuscript	Based on 2 SD of sex-specific young normal people	Sarcopenia class I, II, overall Men: 32.5%, 15.7%, 35.33 % Women: 30.5%, 10%, 34.74 %	Thailand	72	
		RASM index Men: 7.27 kg/m ² Women: 5.44 kg/m ²	Based on the lower 20% of study group	Men: 10.8% Women: 3.7%	Taiwan	47	
		SMI (% of skeletal muscle index) Men: 37.4% Women: 28.0%	Based on the lower 20% of study group	Men: 14.9% Women: 19%			
		BIA	SMI Men <8.87 kg/m ² Women <6.42 kg/m ²	Based on 2 SD below the normal sex-specific mean for young people	18.6% in elderly women and 23.6% in elderly men age 65 and older	Taiwan	40
			ASM/height ² Men <7.0 kg/m ² Women <5.8 kg/m ²	Based on 2 SD below young adult values	Men: 11.3% Women: 10.7% using EWGSOP criteria	Japan	13
			ASM/height ² Women ≤ 6.42 kg/m ²		Women: 22.1%	Japan	6
			ASM/height ² Men <6.75 kg/m ² Women <5.07 kg/m ²	Based on 2 SD below young adult values	Men: 21.8% Women: 22.1% using EWGSOP criteria	Korea/Health ABC data	15
Muscle strength	Handgrip strength	Men: 30.3 kg Women: 19.3 kg	Based on lowest quartile of study group		Japan	13	
		Men <22.4 kg Women <14.3 kg	Based on EWGSOP recommendation and adjusted according to Asian data ⁴⁹		Taiwan	50	
		Women ≤1.01 Nm/kg			Japan	6,73	
Physical performance	Gait speed	Gait speed Men <1.27 m/s Women <1.19 m/s	Based on the lowest quartile of study group, gait speed obtained from the middle 5 m of a total of 11 m walking	Men: 11.3% Women: 10.7% using EWGSOP criteria	Japan	13	
		Gait speed ≤ 1 m/s Gait speed ≤ 1.22 m/s		Women: 22.1%	Taiwan Japan	50 6,73	
		SPPB SPPB scores <9			Japan Korea	74	

ASM, appendicular skeletal muscle mass; BIA, bioimpedance analysis; DXA, dual x-ray absorptiometry; EWGSOP, European Working Group on Sarcopenia in Older People; Health ABC, The Health Aging and Body Composition Study; RASM, relative appendicular skeletal muscle; SD, standard deviation; SPPB, Short Physical Performance Battery; SMI, skeletal muscle mass index.

¹SMI (%) = total skeletal muscle mass (kg)/weight (kg) × 100.

²The author also named it modified skeletal muscle mass index (SMI).

events like severe mobility limitation and mortality.⁵³ TUG is an assessment of ambulation and dynamic balance. Poorer TUG has been demonstrated to be associated with poorer physical and mental function and mood status, as well as low fat-free mass by BIA

measurements.⁵⁴ Although TUG has been proposed as a suitable measurement for physical performance in EWGSOP, abnormal TUG may result from a great variety of underlying conditions. AWGS is more conservative in the use of TUG as a measurement for physical

performance, and we recommend using 6-meter usual gait speed for measurement of physical performance.

Ideally, determination of the cutoff values of these measurements should be based on longitudinal outcome-based studies instead of a simply statistical approach.⁵⁵ Although the association between sarcopenia and functional decline or even mortality has been established,⁵⁶ selection of universal outcome indicators in subsequent research may facilitate international comparisons. Table 3 summarized the epidemiology and proposed cut-off points in different cases of Asian sarcopenia research. EWGSOP has developed a suggested algorithm based on gait speed measurement with a cutoff point of <0.8 m/s.³³ The association of slow usual gait speed in the elderly with adverse clinical outcomes has been reported extensively, but the application was also dependent on the determination of appropriate cutoff points. Meanwhile, the prevalence of low muscle mass in the Asian population as determined using the classical approach is very low, which is confusing. The potential cohort effect may partially explain the phenomenon of older people today engaging in more physical activities than younger people, which made the prevalence of sarcopenia lower than expected. Specific consideration of this potential cohort effect deserves further attention in the diagnosis of sarcopenia in Asia. Although there is a potential gender difference in the cutoff value of usual gait speed and a wide range of walking speed (from 0.6 to 1.2 m/s) being reported in this special issue, AWGS suggested using <0.8 m/s as the cutoff for low physical performance after extensive consideration of data available in Asian studies.

Therapeutic Implications

Physical activities, including aerobics, endurance exercise,⁵⁷ and resistance exercise training^{58,59} have been demonstrated to significantly increase muscle mass and strength in sarcopenic older people. Although the recommended frequency of exercise training to improve muscle strength and functional performance has been shown,⁶⁰ a consensus has not yet been reached concerning the content of the prescribed exercise and the most optimal frequency and intensity. Inappropriate exercise training in the elderly may result in unfavorable adverse outcomes such as musculoskeletal complaints,⁶¹ which is not uncommon. Further research should be focused on the development of suitable exercise prescription, especially for older people at risk of functional decline or sarcopenia. The Society for Sarcopenia, Cachexia, and Wasting Disease developed nutritional recommendations for the prevention and management of sarcopenia, which combined exercise with adequate protein and energy intake.⁶² A leucine-enriched balanced essential amino acid or balanced amino acid supplementation is suggested for sarcopenia. Recently, Kim et al⁶ demonstrated that exercise and amino acid supplementation (3 g of a leucine-rich essential amino acid mixture twice a day) together may actually be effective in enhancing muscle strength, variables of muscle mass, and walking speed in sarcopenic women. Aside from exercise and nutritional supplementation, the pharmaceutical approach to sarcopenia is still under development. Growth hormone replacement was not successful because the effect of increased muscle mass by growth hormone replacement was not associated with the improvement of muscle performance,^{63–65} unless it is used for growth hormone deficiency patients for a period longer than 12 months.^{66–68} In addition, the effects of antimyostatin antibodies on sarcopenia have been demonstrated and may be marketed in a few years. Therefore, sarcopenia should be treated through a multi-level approach employing combined physical activities and nutritional supplementation. Currently, there is no well-established evidence for pharmaceutical approach for sarcopenia intervention, but a few agents may be available in future.

Future Challenge and Conclusion

Sarcopenia significantly impacts daily activities, functional status, disability, and quality of life in older populations. Although Asian populations are rapidly ageing, from the clinical practice or public health points of view, the understanding of and preparation for sarcopenia remain inadequate. Hence, this consensus collected as many Asian studies as possible and offers a working diagnosis of sarcopenia for Asian people. The main aims of AWGS were to promote sarcopenia research in Asian countries through providing recommended diagnostic strategies and cutoff values based on Asian studies, and to foster the importance of implementing sarcopenia in clinical practice and in community health promotion programs.

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ORIGINAL ARTICLE

Age-dependent changes in skeletal muscle mass and visceral fat area in Japanese adults from 40 to 79 years-of-age

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Aim: The age-dependent loss of skeletal muscle mass is highly concerning in diverse aging populations. However, age-dependent changes in muscle mass and the visceral fat area have not been well documented in Asian populations. The aim of the present study was to evaluate the age-dependent changes in skeletal muscle mass and the visceral fat area in Japanese adults from 40 to 79 years-of-age.

Methods: This was a cross-sectional study. Healthy men ($n = 16\,379$) and women ($n = 21\,660$) aged 40–79 years participated in the present study. The skeletal muscle mass and visceral fat area were measured in the study participants by bioelectrical impedance. The muscle mass data were converted into the skeletal muscle mass index (SMI) by dividing the weight by the height squared (kg/m^2).

Results: The SMI showed an age-dependent decrease in both sexes. Between 40 and 79 years, the total SMI decreased by 10.8% in men and by 6.4% in women. The arm SMI decreased by 12.6% in men and 4.1% in women, and the leg SMI decreased by 10.1% in men and by 7.1% in women in the same period. In contrast, the visceral fat area showed an age-dependent increase in both sexes. The visceral fat area increased by 42.9% in men and by 65.3% in women. The multiple regression analysis showed that the SMI was negatively associated with visceral obesity in both sexes.

Conclusions: In Japanese adults, sex-specific changes in skeletal muscle mass are more prominent in the arm than in the leg. Furthermore, the age-dependent increases in visceral adipose tissue might lead to loss of skeletal muscle mass. *Geriatr Gerontol Int* 2014; 14 (Suppl. 1): 8–14.

Keywords: age-dependent, Japanese, skeletal muscle mass, visceral fat area.

Introduction

Sarcopenia is an age-dependent loss of skeletal muscle mass, and is a serious medical concern in older populations.^{1,2} Sarcopenia is characterized by an impaired state of health associated with mobility disorders, an increased risk of falls and fractures, an impaired ability to carry out activities of daily living, disabilities, and a loss of independence.^{3–5}

Previous epidemiological studies of sarcopenia in several countries have shown a disease prevalence of 5–40% in older men and 7–70% in older women.^{6–18} In general, the prevalence of sarcopenia is approximately 25% in older men and 20% in older women. Notably,

previous work from this laboratory has shown that sarcopenia is highly prevalent among Japanese adults aged 80 years and older.¹⁸ Because older adults have a greater potential for health problems than young adults, it is very important to begin prevention of sarcopenia early, possibly before the age of 65 years. Two previous studies from the USA and Europe have shown that the age-dependent loss of skeletal muscle mass starts at approximately 50 years-of-age, and that skeletal muscle mass declines by 6.6–23.3% until 79 years-of-age.^{19,20} However, age-dependent changes in muscle mass in Asians are not well documented.

Visceral adiposity, which is the basis of metabolic syndrome and cardiovascular disease, is aggravated with age.²¹ The visceral adipose tissue produces many inflammatory cytokines, such as tumor necrosis factor-alpha (TNF- α) and interleukin (IL)-6,²² and expression of these inflammatory cytokines can lead to increased skeletal muscle breakdown.²³ Furthermore, previous studies have shown that increased visceral fat area is associated with decreased skeletal muscle mass in a

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small sample of older adults.²⁴ However, the association of skeletal muscle mass with age-dependent changes in visceral fat in a large population has not previously been shown.

The primary aim of the present study was to evaluate the age-dependent changes in skeletal muscle mass and visceral fat area using a large cross-sectional cohort of Japanese adults between 40 and 79 years-of-age. We also evaluated sex differences in skeletal muscle loss in the arms and legs. The secondary aim of the present study was to evaluate the association between the skeletal muscle mass and visceral fat area.

Methods

Participants

Participants were recruited by advertisements at several fitness and community centers. The participants in the present study were limited to visitors to these centers in the Kyoto, Osaka, and Hyogo prefectures in Japan. The inclusion criteria were an age of 40–79 years, living in the community and the ability to walk independently (including with a cane). The exclusion criteria were a certification of frailty status by the long-term care insurance service in Japan and artificial implants, such as cardiac pacemakers and replacement joints, which would interfere with accurate bioimpedance measurements. An interview was also used to identify those with the following exclusion criteria: severe cognitive impairment; severe cardiac, pulmonary, or musculoskeletal disorders; and comorbidities associated with greater risk of falls, such as Parkinson's disease or stroke. Because the purpose of the present study was to address physiological age-dependent changes in body composition, we excluded frail elderly and adults with those comorbidities. The present study was carried out in accordance with the guidelines of the Declaration of Helsinki, and the study protocol was reviewed and approved by the Ethics Committee of the Kyoto University Graduate School of Medicine.

Healthy men ($n = 16\,379$) and women ($n = 21\,660$) aged 40–79 years participated in the present study. The male participants were divided into eight groups according to age: 40–44 ($n = 3697$), 45–49 ($n = 3151$), 50–54 ($n = 2202$), 55–59 ($n = 1952$), 60–64 ($n = 2274$), 65–69 ($n = 1683$), 70–74 ($n = 1030$), and 75–79 ($n = 390$) years. The female participants were similarly divided into eight groups according to age: 40–44 ($n = 3828$), 45–49 ($n = 3686$), 50–54 ($n = 3597$), 55–59 ($n = 3002$), 60–64 ($n = 3490$), 65–69 ($n = 2314$), 70–74 ($n = 1269$), and 75–79 ($n = 474$) years.

Skeletal muscle mass index and visceral fat area

A bioelectrical impedance data acquisition system (Inbody 720; Biospace, Seoul, Korea) was used to deter-

mine bioelectrical impedance.²⁵ This system uses an electrical current at different frequencies (5, 50, 250, 500, and 1000 kHz) to directly measure the amount of extracellular and intracellular water in the body. The study participants stood on two metallic electrodes and held metallic grip electrodes. Using segmental body composition and muscle mass, a value for the appendicular skeletal muscle mass was determined and used for further analysis. The muscle mass was converted into the skeletal muscle mass index (SMI) by dividing the weight by the height squared (kg/m^2). This index has been used in several epidemiological studies.^{6,26} Additionally, the SMI of the arms and legs was calculated. The visceral fat area was determined by evaluating a transverse cross-section of the fourth and fifth abdominal lumbar area.

Statistical analysis

Differences in the total SMI, arm SMI, leg SMI, and visceral fat area among the eight age groups were examined using an analysis of variance. Multiple regression models were applied to determine the relationship between the visceral fat area and the SMI, adjusted for age and weight in each sex. The data were managed and analyzed using SPSS (Windows version 18.0; SPSS, Chicago, IL, USA). A P -value of <0.05 was considered to show statistical significance for all analyses.

Results

The mean age of the study participants was 54.5 ± 9.9 years, and 21 660 (56.9%) of the participants were women. The total SMI showed an age-dependent decrease in both sexes (men, $F = 251.1$, $P < 0.001$; women, $F = 135.6$, $P < 0.001$; Table 1). The percentage change in the total SMI at 40–44 years showed an age-dependent decrease in both sexes (Fig. 1, Table 1). In those aged over 65 years, the percentage change in the total SMI was greater in men than in women. In addition, the 20th percentile of total SMI in men and women aged 65–79 years was $7.02 \text{ kg}/\text{m}^2$ and $5.61 \text{ kg}/\text{m}^2$, respectively (Table 2).

To compare the age-dependent changes in muscle mass in the upper and lower limbs in this cohort, we analyzed the arm and leg SMI. The arm SMI showed an age-dependent decrease in both sexes (men, $F = 132.1$, $P < 0.001$; women, $F = 24.1$, $P < 0.001$; Table 1). The percentage change in the arm SMI using the 40–44 years group as a reference also showed an age-dependent decrease in both sexes (Fig. 2, Table 1).

Similarly to the arm SMI, the leg SMI also showed an age-dependent decrease in both sexes (men, $F = 273.2$, $P < 0.001$; women, $F = 192.2$, $P < 0.001$; Table 1). The percentage change in the leg SMI also showed an

Table 1 Participant characteristics by age half decade

		Overall			40–44 years			45–49 years			50–54 years			55–59		
		Men (<i>n</i> = 16 379)	Women (<i>n</i> = 21 660)		Men (<i>n</i> = 3697)	Women (<i>n</i> = 3828)		Men (<i>n</i> = 3151)	Women (<i>n</i> = 3686)		Men (<i>n</i> = 2202)	Women (<i>n</i> = 3597)		Men (<i>n</i> = 1952)	Women (<i>n</i> = 3002)	
		Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years
Total SMI (kg/m ²)	Men	7.97	0.73	–	8.20	0.78	–	8.11	0.66	–1.0	8.11	0.67	–1.1	7.98	0.64	–2.7
	Women	6.26	0.64	–	6.41	0.67	–	6.39	0.64	–0.3	6.33	0.64	–1.3	6.23	0.59	–2.8
Arm SMI (kg/m ²)	Men	2.08	0.28	–	2.14	0.31	–	2.11	0.26	–1.4	2.11	0.26	–1.2	2.08	0.24	–3.0
	Women	1.47	0.22	–	1.49	0.24	–	1.49	0.23	–0.5	1.47	0.22	–1.4	1.46	0.21	–2.3
Leg SMI (kg/m ²)	Men	7.98	0.73	–	6.06	0.51	–	6.00	0.46	–0.9	5.99	0.46	–1.1	5.91	0.45	–2.5
	Women	6.26	0.64	–	4.92	0.48	–	4.91	0.45	–0.3	4.85	0.46	–1.3	4.77	0.42	–3.0
Visceral fat area (cm ²)	Men	100.6	29.2	–	88.4	28.8	–	91.9	27.1	4.0	98.9	28.8	11.9	103.5	25.7	17.1
	Women	84.7	27.4	–	68.0	25.3	–	72.1	23.9	6.0	79.3	23.6	16.5	89.4	23.0	31.5
		60–64 years			65–69 years			70–74 years			75–79 years			ANOVA		
		Men (<i>n</i> = 2274)			Men (<i>n</i> = 1683)			Men (<i>n</i> = 1030)			Men (<i>n</i> = 390)					
		Women (<i>n</i> = 3490)			Women (<i>n</i> = 2314)			Women (<i>n</i> = 1269)			Women (<i>n</i> = 474)					
		Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years	Mean	SD	% change over 40–44 years	<i>F</i> -value	<i>P</i> -value	
Total SMI (kg/m ²)	Men	7.84	0.68	–4.3	7.64	0.67	–6.9	7.59	0.66	–7.4	7.32	0.62	–10.8	251.1	<0.001	
	Women	6.14	0.61	–4.2	6.08	0.60	–5.2	6.09	0.55	–5.1	6.00	0.60	–6.4	135.6	<0.001	
Arm SMI (kg/m ²)	Men	2.05	0.25	–4.4	1.99	0.25	–6.9	1.96	0.24	–8.5	1.87	0.26	–12.6	132.1	<0.001	
	Women	1.45	0.22	–3.1	1.44	0.21	–3.6	1.46	0.20	–2.5	1.43	0.21	–4.1	24.1	<0.001	
Leg SMI (kg/m ²)	Men	5.80	0.48	–4.3	5.64	0.46	–6.9	5.64	0.51	–7.0	5.45	0.45	–10.1	273.2	<0.001	
	Women	4.69	0.43	–4.6	4.64	0.44	–5.7	4.63	0.41	–5.9	4.57	0.45	–7.1	192.2	<0.001	
Visceral fat area (cm ²)	Men	108.3	26.2	22.5	113.0	25.7	27.8	122.3	25.1	38.3	126.4	25.2	42.9	376.9	<0.001	
	Women	94.0	23.3	38.2	101.6	23.0	49.4	108.5	24.1	59.5	112.4	29.3	65.3	966.7	<0.001	

Percentage change of 40–44 years = (absolute change value / 40–44 years value) × 100. SMI, skeletal muscle mass index.

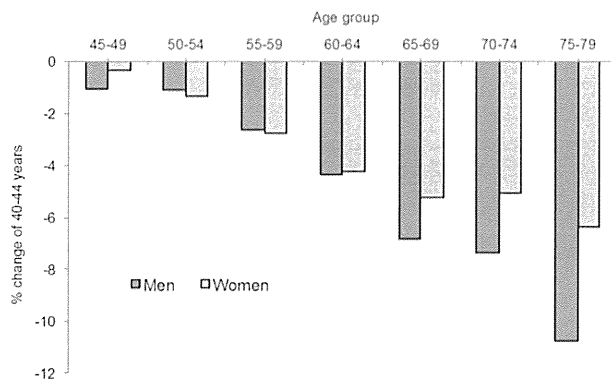


Figure 1 The percentage of change in the total skeletal muscle mass index in each sex and each age group, using 40–44 years-of-age as a reference.

Table 2 20th percentile of total skeletal muscle mass index (kg/m^2) in both sexes

Age group (years)	20th percentile of SMI	
	Men	Women
65–69	7.06	5.61
70–74	7.09	5.63
75–79	6.83	5.54
65–79	7.02	5.61

SMI, skeletal muscle mass index.

age-dependent decrease in both sexes (Fig. 2, Table 1). The age-dependent changes in the leg SMI were similar in men and women. However, the age-dependent changes in the arm SMI were greater in men than in women.

Next, we examined the age-dependent changes in visceral obesity. The visceral fat area showed an age-dependent increase in both sexes (men, $F = 376.9$, $P < 0.001$; women, $F = 966.7$, $P < 0.001$; Table 1). The percentage change from 40–44 years in the visceral fat area showed an age-dependent increase in both sexes (Fig. 3, Table 1).

To examine the association between skeletal muscle mass and visceral obesity, we carried out a multiple regression analysis using the SMI as an outcome. We found that the visceral fat area, age, and weight were significant and independent determinants of the SMI in both men ($\beta = -0.586$) and women ($\beta = -0.627$; Table 3). Therefore, the age-dependent change in the SMI was negatively associated with the visceral-fat area in both sexes.

Discussion

The current cross-sectional study was carried out to evaluate the SMI in Japanese adults aged between 40

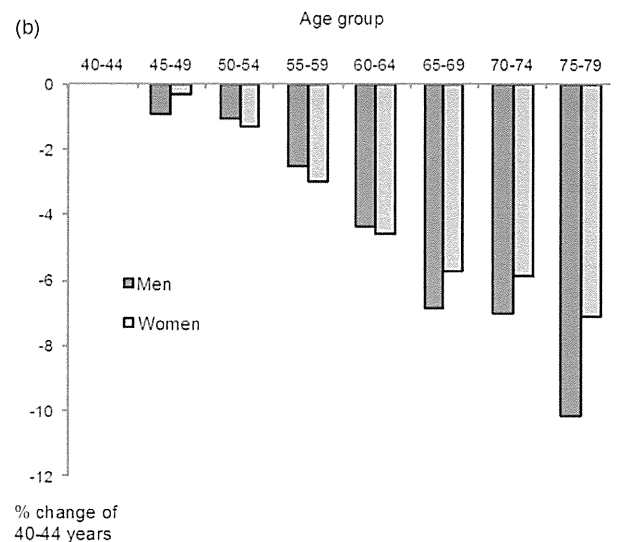
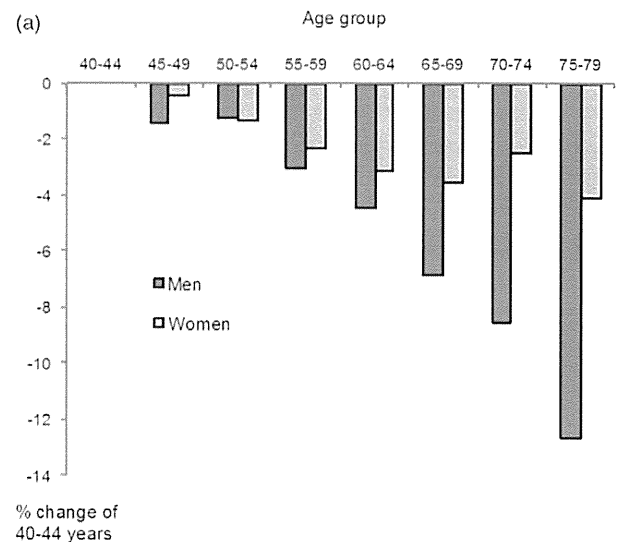


Figure 2 The percentage of change in the (a) arm and (b) leg skeletal muscle mass index (SMI) in each sex and each age group using 40–44 years-of-age as a reference.

and 79 years. Our data show that the SMI decreased age-dependently in both sexes. Notably, regarding the age-dependent decreases in the total SMI and in those aged over 65 years, the percentage change in the total SMI was greater in men than in women. From 40 to 79 years, the total SMI decreased by 10.8% in men and by 6.4% in women. Previous epidemiological studies of body composition have shown that between 40 and 79 years, the fat-free mass decreases by 6.6–23.3% in both sexes.^{19,20} The age-dependent increases in inflammatory cytokines, such as IL-6 and TNF- α , can result in increased skeletal muscle breakdown.²³ In contrast, the age-dependent decrease in anabolic hormones, such as testosterone, growth hormone, and insulin-like growth factor-1 (IGF-1), might lead to a loss of skeletal muscle