

古田勝経、溝神文博、宮川哲也、森川拓、永田治、永田実、福澤悦子、油座マミ、櫻井淳二、庄司理恵、藤井聡	医師・薬剤師・看護師による褥瘡チーム医療の経済的側面に関する考察	日本医療・病院管理学会誌	Vol. 50, No. 3	15-23 (199-207)	2013
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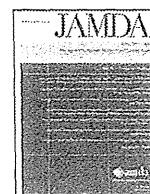
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## Review

## Sarcopenia in Asia: Consensus Report of the Asian Working Group for Sarcopenia

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### ABSTRACT

#### Keywords:

Sarcopenia  
 frailty  
 muscle mass  
 muscle quality  
 muscle strength  
 physical performance

Sarcopenia, a newly recognized geriatric syndrome, is characterized by age-related decline of skeletal muscle plus low muscle strength and/or physical performance. Previous studies have confirmed the association of sarcopenia and adverse health outcomes, such as falls, disability, hospital admission, long term care placement, poorer quality of life, and mortality, which denotes the importance of sarcopenia in the health care for older people. Despite the clinical significance of sarcopenia, the operational definition of sarcopenia and standardized intervention programs are still lacking. It is generally agreed by the different working groups for sarcopenia in the world that sarcopenia should be defined through a combined approach of muscle mass and muscle quality, however, selecting appropriate diagnostic cutoff values for all the measurements in Asian populations is challenging. Asia is a rapidly aging region with a huge population, so the impact of sarcopenia to this region is estimated to be huge as well. Asian Working Group for Sarcopenia (AWGS) aimed to promote sarcopenia research in Asia, and we collected the best available evidences of sarcopenia researches from Asian countries to establish the consensus for sarcopenia diagnosis. AWGS has agreed with the previous reports that sarcopenia should be described as

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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<sup>2</sup> for men and 5.4 kg/m<sup>2</sup> for women by using dual X-ray absorptiometry, and 7.0 kg/m<sup>2</sup> for men and 5.7 kg/m<sup>2</sup> for women by using bioimpedance analysis), handgrip strength (<26 kg for men and <18 kg for women), and usual gait speed (<0.8 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,<sup>1</sup> 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.,<sup>2</sup> the etiology, pathophysiology, risk factors, and consequences of sarcopenia have gradually become clearer.<sup>3</sup> Moreover, a number of therapeutic approaches and clinical trials have been developed and are still evolving.<sup>4–7</sup> 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.<sup>8–10</sup>

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),<sup>11</sup> which may result in reduced physical capability,<sup>12–14</sup> poorer quality of life, impaired cardiopulmonary performance,<sup>15,16</sup> unfavorable metabolic effects,<sup>17</sup> falls,<sup>18</sup> disability, and mortality in older people,<sup>19,20</sup> as well as high health care expenditure.<sup>21</sup> Furthermore, sarcopenia is also associated with multimorbidity,<sup>22,23</sup> cigarette smoking,<sup>22,24</sup> low body mass index,<sup>25</sup> underweight,<sup>26</sup> physical inactivity,<sup>12</sup> and low serum levels of testosterone in men.<sup>27,28</sup> In general, the association between sarcopenia and functional decline is more significant in men than in women,<sup>29,30</sup> 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.<sup>31,32</sup> 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.<sup>33</sup> 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.<sup>34</sup> 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).<sup>35</sup> Moreover, IWGS recommends assessing patients with reduced physical functioning (or weakness) or patients with habitual gait speed <1.0 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

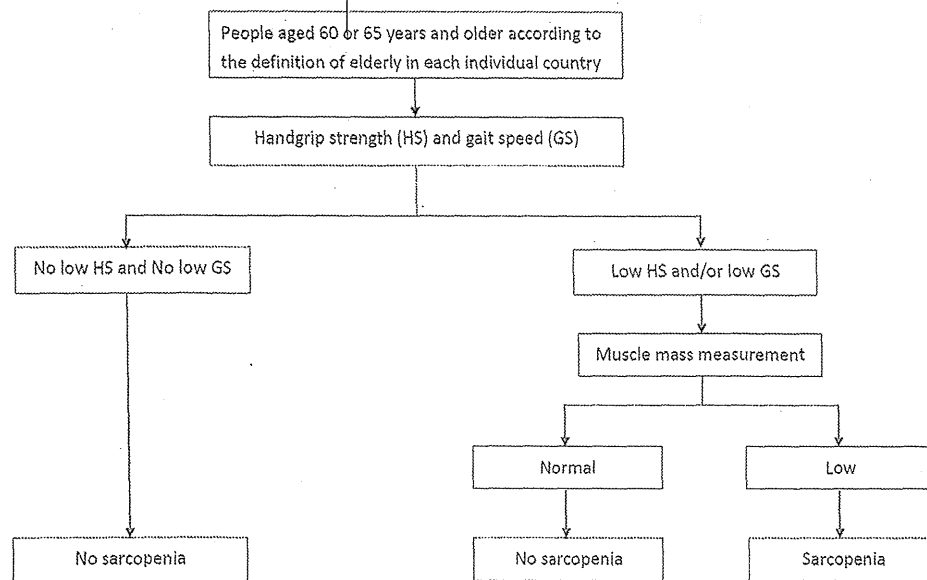


Fig. 1. Recommended diagnostic algorithm of Asian Working Group for Sarcopenia.

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,<sup>36</sup> progresses faster after the age of 60,<sup>37</sup> and accelerates even faster after the age of 75.<sup>38</sup> 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.<sup>33</sup> 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).

#### 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 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)



**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,<sup>39–41</sup> it is heavily dependent on the accuracy of the equation of the equipment and the conditions of assessments, eg, temperature, humidity, skin condition, etc.<sup>42</sup> 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.<sup>43,44</sup> 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.<sup>45</sup> 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 al<sup>46</sup> 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.<sup>26,47,48</sup> Lau et al<sup>26</sup> also found that the relative total skeletal muscle of Hong Kong Chinese (total skeletal muscle /height<sup>2</sup>) was 17% lower among young Chinese men than that of Caucasian men.<sup>26</sup> 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/m<sup>2</sup> in men and 5.4 kg/m<sup>2</sup> in women by using DXA. By using BIA, the suggested cutoff values were 7.0 kg/m<sup>2</sup> in men and 5.7 kg/m<sup>2</sup> in women, defined by appendicular skeletal muscle mass/height<sup>2</sup>.

## 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 al<sup>49</sup> 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,<sup>50</sup> 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).<sup>51</sup> Timed usual gait is highly predictive for the onset of disability,<sup>52</sup> 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 <sup>2</sup> Class 1 and class 2 sarcopenia Men: 7.77 and 6.87 kg/m <sup>2</sup> Women: 6.12 and 5.46 kg/m <sup>2</sup>	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 <sup>2</sup> Men <5.72 kg/m <sup>2</sup> Women <4.82 kg/m <sup>2</sup>	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	265	
		ASM/height <sup>2</sup> Men: 7.40 kg/m <sup>2</sup> Women: 5.14 kg/m <sup>2</sup>	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 (%) <sup>†</sup> 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 <sup>2</sup> Class I and class II sarcopenia Men: 7.50 and 6.58 kg/m <sup>2</sup> Women: 5.38 and 4.59 kg/m <sup>2</sup>	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 (%) <sup>†</sup> 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 <sup>2</sup> Women: 5.44 kg/m <sup>2</sup>	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 <sup>2</sup> Women <6.42 kg/m <sup>2</sup>	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 <sup>2</sup> Men <7.0 kg/m <sup>2</sup> Women <5.8 kg/m <sup>2</sup>	Based on 2 SD below young adult values	Men: 11.3% Women: 10.7% using EWGSOP criteria	Japan
ASM/height <sup>2</sup> Women ≤ 6.42 kg/m <sup>2</sup>				Women: 22.1%	Japan	6	
ASM/height <sup>2</sup> Men <6.75 kg/m <sup>2</sup> Women <5.07 kg/m <sup>2</sup>	Based on 2 SD below young adult values			Men: 21.8% Women: 22.1% using EWGSOP criteria	Korea/Health ABC data	15	
Handgrip strength Men: 30.3 kg Women: 19.3 kg	Based on lowest quartile of study group				Japan	13	
Muscle strength	Knee extension speed	Men <22.4 kg Women <14.3 kg	Based on EWGSOP recommendation and adjusted according to Asian data <sup>49</sup>		Taiwan	50	
		Women ≤1.01 Nm/kg			Japan	6,73	
		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	
Physical performance	SPPB	Gait speed ≤ 1 m/s Gait speed ≤ 1.22 m/s		Women: 22.1%	Taiwan	50	
		SPPB scores <9			Japan	6,73	
					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.

<sup>†</sup>SMI (%) = total skeletal muscle mass (kg)/weight (kg) × 100.

<sup>‡</sup>The author also named it modified skeletal muscle mass index (SMI).

events like severe mobility limitation and mortality.<sup>53</sup> 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.<sup>54</sup> 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.<sup>55</sup> Although the association between sarcopenia and functional decline or even mortality has been established,<sup>56</sup> 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.<sup>33</sup> 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  $\leq 0.8$  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,<sup>57</sup> and resistance exercise training<sup>58,59</sup> 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,<sup>60</sup> 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,<sup>61</sup> 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.<sup>62</sup> A leucine-enriched balanced essential amino acid or balanced amino acid supplementation is suggested for sarcopenia. Recently, Kim et al<sup>6</sup> 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,<sup>63–65</sup> unless it is used for growth hormone deficiency patients for a period longer than 12 months.<sup>66–68</sup> 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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## Growing research on sarcopenia in Asia

We, the Guest Editors of this special issue, are proud to publish 16 articles on sarcopenia from six Asian countries, including seven articles from Japan, four from Taiwan, two from Hong Kong, and one each from Korea, China, and Thailand. We searched PubMed using the key words “sarcopenia” and “human,” and found 97 original articles that were published in English in 2013 (from January to November). Among the articles, 17 were from Asian countries. Thus, researchers in Asian countries have contributed significantly to sarcopenia research.

Aging is an inevitable phenomenon, and the aging of skeletal muscle is no exception. It has been more than 20 years since Rosenberg first coined the term “sarcopenia,”<sup>1</sup> indicating that age-related muscle decline is associated with poor health status and adverse health outcomes in older adults. Along with the tremendous increase in the older population in Asia, sarcopenia has exerted a great impact on Asian populations. However, until recently, Asian researchers have not given great attention to sarcopenia research. Additionally, factors such as population aging, economic development and ethnic background vary extensively in Asian countries. Therefore, sarcopenia experts and researchers from China, Hong Kong, Japan, Korea, Malaysia, Taiwan, and Thailand organized the Asian Working Group for Sarcopenia (AWGS). Since March 2013, this working group has held several meetings in Taipei, Seoul and Kyoto to promote further sarcopenia research development in Asia. The AWGS also aims to focus on the epidemiology of sarcopenia in Asian countries, and has proposed a diagnostic algorithm based on currently available evidence in Asia. As a result of the efforts of AWGS, we are happy to announce that our consensus paper on the diagnostic algorithm and a systematic review of Asian evidence was published in the *Journal of the American Medical Directors Association*.<sup>2</sup> We hope that all of the articles in this special issue and the consensus paper will further inspire sarcopenia research in Asia.

In terms of the definition of sarcopenia, the European Working Group on Sarcopenia in Older People (EWGSOP) proposed an operational definition and diagnostic strategy that have become the most widely used in the world.<sup>3</sup> The EWGSOP definition requires measurements of muscle mass, muscle strength and/or physical performance for the diagnosis of sarcopenia. Based on discussions at the AWGS meetings, we

decided to take similar approaches to sarcopenia diagnosis. However, unlike the EWGSOP definition, we recommend measuring both muscle strength (grip strength) and physical performance (usual gait speed) as the initial screening test. For the usual gait speed, we recommend using 6-m usual gait speed without deceleration. Although the cut-offs of these measurements in Asians might differ from those in Caucasians because of variations in ethnicities, body size, lifestyles and cultural backgrounds, we utilize the EWGSOP definition of slow gait speed (0.8 m/s or less) due to a lack of outcome-based evidence. However, if we use the lowest 20th percentile of gait speed in community settings, according to most Asian studies, the cut-off would be higher than 1 m/s. Meanwhile, we have more data on the cut-offs of grip strength and muscle mass in Asian populations. Based on several epidemiological studies in Asia, we define low grip strength as <26 kg for men and <18 kg for women. The AWGS recommends using height-adjusted skeletal muscle mass, with the suggested cut-off values of 7.0 kg/m<sup>2</sup> in men and 5.4 kg/m<sup>2</sup> in women using dual X-ray absorptiometry (DXA). The suggested cut-off values are 7.0 kg/m<sup>2</sup> in men and 5.7 kg/m<sup>2</sup> in women when bioelectrical impedance analysis (BIA) is used. However, we should keep in mind that DXA and BIA are not yet available in many Asian countries for the screening of muscle mass. Therefore, we must develop an inexpensive measurement for assessing muscle mass.

In this special issue, to maintain consistency, we referred to “sarcopenia” only if authors measured gait speed, grip strength (quadriceps strength was acceptable) and muscle mass. Therefore, “low muscle mass” was used when authors only measured muscle mass. Additionally, many articles used different cut-off values for the grip strength and muscle mass measurements. Table 1 summarizes these data and the prevalence of sarcopenia. We also compared the difference in the diagnostic flow of sarcopenia across the AWGS, EWGSOP and International Working Group on Sarcopenia (IWGS), as shown in Table 2.

As described in the articles of this special issue, sarcopenia has a substantial impact on the health care of older adults. Therefore, additional research is required to further develop the diagnosis and treatment of sarcopenia. We hope that this special issue will inspire more Asian researchers to carry out sarcopenia research.

**Table 1** Surrogates comparison for Asian consensus

1 <sup>st</sup> Author and nationality	Available measurements	Cut-off definition	Cut-off values	Prevalence of sarcopenia	Research population	Reference population	Ref. no.
Assantachai Thailand	<ul style="list-style-type: none"> <li>• QS measured by a hand-held dynamometer: Lafayette Manual Muscle Test System (MMT)® model 01163 (Lafayette Instrument, Lafayette, IN, USA)</li> <li>• Total lean body mass, using BIA Model 450 (Biodynamics Corp. Seattle, WA, USA)</li> <li>• Timed 5-step test</li> <li>• Timed 5-chair stand test</li> <li>• 6-min walk test</li> </ul>	—	<b>QS</b> 18 kg in men 16 kg in women	Low QS: 32.9%	n = 950, aged ≥60 years	—	4
Wu Taiwan	<ul style="list-style-type: none"> <li>• Body composition by BIA (Tanita BC-418, Tanita Corp., Tokyo, Japan)</li> <li>• GS</li> <li>• Handgrip strength</li> </ul>	<b>ASM/ht<sup>2</sup></b> : ① mean – 2SD of young adults ② 1 <sup>st</sup> quintile of study population <b>GS</b> : Sex- and height- specific 1 <sup>st</sup> quintile <b>Handgrip strength</b> : Sex- and BMI-specific 1 <sup>st</sup> quintile	① 6.76 kg/m <sup>2</sup> for men; 5.28 kg/m <sup>2</sup> for women ② 7.09 kg/m <sup>2</sup> for men; 5.70 kg/m <sup>2</sup> for women <b>GS</b> : Men: height ≤163 cm, 0.67 m/s, height >163 cm, 0.71 m/s Women: height ≤152 cm, 0.57 m/s, height >152 cm, 0.67 m/s <b>Handgrip strength</b> Men: BMI <22.1 kg/m <sup>2</sup> , 25.0 kg, BMI 22.1–24.3 kg/m <sup>2</sup> , 26.5 kg, BMI 24.4–26.3 kg/m <sup>2</sup> , 26.4 kg, BMI >26.3 kg/m <sup>2</sup> , 27.2 kg Women: BMI <22.3 kg/m <sup>2</sup> , 14.6 kg, BMI 22.3–24.2 kg/m <sup>2</sup> , 16.1 kg, BMI 24.3–26.8 kg/m <sup>2</sup> , 16.5 kg, BMI >26.8 kg/m <sup>2</sup> , 16.4 kg	① Using young ref. 5.4% in men 2.5% in women ② Using study ref. 8.2% in men 6.5% in women	2867 community-dwelling older adults Mean age: 74 ± 6.0 years, 50% women	998 healthy adults aged 20–40 years	5
Hsu Taiwan	<ul style="list-style-type: none"> <li>• Muscle mass by BIA (InBody 220, Seoul, South Korea)</li> <li>• GS: A 6-m walk</li> <li>• Handgrip strength by using a digital dynamometer (TTM-YD, Tokyo, Japan; 3 trials for each hand; using the best reading)</li> </ul>	<b>FFM/m<sup>2</sup></b> : mean – 2SD of young adults <sup>6</sup> <b>GS</b> : EWGSOP cut-off <b>Handgrip strength</b> : <sup>7</sup>	<b>Muscle mass index</b> : 8.87 kg/m <sup>2</sup> in men 6.42 kg/m <sup>2</sup> in women <b>GS</b> : ≤0.8 m/s <b>Handgrip strength</b> : 22.5 kg	30.9% (109/353)	353 men living in facilities aged ≥65 years Mean age: 82.7 ± 5.3 years	—	8
Meng and Hu China	<ul style="list-style-type: none"> <li>• Muscle mass by DXA (GE Lunar)</li> <li>RASM: ASM/ht<sup>2</sup></li> <li>SMI%: ASM/weight × 100</li> <li>• Handgrip strength by a dynamometer (Jamar Plus+ digital hand dynamometer, USA; 1 trial for each hand, using the best reading)</li> <li>• GS: 6-m walk</li> </ul>	<b>RASM</b> : mean – 2SD of young adults <b>Handgrip strength</b> : <sup>7</sup> <b>GS</b> : EWGSOP cut-off	6.85 kg/m <sup>2</sup> by RASM, 28.0% by SMI% <b>Handgrip strength</b> : 22.4 kg <b>GS</b> : ≤0.8 m/s	Sarcopenia, 45.7%, Sarcopenic obesity, 4.9% by RASM Sarcopenia, 53.2%, Sarcopenic obesity, 11.5% by SMI%	Community-dwelling men aged ≥80 years, n = 101, mean age 88.8 ± 3.7 years	75 healthy young volunteers (male) aged 20–40 years	9

Liu Taiwan	<ul style="list-style-type: none"> <li>• Muscle mass by DXA (GE Healthcare, Madison, WI, USA)</li> <li>• Handgrip strength by a dynamometer (Smedley's Dynamo Meter; TTM, Tokyo, Japan; 3 trials for the dominant hand, using the highest reading)</li> <li>• GS: 6-m walk</li> </ul>	<p>ASM/ht<sup>2</sup>: 1st quintile of study population</p> <p>Handgrip strength &amp; GS: 1st quintile of study population</p>	<p>Muscle mass index: 7.0 kg/m<sup>2</sup> in men, 5.9 kg/m<sup>2</sup> in women</p> <p>Handgrip strength: 25 kg in men, 16 kg in women</p> <p>GS: 1.0 m/s in men, 0.9 m/s in women</p>	9.4% in men, 9.8% in women	481 aged ≥65 years, male 55.5%	–	10
Wu Taiwan	<ul style="list-style-type: none"> <li>• Muscle mass by BIA (Tanita BC-418; Tanita, Tokyo, Japan)</li> <li>• Handgrip strength (Grip-D, TKK 5401, Japan; 2 trials for both hands, using the highest reading)</li> <li>• GS: 15-ft walking test</li> </ul>	<p>Total muscle mass/ ht<sup>2</sup>: mean – 2SD of young adults<sup>8</sup></p> <p>Handgrip strength: EWGSOP cut-off</p> <p>GS: EWGSOP cut-off</p>	<p>Muscle mass index: 7.70 kg/m<sup>2</sup> in men, 5.67 kg/m<sup>2</sup> in women</p> <p>Handgrip strength: Men: BMI ≤24 kg/m<sup>2</sup>, 24.1–28 kg/m<sup>2</sup> and &gt;28 kg/m<sup>2</sup> were ≤29 kg, ≤30 kg and ≤32 kg Women: BMI ≤23 kg/m<sup>2</sup>, 23.1–26 kg/m<sup>2</sup>, 26.1–29 kg/m<sup>2</sup> and &gt;29 kg/m<sup>2</sup> were ≤17 kg, ≤17.3 kg, ≤18 kg and ≤21 kg GS: ≤0.8 m/sec</p>	Sarcopenia, 7.1%, Severe sarcopenia, 5.6%	Total 549 study subjects, 285 male and 264 female aged ≥ 65 years Mean age: 76.0 ± 6.2 years	–	11
Kim Korea	<ul style="list-style-type: none"> <li>• Muscle mass by DXA (Discovery-W, Hologic, Bedford, MA)</li> </ul>	<p>Muscle indices: ASM/ht<sup>2</sup> and ASM/Wt: mean – 2SD of young adults or &lt;1<sup>st</sup> quintile of total body skeletal muscle mass/weight (TSM/Wt) from control subjects</p>	<p>ASM/ht<sup>2</sup>: 7.40 kg/m<sup>2</sup> in men, 5.14 kg/m<sup>2</sup> in women</p> <p>ASM/Wt: 29.5% in men, 23.2% in women</p> <p>TSM/Wt: 34.9% in men, 25.8% in women</p>	–	414 adults aged ≥65 years Mean age: men 70.6 years and women 70.9 years	<p>ASM/ht<sup>2</sup>: young healthy volunteers, aged 20–40, n = 145 (54 men, 91 women)</p> <p>ASM/Wt: 2392 healthy adults aged 20–40 years (1054 men, 1338 women)</p>	12
Ishii Japan	<ul style="list-style-type: none"> <li>• Muscle mass by BIA (Inbody 430, Biospace, Seoul, Korea)</li> <li>• Handgrip strength by a grip strength dynamometer (Takei Scientific Instruments, Niigata, Japan)[2 trials for dominant hand, using the higher reading]</li> <li>• GS: middle 5 m over an 11-m straight course at their usual speed</li> </ul>	<p>ASM/ht<sup>2</sup>: mean – 2SD of young adults<sup>13</sup></p> <p>Handgrip strength: 1<sup>st</sup> quintile of study population</p> <p>GS: 1<sup>st</sup> quintile of study population</p>	<p>Muscle mass index: &lt;7.0 kg/m<sup>2</sup> in men, &lt;5.8 kg/m<sup>2</sup> in women</p> <p>Handgrip strength: 30 kg in men, 20 kg in women</p> <p>GS: ≤1.26 m/s</p>	14.2% in men, 22.1% in women	1971 functionally independent, community-dwelling adults aged ≥65 years 977 men, 994 women	–	14
Sampaio Japan	<ul style="list-style-type: none"> <li>• Muscle mass by BIA (Inbody 430; Biospace, Seoul, Korea)</li> <li>• Handgrip strength using a dynamometer (Smedley's Dynamo Meter, TTM, Tokyo, Japan; 1 trial for each hand, using the higher reading)</li> <li>• GS: 10-m walking in a 12-m length</li> </ul>	<p>Total muscle mass/ht<sup>2</sup>: 1<sup>st</sup> quintile of study population</p>	<p>Total muscle mass/ht<sup>2</sup>: 8.81 kg/m<sup>2</sup> in men, 7.57 kg/m<sup>2</sup> in women</p>	–	Community-dwelling Japanese older adults (n = 175; male = 84, female = 91)	–	15

Table 1 Continued

1 <sup>st</sup> Author and nationality	Available measurements	Cut-off definition	Cut-off values	Prevalence of sarcopenia	Research population	Reference population	Ref. no.
Shimokata, Japan	<ul style="list-style-type: none"> <li>Muscle mass by DXA (QDR-4500; Hologic, Bedford, MA, USA)</li> <li>Leg extension power measured using the T.K.K.4236 adjustable seat and foot plate (Takei, Niigata, Japan; the maximum values of 8 tests were analyzed)</li> <li>Grip strength was measured using the T.K.K.4301 (Takei; maximum values of 2 tests for dominant hand were analyzed)</li> </ul>	ASM/ht <sup>2</sup> : mean - 2SD of young adults <sup>16</sup>	ASM/ht <sup>2</sup> : <6.87 kg/m <sup>2</sup> in men <5.46 kg/m <sup>2</sup> in women	The prevalence of low muscle mass: 27.1% in men 16.4% in women	NILS-LSA 1090 men, mean age 59.3 ± 11.0 years 1081 women, mean age 59.3 ± 10.9 years	—	17
Yamada Japan	<ul style="list-style-type: none"> <li>Muscle mass by BIA (Inbody 720; Biospace, Seoul, Korea)</li> </ul>	ASM/ht <sup>2</sup> : 1 <sup>st</sup> quintile of study population	<b>ASM/ht<sup>2</sup></b> <b>For men</b> 65-69; 7.06 kg/m <sup>2</sup> 70-74; 7.09 kg/m <sup>2</sup> 75-79; 6.83 kg/m <sup>2</sup> 65-79; 7.02 kg/m <sup>2</sup> <b>For women</b> 65-69; 5.61 kg/m <sup>2</sup> 70-74; 5.63 kg/m <sup>2</sup> 75-79; 5.54 kg/m <sup>2</sup> 65-79; 5.61 kg/m <sup>2</sup>	—	Community healthy men (n = 16 379) and women (n = 21 660) aged 40-79 years Mean age: 54.5 ± 9.9 years, 56.9% women	—	18
Yoshida Japan	<ul style="list-style-type: none"> <li>Muscle mass by BIA (MC-980A; Tanita, Tokyo, Japan)</li> <li>Handgrip strength by a hand dynamometer (Grip-D (Takei; 1 trial for the dominant hand)</li> <li>GS: middle 2.4 m in a 6.4 m walking at their usual pace for five times, using the average value</li> </ul>	<b>ASM/ht<sup>2</sup> and Handgrip strength:</b> sex-specific 1st quintile of study population <b>GS:</b> EWGSOP cut-off	<b>ASM/ht<sup>2</sup>:</b> 7.09 kg/m <sup>2</sup> in men, 5.91 kg/m <sup>2</sup> in women <b>Handgrip strength:</b> 28.8 kg in men, 18.2 kg in women <b>GS:</b> ≤0.8 m/s	age ≥65 years: 8.2% in men and 6.8% in women age ≥80 years: 25.0% in men and 12.2% in women	4811 people aged 65 years and over, 48.7% men: (n = 2343, mean age 72.2 ± 5.5 years) women: (n = 2468, mean age 72.1 ± 5.7 years)	—	19
Yu Hong Kong	<ul style="list-style-type: none"> <li>Muscle mass by DXA (Hologic Delphi W4500 densitometer; Hologic, Bedford, MA, USA)</li> <li>Grip strength using a dynamometer (JAMAR Hand Dynamometer S030)O; 2 trials for each hand, using the average value between right and left hand)</li> <li>Walking speed: a 6-m walking speed (2 trials, using best time recorded)</li> </ul>	<b>ASM/ht<sup>2</sup>:</b> 1st quintile of study population <b>Handgrip strength:</b> 1st quintile of study population <b>GS:</b> EWGSOP cut-off	<b>ASM/ht<sup>2</sup></b> <6.52 kg/m <sup>2</sup> in males <5.44 kg/m <sup>2</sup> in females <b>Handgrip strength:</b> ≤28 kg in males ≤18 kg in females <b>GS</b> ≤0.8 m/s	361 (9.0%)	4000 community-dwelling men and women aged 65 years and above, men 50% Mean age: 72.5 ± 5.2 years	—	20

ASM, appendicular skeletal mass; BIA, bioelectrical impedance analysis; BMI, body mass index; DXA, dual X-ray absorptiometry; EWGSOP<sup>19</sup>, European Working Group on Sarcopenia in Older People; FFM, fat free mass; GS, gait speed; QS, quadriceps strength; RASM, relative appendicular skeletal muscle mass; SMI, skeletal muscle index.



**Table 2** Comparison of diagnostic algorithm of sarcopenia among Asian Working Group for Sarcopenia, European Working Group on Sarcopenia in Older People, and International Working Group on Sarcopenia

	AWGS	EWGSOP	IWGS
Target for screening	Community-dwelling older adults and older people with certain clinical conditions, such as 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, malnutrition, chronic conditions, such as chronic heart failure, chronic obstructive lung disease, diabetes mellitus, chronic kidney disease, connective tissue disease, tuberculosis infection, and other chronic wasting conditions	Community-dwelling people aged $\geq 65$ years	Individuals with functional decline, mobility-related difficulties, history of recurrent falls, recent unintentional body weight loss, post-hospitalization, and chronic conditions, such as type 2 diabetes, congestive heart failure, chronic kidney disease, chronic obstructive lung disease, rheumatoid arthritis, and cancer
Target age group	$\geq 60$ years or $\geq 65$ years depending on the definition of older adults in each country	$\geq 65$ years	Not specified
Screening	Gait speed and handgrip strength	Gait speed	Gait speed
Cut-off of gait speed	0.8 m/s	0.8 m/s	1.0 m/s
Cut-off of handgrip strength	26 kg in men and 18 kg in women	30 kg in men and 20 kg in women	NA
Cut-off of muscle mass (appendicular muscle mass/ht <sup>2</sup> )	7.0 kg/m <sup>2</sup> in men and 5.4 kg/m <sup>2</sup> in women by DXA, 7.0 kg/m <sup>2</sup> in men and 5.7 kg/m <sup>2</sup> in women by BIA	Mean - 2SD of young adults	7.23 kg/m <sup>2</sup> in men and 5.67 kg/m <sup>2</sup> in women

AWGS, Asian Working Group for Sarcopenia; BIA, bioelectrical impedance analysis; BMI, body mass index; DXA, dual X-ray absorptiometry; EWGSOP, European Working Group on Sarcopenia in Older People; IWGS, International Working Group on Sarcopenia.

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## Disclosure statement

The authors declare no conflict of interest.

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## Association between serum uric acid and lumbar spine bone mineral density in peri- and postmenopausal Japanese women

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### Abstract

**Summary** Previous studies on the association between uric acid and bone mineral density yielded conflicting results. In this study, we demonstrated positive association between uric acid and lumbar spine bone mineral density in peri- and postmenopausal Japanese women. Further research is needed to elucidate the underlying mechanism.

**Introduction** Oxidative stress has been implicated in the pathogenesis of osteoporosis. Uric acid, a potent antioxidant substance, has been associated with bone mineral density but previous studies have yielded conflicting results. The objective of the study was to examine the association between serum uric acid and lumbar spine bone mineral density (BMD).

**Methods** This was a retrospective analysis of medical records of 615 women, aged 45–75 years, who had lumbar spine BMD measurement by dual-energy X-ray absorptiometry as a part of health checkup from August 2011 to July 2012.

**Results** Mean serum uric acid level was 4.7 mg/dL. Serum uric acid level was positively and significantly associated with lumbar spine BMD independent of age, body mass index, smoking, drinking, physical activity, years after menopause, diabetes mellitus, hypertension, serum calcium, estimated

glomerular filtration rate, plasma C-reactive protein, and serum alkaline phosphatase (standardized  $\beta=0.078$ ,  $p=0.049$ ). Uric acid rapidly increased until the age of 60 years, and then decelerated but continued to increase thereafter. The association between lumbar spine BMD and uric acid remained significantly positive after excluding women older than 60 years.

**Conclusion** The present study showed that higher uric acid levels were linearly associated with higher lumbar spine BMD in peri- and postmenopausal Japanese women. Further research is needed to elucidate the underlying mechanism of the association between uric acid and BMD.

**Keywords** Bone mineral density · Menopause · Osteoporosis · Uric acid

### Introduction

Osteoporosis, a disease characterized by bone fragility and increased risk of fracture, has been chiefly attributed to the decline of ovarian function at menopause and resulting sex steroid deficiency [1]. On the other hand, oxidative stress has also been implicated in the pathogenesis of osteoporosis [1–12]. For example, observational studies suggested that a higher intake of the antioxidant vitamin C was associated with slower decline of bone mineral density (BMD) [10] and lower risk of hip and nonvertebral fractures [9], and that diminution in plasma antioxidant activity or high oxidative stress was observed in patients with osteoporosis compared with those without [4, 6, 8, 11, 12].

In agreement with accumulating evidence supporting the role of oxidative stress as one of the underlying mechanisms of osteoporosis, uric acid, a potent antioxidant substance [13], has been associated with osteoporosis. In a large population-based, cross-sectional study on older men, higher serum uric acid levels were significantly associated with higher BMD at

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