European Geriatric Medicine
https://doi.org/10.1007/s41999-022-00652-2

RESEARCH PAPER

Extracellular water-to-total body water ratio is an essential confounding factor in bioelectrical impedance analysis for sarcopenia diagnosis in women

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Received: 5 February 2022 / Accepted: 15 April 2022

Key summary points

Aim To examine the relationships of extracellular water-to-total body water ratio (ECW/TBW) with handgrip strength, gait speed, and skeletal muscle mass index (SMI) in older women.

Findings This study reveals an association between SMI and handgrip strength in community-dwelling older women with ECW/TBW values less than 0.40, although there was no such association in women with ECW/TBW values of 0.40 or higher.

Message The ECW/TBW ratio represents a confounding factor, which should be considered when using bioelectrical impedance analysis for sarcopenia diagnosis.

Abstract

Purpose The extracellular water-to-total body water ratio (ECW/TBW) is used in bioelectrical impedance analysis (BIA) for measuring muscle mass; however, ECW/TBW may be affected by several factors common in older individuals. Here, we assessed the relationships of ECW/TBW with handgrip strength, gait speed, and skeletal muscle mass index (SMI) in older women.

Methods In this cross-sectional study, 73 community-dwelling women aged ≥ 65 years who could independently perform activities of daily living were included. ECW/TBW was measured using direct segmental multifrequency BIA. The participants were divided into ECW/TBW < 0.40 (n = 54) and ECW/TBW ≥ 0.40 (n = 19) groups, with the latter indicating overhydration. SMI was calculated as appendicular skeletal muscle mass/(height)^2 (kg/m^2). The relationships of SMI with handgrip strength and gait speed were assessed using partial correlation coefficients. Age, number of medications, pain, and medical history were treated as control variables.

Results The average age of participants was 77.6 ± 6.0 years. The SMI was significantly related to handgrip strength (partial correlation coefficient = 0.293, P = 0.016) but not to gait speed (partial correlation coefficient = − 0.183, P = 0.138). Similarly, the SMI of the ECW/TBW < 0.40 group was significantly related to handgrip strength (partial correlation coefficient = 0.372, P = 0.009) but not gait speed (partial correlation coefficient = − 0.267, P = 0.066); however, the SMI of the ECW/TBW ≥ 0.40 group was not related to either variable.

Conclusion ECW/TBW represents a confounding factor, which should be considered when using BIA for sarcopenia diagnosis.

Keywords Sarcopenia · Bioelectrical impedance analysis · Handgrip strength · Gait speed · Skeletal muscle mass index

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Introduction

Sarcopenia is a condition characterized by progressive loss of skeletal mass and is associated with decreased activities of daily living and increased mortality; this condition is recognized as a serious health problem in older individuals [1]. To date, several diagnostic criteria for sarcopenia have

Published online: 10 May 2022

been proposed. According to the European Working Group of Sarcopenia in Older People 2 (EWGSOP2) and Asian Working Group of Sarcopenia (AWGS) 2019, sarcopenia is defined by a certain decrease in muscle strength or physical function in addition to a decrease in muscle mass [2, 3]. Typically, dual-energy X-ray absorptiometry (DEXA) and bioelectrical impedance analysis (BIA) are used for muscle mass measurement, which is then used to calculate the skeletal muscle mass index (SMI) [2, 3].

The EWGSOP2 reported the importance of assessing muscle mass and muscle quality as a diagnostic tool for sarcopenia [2]. In BIA measurements, not only muscle mass but also intracellular water (ICW) and extracellular water (ECW) can be measured to determine the state of muscle quality [4]. The skeletal muscles retain large amount of water, which accounts for approximately 75% of the muscle mass [5]. Water in the skeletal muscles is classified as either ICW or ECW according to its placement within the muscle cell membranes, and the sum of ICW and ECW constitutes the total body water (TBW) [6]. The ICW reflects the muscle cell mass, whereas the ECW represents the sum of interstitial fluid and blood plasma in the extracellular space [6]. The ECW/TBW ratio is used in clinical settings to predict the prognosis of patients with heart failure, dialysis, and cirrhosis [7–9], and is also a standard edema index [10]. The presence of edema increases both ICW and ECW, with a higher increase in latter than in the former, resulting in an increased ECW/TBW ratio [11]. When excess water accumulation in the muscle tissue due to edema results in overhydration, the muscle mass value measured using BIA increases (i.e., overestimation of muscle mass) [11]. However, a high ECW/TBW ratio does not necessarily indicate edema. For example, the ICW can decrease owing to a decrease in muscle cell mass related to aging and nutritional deterioration, also resulting in high ECW/TBW [12] and decreased muscle quality.

In a previous study, participants with high ECW/TBW had lower physical function and more severe sarcopenia than those with low ECW/TBW [13]. These results were considered to be related to muscle overhydration owing to edema; thus, the muscle mass value is overestimated or ICW is decreased owing to decreased muscle cell mass related to aging and nutritional deterioration. According to this hypothesis, the relationships between SMI and muscle strength or physical function may be studied in participants with a reference ECW/TBW value, although these relationships may not be observed in participants with an ECW/TBW value above the reference value. However, the differences between individuals with an ECW/TBW ratio close to or above the reference value in the associations between handgrip strength, gait speed, and SMI are unclear. Clarifying such differences would highlight the importance of considering the ECW/TBW when determining the muscle mass value using BIA. This is particularly important when investigating the prevalence of sarcopenia. Thus, the aim of this study was to investigate the associations between the ECW/TBW and handgrip strength, gait speed, and SMI in community-dwelling older women.

Methods

Study design and participants

This study adopted a cross-sectional design. We recruited 73 older women (aged $\geq$ 65 years) who could independently perform activities of daily living and resided in Yoshinogawa City, Tokushima, Japan. To recruit participants from among community-dwelling older women, an advertisement was placed in the public magazine of the Yoshinogawa City office. Individuals with a cardiac pacemaker were excluded as BIA measurements could not be conducted in them. Each participant provided written informed consent prior to participation. The study was approved by the Ethics Committee of our institution, and was conducted in accordance with the Declaration of Helsinki of 1996.

Bioelectrical impedance analysis

The ECW/TBW and SMI were measured while participants were in the standing position using a direct segmental multifrequency bioelectrical impedance analysis (DSM-BIA) (S10, InBody, Tokyo, Japan). The DSM-BIA analysis was employed using an 8-point tactile electrode system, with 30 impedance measurements taken using 6 frequencies (1, 5, 50, 250, 500, and 1000 kHz). The tool is not statistically corrected based on age, sex, and race for measuring body water and skeletal muscle mass and calculates ECW, ECW/TBW, and ICW using a formula in the software based on the measured height, weight, and impedance. Next, fat-free mass was calculated from the body water information, and skeletal muscle mass was calculated from the fat-free mass [14, 15]. The water content and muscle mass determined using DSM-BIA have been compared and verified by deuterium (D2O) dilution and DEXA, and they have been reported to be highly reliable [16, 17].

Touch-type electrodes were attached between the heel and the ankle of the participants' right and left feet and on their right and left middle fingers and thumbs. The participants held their arms and legs out to avoid contact with any other body segment during the measurement. SMI was calculated using the appendicular skeletal muscle mass/(height)^2 (kg/m^2). The reference range of ECW/TBW was previously established to be 0.36–0.40 [18–20], and ECW/TBW $\geq$ 0.40 is considered to indicate overhydration [21].

Therefore, the participants were divided into two groups: ECW/TBW < 0.40 (n = 54) and ECW/TBW ≥ 0.40 (n = 19).

Handgrip strength, gait speed, and other measurements

Handgrip strength was measured using a Jamar dynamometer (563213, Patterson Medical, Nottinghamshire, UK). The measurement position was 90° elbow flexion while sitting [3] and the measurement was performed on the right side. Handgrip strength was assessed twice, and the maximum score was recorded. To measure gait speed, we asked the participants to walk a distance of 6 m at a comfortable speed [2, 22]. The gait speed (m/s) was calculated based on the time required to walk the middle 4 m of the route. Other parameters including age, height, weight, body mass index, number of medications, pain (presence or absence), and medical history (presence or absence) were also considered. The body mass index was calculated as weight/(height)^2 (kg/m^2). An increased number of medications and presence of pain are reportedly associated with decreased motor function in the community-dwelling older population [23–25]. Thus, we measured the number of medications, pain, and medical history using a self-reported questionnaire. Medical history was investigated for the presence of the following conditions: hypertension, diabetes, dyslipidemia, heart disease, cerebrovascular disease, fractures, and osteoarthritis.

According to the recommendations of the AWGS 2019, sarcopenia was assessed based on muscle mass, muscle strength, and physical performance. Participants were considered to have sarcopenia if they presented a low handgrip strength (< 18 kg) and/or a low gait speed (< 1.0 m/s) along with a low SMI (< 5.7 kg/m^2) as per the AWGS 2019 criteria.

Statistical analysis

All statistical analyses were conducted using the SPSS software (version 24, IBM SPSS Japan, Tokyo, Japan). Variables were assessed for normality using the Shapiro–Wilk test. Parametric data are reported as mean ± SD, whereas non-parametric data are expressed as median (25th–75th percentile).

The characteristics of both groups—ECW/TBW < 0.40 and ECW/TBW ≥ 0.40—were compared using Student's t-test, Mann−Whitney U test, and Chi-square test as appropriate. The relationship between SMI and handgrip strength or gait speed was assessed in the participants of both groups using partial correlation coefficients. Age, number of medications, pain, and medical history were considered as control variables. Statistical significance was set at $P < 0.05$.

Results

Table 1 shows the characteristics of all participants and the results of comparisons between characteristics of the two groups (ECW/TBW < 0.40 and ECW/TBW ≥ 0.40). The mean ± SD of ECW/TBW of all participants, ECW/TBW < 0.40 group, and ECW/TBW ≥ 0.40 group were 0.395 ± 0.006, 0.392 ± 0.004, and 0.404 ± 0.003, respectively. Age, rate of medical history of hypertension, prevalence of sarcopenia, and ECW/TBW of the ECW/TBW ≥ 0.40 group were significantly higher than those of the ECW/TBW < 0.40 group. The ICW, handgrip strength, and gait speed of the ECW/TBW ≥ 0.40 group were significantly lower than those of the ECW/TBW < 0.40 group.

The results of the partial correlation analyses are shown in Table 2. The SMI of all participants was significantly related to handgrip strength but not gait speed. The SMI of the ECW/TBW < 0.40 group was significantly related to handgrip strength but not to gait speed. However, the SMI of the ECW/TBW ≥ 0.40 group was not significantly related to handgrip strength and gait speed.

Discussion

Our results indicate that the SMI was independently associated with handgrip strength in community-dwelling older women with an ECW/TBW less than 0.40. Conversely, no such association was observed in women with an ECW/TBW of 0.40 or higher. The ECW/TBW cutoff value in the presence or absence of overhydration is considered as 0.40 (normal reference range: 0.36–0.40) [18–21], which was adopted in our study. A previous study reported that the ECW/TBW cutoff value of 0.391 can be used for detecting locomotive syndrome [26]. Park et al. [13] reported that people with low muscle strength and muscle mass have a higher ECW/TBW value (i.e., 0.391 or higher) than that of healthier individuals. Although the cutoff value of ECW/TBW in this study was different from that used in the study by Park et al. [13], the results of both the studies are comparable.

In previous studies [16, 17], high reliabilities were observed between values of the body water and muscle mass measured with the DSM-BIA analysis and deuterium (D2O) dilution and DEXA. In addition, the DSM-BIA device used in this study calculates body water and muscle mass based on height, weight, and impedance without statistical corrections for age, sex, and race. Therefore, body water and muscle mass can be accurately assessed with DSM-BIA in older, obese, or athletic people [14, 15]. Taken together, values of body water and muscle mass

Table 1 Characteristics of all participants and comparisons between the ECW/TBW less than 0.40 group and ECW/TBW 0.40 or higher group

	All participants ($n=73$)	ECW/TBW less than 0.40 group ($n=54$)	ECW/TBW 0.40 or higher group ($n=19$)	P value
Age (years)	77.6 ± 6.0	76.1 ± 5.5	81.8 ± 5.3	< 0.001[f]
Height (cm)	150.0 (145.9–152.3)	150.8 (146.9–152.5)	147.2 (145.2–151.9)	0.113[g]
Weight (kg)	51.2 ± 8.0	51.7 ± 7.1	49.5 ± 10.1	0.302[f]
BMI[a] (kg/m^2)	23.0 ± 3.1	23.1 ± 2.8	22.6 ± 3.7	0.594[f]
Number of medications	2.0 (1.0–4.0)[i]	2.0 (1.0–4.0)	3.0 (1.0–4.0)	0.604[g]
Pain	29 (40.3)[i]	20 (37.7)[j]	9 (47.3)	0.463[h]
Medical history				
Hypertension	28 (38.4)	17 (31.5)	11 (57.9)	0.042[h]
Diabetes	4 (5.5)	3 (5.6)	1 (5.3)	0.724[h]
Dyslipidemia	12 (16.4)	11 (20.4)	1 (5.3)	0.118[h]
Heart disease	3 (4.1)	2 (3.7)	1 (5.3)	0.601[h]
Cerebrovascular disease	6 (8.2)	4 (7.4)	2 (10.5)	0.495[h]
Fracture	9 (12.3)	7 (13.0)	2 (10.5)	0.570[h]
Osteoarthritis	18 (24.7)	14 (25.9)	4 (21.1)	0.465[h]
Prevalence of sarcopenia	16 (21.9)	8 (14.8)	8 (42.1)	0.019[h]
SMI[b] (kg/m^2)	5.8 ± 0.6	5.9 ± 0.5	5.7 ± 0.9	0.343[f]
ECW[c] (L)	9.9 ± 1.0	10.0 ± 0.9	9.8 ± 1.3	0.639[f]
ICW[d] (L)	15.2 ± 1.7	15.4 ± 1.5	14.5 ± 2.0	0.034[f]
ECW/TBW[e]	0.395 ± 0.006	0.392 ± 0.004	0.404 ± 0.003	< 0.001[f]
Handgrip strength (kg)	20.3 ± 5.0	21.3 ± 5.0	17.6 ± 3.8	0.004[f]
Gait speed (m/s)	1.2 ± 0.3	1.2 ± 0.3	1.0 ± 0.3	0.002[f]

Data are presented as mean ± standard deviation, median (25th–75th percentile), or n (%)

[a]BMI, Body mass index

[b]SMI, Skeletal muscle mass index

[c]ECW, Extracellular water

[d]ICW, Intracellular water

[e]ECW/TBW, Extracellular water-to-total body water ratio

[f]Student's t test

[g]Mann–Whitney U test

[h]χ^2 test

[i]$n=72$

[j]$n=53$

measured with the DSM-BIA tool used in this study are valid, and reveal the influence of ECW/TBW on the associations between muscle strength and muscle mass.

We found a different relationship between handgrip strength and SMI between the ECW/TBW < 0.40 and ECW/TBW ≥ 0.40 groups. Thus, our study outcomes suggest that a relationship between SMI and handgrip strength exists only when the ECW/TBW is less than 0.40. We speculate that these different relationships may be attributable to overhydration of the muscle or a decrease in muscle cell mass due to aging and nutritional deterioration. ECW/TBW has not been fully considered in previous studies wherein muscle mass was measured using BIA to investigate the prevalence of sarcopenia [1, 27]. Therefore, sarcopenia prevalence reported in previous studies may have been calculated with the inclusion of people with an ECW/TBW value of 0.40 or higher [1, 27]. The results of this study provide evidence that ECW/TBW must be treated as a confounding factor when using BIA for sarcopenia diagnosis to avoid the potential influence of overhydration.

In this study, the majority of participants were in the ECW/TBW < 0.40 group (54/73, 74%); thus, only 26% of the total participants had an ECW/TBW of 0.40 or higher. Although there are limits to generalizations, other populations may show similar results. We consider that paying attention to ECW/TBW (i.e., whether or not the ratio is 0.40 or higher) is essential when diagnosing sarcopenia using BIA. Moreover, attention to this aspect may be crucial in

Table 2 Relationships between SMI and handgrip strength or gait speed in all participants and ECW/TBW less than 0.40 and ECW/TBW 0.40 or higher groups

	SMI[a]	
	Partial correlation coefficient	P value
All participants ($n = 73$)		
Handgrip strength	0.293	0.016[c]
Gait speed	− 0.183	0.138[c]
ECW/TBW[b] less than 0.40 group ($n = 54$)		
Handgrip strength	0.372	0.009[c]
Gait speed	− 0.267	0.066[c]
ECW/TBW[b] 0.40 or higher group ($n = 19$)		
Handgrip strength	0.194	0.487[c]
Gait speed	0.040	0.886[c]

[a]SMI, Skeletal muscle mass index

[b]ECW/TBW, Extracellular water-to-total body water ratio

[c]Adjusted for age, number of medications, pain, and medical history

clinical settings because many patients in the at-risk population for sarcopenia have edema [9, 18–21].

Despite presenting some credible evidence, this study has four main limitations. First, because of the cross-sectional study design, the longitudinal associations between ECW/TBW, handgrip strength, and gait speed are not clear; thus, additional research is required to clarify the causal associations between these factors. Second, the participants in this study were community-dwelling older women. Therefore, whether similar associations exist in community-dwelling older men remains unclear. Third, the prevalence rate of sarcopenia in all the participants in this study was 21.9%. This prevalence rate was higher than that in previous studies. In recent studies, the prevalence rate of sarcopenia was reported to be influenced by aging as well as by the presence of pain [28, 29]. The mean age of the participants in this study was 77.6 ± 6.0 years, and 40.3% of all the participants presented with pain. Taken together, the background for the high prevalence rate of sarcopenia in this study may be attributable to higher age and higher rate of presence of pain in the participants. Further studies examining the influence of ECW/TBW on the associations between muscle strength and muscle mass, based on the participants categorized for age and nutrition and pain status, will be needed. Finally, although this study targeted the participants who could independently perform activities of daily living, those who had symptoms, such as hypertension, dyslipidemia, and osteoarthritis, were also included. These participants may have had attended a hospital for the management of symptoms. However, we were not able to examine whether the participants had gone to the hospital and the number of visits to the hospital. In addition, we did not examine information on heart failure, renal failure, liver cirrhosis, and the use of diuretics, which could increase ECW/TBW. In future studies, we would examine these factors.

This study revealed an association between SMI and handgrip strength in community-dwelling older women with ECW/TBW values less than 0.40, although there was no such association in women with ECW/TBW values of 0.40 or higher. Thus, when using BIA for sarcopenia diagnosis, ECW/TBW must be considered as a confounding factor.

Acknowledgements We thank the participants and the Yoshinogawa City office for assistance with participant recruitment.

Funding This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declarations

Conflict of interest The authors declare that there is no conflict of interest.

Ethical approval The study was approved by the Ethics Committee of our institution, and was conducted in accordance with the Declaration of Helsinki of 1996.

Informed consent Each participant provided written informed consent prior to participation.

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