



Association between Disability and Edema Index Values in Rural Older Adult Osteosarcopenia Patients

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Purpose: This study analyzed the relationship between degree of disability and edema index [extracellular water/total body water (ECW/TBW) ratio] values in a rural population of older adult patients with osteopenia, sarcopenia, or osteosarcopenia (OS).

Materials and Methods: This study used data from the Namgaram-2 cohort. The degree of disability was measured using the World Health Organization Disability Assessment Schedule (WHODAS) 12, and ECW/TBW ratio was calculated using bioelectrical impedance analysis. Based on ECW/TBW ratio, the participants were stratified into normal (<0.391) and abnormal (≥0.391) groups, and the mean WHODAS 12 scores were compared between the two groups. Multiple regression analysis corrected for demographic factors, smoking history, hypertension, diabetes, and serological test results was also conducted.

Results: Significant differences in mean WHODAS 12 scores were observed in the healthy group (5.8±7.4 vs. 9.2±9.7, $p=0.008$), the osteopenia only group (7.4±8.7 vs. 12.9±12.0, $p<0.001$), and the OS group (16.0±13.2 vs. 23.1±17.1, $p=0.004$). However, no significant difference in mean WHODAS 12 score was observed in the sarcopenia only group (14.9±13.4 vs. 20.7±14.8, $p=0.051$). There were significant differences in ECW/TBW ratio values between the abnormal and normal groups in the osteopenia only group ($B=4.646$ and $p=0.001$), the sarcopenia only group ($B=5.097$ and $p=0.016$), and the OS group ($B=5.653$ and $p=0.043$).

Conclusion: This study found that the degree of disability is related to the edema index in older patients with osteopenia, sarcopenia, or OS. Since the edema index indicates the nutritional status of an individual, proper nutrition and fluid intake are important to reduce disability.

Key Words: Osteosarcopenia, disability, bioimpedance analysis, edema

INTRODUCTION

Recently, as the population of older adults continues to rapidly increase, their health care has become a social issue. The World Health Organization has stated that health programs for older

adults should focus on function rather than disease.¹ Bones and muscles are important for physical function. Aging causes physiological and biochemical changes in the body, resulting in quantitative and qualitative changes in body composition, particularly in muscles and bones. Muscle mass peaks at the age of 30, gradually decreases after the age of 40, and decreases by 8% every 10 years until the age of 70; thereafter, a more rapid decrease occurs, up to 15% every 10 years.² Changes in muscle strength with increasing age do not appear to rapidly decrease before the age of 70 for male and the age of 75 for female, but thereafter, muscle strength gradually and continuously decreases, with acceleration patterns steeper in female than in male.³ Similarly, the amount of bone formed is at its maximum around the age of 30, and a slight decrease in bone mass occurs between the ages of 30 and 50.⁴ In female, after menopause, bone mass rapidly decreases by 1% to 2% every year, leading to an increase

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in osteopenia and osteoporosis.⁵

Recently, sarcopenia was named as a disease that should be managed medically.^{6,7} Furthermore, in Asia, diagnostic criteria for sarcopenia were newly announced, making them important to be managed nationally.⁸ According to these criteria, sarcopenia is defined as a severe decrease in muscle mass and strength, in addition to a decrease in physical function. Sarcopenia, along with osteoporosis, has been found to be closely related to frailty, fractures, hospitalizations, and death and to significantly contribute to an increase in medical expenses.⁹⁻¹² Therefore, it is important to prevent deterioration of physical function older adults by preventing and managing decreases in muscle strength and muscle mass.

Studies have shown that risk factors and biological pathways are similar for sarcopenia and osteopenia [including osteosarcopenia (OS), which is a combination of the two conditions]. OS had been proposed as a “hazardous duet” by exacerbating bone weakness due to sarcopenia in osteopenic patients.^{13,14} Sarcopenia and osteopenia are the two main risk factors affecting frailty, which refers to decreased physical, mental, and social functioning in older individuals. Frailty has also been shown to be associated with disability,¹⁵ and sarcopenia, osteopenia, and OS in association with frailty might be associated with disability.

The International Classification of Functioning, Disability, and Health (ICF) defines disability as a comprehensive concept that includes impairment of bodily functions and structures, activity restrictions, and social participation restrictions, considering social activities and psychological functions. Üstün, et al.¹⁶ developed a questionnaire tool for the World Health Organization Disability Assessment Schedule (WHODAS) 12 to measure disability in accordance with the ICF criteria that can also be used measure difficulty in daily living activities among older adults in the community.

In community health programs designed to evaluate sarcopenia, muscle mass is measured by bioelectrical impedance analysis (BIA), and the extracellular water/total body water (ECW/TBW) ratio is also measured. Recent studies^{17,18} have reported this ratio as an index related to sarcopenia and frailty. Another study found that ECW/TBW is related to grip strength and physical function, which are major risk factors for sarcopenia.¹⁹ However, there have been no studies on its association with degree of disability.

The purpose of this study was to determine whether the degree of disability is associated with the edema index (ECW/TBW) in sarcopenia, osteopenia, and OS groups with increasing prevalences of muscle and bone weakness among older adults.

MATERIALS AND METHODS

Participants

The analyzed data were collected from the Namgaram-2 co-

hort data, collected from 1010 people over 3 years from 2016 to 2018 in order to identify relationships between musculoskeletal disorders and health outcomes (frailty, cognitive impairment) among farmers in rural areas.²⁰ The Namgaram-2 cohort consists of a group of people living in three rural communities who answered questionnaires and underwent physical examinations, blood tests, and radiographic examination. Participants with a prior history of cardiovascular disease were not candidates for this cohort. We included only 885 adults (87.6%) aged 60 years and above. The questionnaire, physical function evaluation, and medical examination were all conducted at Gyeongsang National University Hospital. The subjects heard the explanation of the study and signed a consent form before the survey was conducted. All research was conducted under the review of the Institutional Review Board (approval number: GIRB-A16-0012).

Materials

Among the questionnaire results, sociodemographic variables of sex, age, marital status, perceived economic level, smoking, and perceived morbidity of hypertension and diabetes were used. Among blood tests known to be related to nutritional status and muscle mass, hemoglobin, cholesterol, albumin, uric acid, gamma-glutamyl transpeptidase (γ -GTP), and creatinine were used.²¹

Osteosarcopenia

The Asian Working Group for Sarcopenia (AWGS 2019) consensus was applied for the definition of sarcopenia.⁹ Data measured by dual energy X-ray absorptiometry (DEXA) were used to reflect muscle mass. Values obtained by dividing the appendicular skeletal muscle mass by the square of the height (m^2) was calculated and used as representing skeletal muscle mass. The cut-off point was less than 7.0 kg/m^2 for male and less than 5.4 kg/m^2 for female.

For muscle strength, a Smedley-type dynamometer (TKK 5401; Takei Scientific Instruments Co., Tokyo, Japan) was used: both hands were alternately measured twice each, and the largest value was less than 28 kg for male and less than 18 kg for female. Decreases in both muscle mass and grip strength were defined as sarcopenia.

Bone mineral density was measured with DEXA (DISCOVERY QDR4500W, Hologic Inc, Bedford, MA, USA). A subject was diagnosed with osteopenia if the value was less than -1.0 and normal if it was greater than -1.0, based on the T-value of each study subject. The presence of both sarcopenia and osteopenia was defined as OS.

Edema index

In this study, ECW/TBW ratio was as the edema index. This was obtained with an Inbody 720 BIA device (Inbody Co. Ltd, Seoul, Korea) using bioimpedance. The cut-off point for ECW/TBW was 0.391, which was recently used in a study related to loco-

motive syndrome.¹⁷ When this value was used, the difference in body function was also significant. The edema index value was abnormal when the ECW/TBW value was greater than 0.391 and normal when the ECW/TBW value was less than 0.391.

Disability

The World Health Organization developed the WHODAS for multi-component measurement of individual function and disabilities in consideration of the ICF.¹⁶ The WHODAS addresses difficulties in six areas of life: 1) understanding and communicating, 2) getting around, 3) self-care, 4) getting along with people, 5) life activities, and 6) participation in society. It is measured by dividing it by participation, and in this study, WHODAS 12, which has proven reliability and validity, was used.¹⁵ The 12-item WHODAS instructs the respondent to report his or her difficulty in engaging in particular activities, as rated on a scale from “none” (no difficulty) to “extreme or cannot do,” corresponding to the six domains of functioning. Total score ranges from 0 to 100, with higher scores indicating a higher degree of disability in daily life.

Statistical analysis

The general characteristics of the subjects are presented as descriptive statistics, and correlations between WHODAS 12 and edema index values was analyzed by Pearson’s correlation analysis for all subjects, in addition to the osteopenia only group, sarcopenia only group, and OS group. In addition, the edema index was used to divide the study population into normal (<0.391) and abnormal (≥ 0.391) groups according to ECW/TBW values, and a t-test was performed for each group to determine differences between them in terms of mean WHODAS 12 values.

Multinomial logistic regression was performed to determine the associations between osteopenia, sarcopenia, and OS and edema index values (reference value: robust).

Finally, multiple regression analysis was performed on the association between WHODAS 12 and ECW/TBW in each of the following groups: osteopenia only, sarcopenia only, and OS (demographic and socioeconomic variables, smoking status, morbidity, and blood tests were included as correction variables). The analysis used the SPSS 25.0 (IBM Corp., Armonk, NY, USA) program, and the significance level was set to less than 0.05.

RESULTS

General characteristics of the participants

Table 1 shows the general characteristics of all subjects. Of all 885 subjects, 594 (67.1%) were female, and the average age was 70.3 \pm 6.2 years. The majority (63.4%) of the subjects had a spouse, 17.2% felt economically affluent, 7.5% were smokers, and the prevalences of hypertension and diabetes were 50.5% and 21.7%, respectively.

The group with only osteopenia comprised 33.7% of the study population, the group with only sarcopenia comprised 13.1%, and the group with both osteopenia and sarcopenia comprised 19.2%. The mean \pm standard deviation value for hemoglobin was 13.4 \pm 1.4 g/dL, for uric acid was 4.8 \pm 1.3 mg/dL, for albumin was 4.4 \pm 0.3 g/dL, for γ -GTP was 33.9 \pm 58.6 IU/L, and for creatinine was 0.7 \pm 0.3 mg/dL.

Association between group and edema index (ECW/TBW)

Table 2 shows the results of multinomial logistic regression analysis comparing the association between the edema index (ECW/TBW) and the presence of osteopenia only, sarcopenia only, or OS in reference to a healthy group. In the group with only osteopenia, compared to the healthy group, female sex [odds ratio (OR)=2.677, $p=0.001$] and creatinine (OR=0.315, $p=0.024$) had

Table 1. General Characteristics of the Study Population (n=885)

Variables	Value
Sex	
Male	291 (32.9)
Female	594 (67.1)
Age, yr	70.3 \pm 6.2
Spouse	
Yes	561 (63.4)
No	324 (36.6)
Economic status	
Poor	268 (30.3)
Middle	465 (52.5)
Rich	152 (17.2)
Smoking	
No	819 (92.5)
Yes	66 (7.5)
Hypertension	
No	438 (49.5)
Yes	447 (50.5)
Diabetes	
No	693 (78.3)
Yes	192 (21.7)
Osteopenia, sarcopenia	
Robust	301 (34.0)
Only osteopenia	298 (33.7)
Only sarcopenia	116 (13.1)
Osteosarcopenia	170 (19.2)
Hemoglobin, g/dL	13.4 \pm 1.4
Uric acid, mg/dL	4.8 \pm 1.3
Albumin, g/dL	4.4 \pm 0.3
γ -GTP, IU/L	33.9 \pm 58.6
Creatinine, mg/dL	0.7 \pm 0.3
Cholesterol, mg/dL	186.8 \pm 38.1

γ -GTP, γ -glutamyl transpeptidase.

Data are presented as mean \pm standard deviation or n (%).

a significant effect, whereas the edema index (ECW/TBW) was not significant. In the group with only sarcopenia, compared to the healthy group, the effects from female sex (OR=3.327, $p=0.003$), age (OR=1.129, $p<0.001$), and γ -GTP (OR=1.006, $p=0.010$) were significantly higher than those of males. ECW/TBW was also significant (OR=3.373, $p<0.001$). Compared to the healthy group, the osteopenia group contained significantly more females than males (OR=7.861, $p<0.001$), subjects with older age (OR=1.217, $p<0.001$), and smokers compared to non-smokers (OR=2.774, $p=0.047$). Albumin (OR=0.384, $p=0.024$) and creatinine (OR=0.194, $p=0.033$) had a significant effect, and the edema index (ECW/TBW) was also significant (OR=1.887, $p=0.016$).

Association between WHODAS 12 and ECW/TBW

As a result of the correlation analysis between the WHODAS 12 values and edema index (ECW/TBW) values, the correlation

coefficient (r) was 0.365 ($p<0.001$) in the osteopenia group and 0.203 ($p=0.008$) in the OS group. However, in the group with only sarcopenia, the correlation coefficient (r) was 0.142 ($p=0.130$), which was not significant (Fig. 1).

After classifying the edema index (ECW/TBW) values into the normal group (<0.391) and the abnormal group (≥ 0.391), the differences between the average WHODAS values were as follows (Fig. 2): In all three groups, the mean WHODAS value was higher in the abnormal group than in the normal group. That is, in the group with only osteopenia, there was a significant difference between values of 7.4 ± 8.7 and 12.9 ± 12.0 ($p<0.001$) for the normal and abnormal groups, respectively; in the group with osteopenia, there was a significant difference between 16.0 ± 13.2 and 23.1 ± 17.1 ($p=0.004$), respectively. In the group with only sarcopenia, there was no significant difference between 14.9 ± 13.4 and 20.7 ± 14.8 ($p=0.051$), respectively.

Multiple regression was performed to examine the associa-

Table 2. Multinomial Logistic Regression Analysis of the Association of ECW/TBW Values with Osteopenia, Sarcopenia, and Osteosarcopenia, Compared to Normal

	Osteopenia (ref: robust) (n=298)			Sarcopenia (ref: robust) (n=116)			Osteosarcopenia (ref: robust) (n=170)		
	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	p value
ECW/TBW									
Normal	1			1			1		
Abnormal	1.083	0.703–1.669	0.718	3.373	1.925–5.910	<0.001	1.887	1.125–3.165	0.016
Sex									
Male	1			1			1		
Female	2.677	1.523–4.705	0.001	3.327	1.501–7.376	0.003	7.861	3.298–18.735	<0.001
Age	1.029	0.993–1.066	0.120	1.129	1.075–1.185	<0.001	1.217	1.161–1.276	<0.001
Spouse									
Yes	1			1			1		
No	1.339	0.868–2.066	0.188	1.509	0.850–2.680	0.161	1.113	0.651–1.901	0.696
Economic									
Poor	1			1			1		
Middle	1.034	0.684–1.562	0.210	0.572	0.332–0.985	0.407	0.750	0.446–1.260	0.848
Rich	0.677	0.400–1.148	0.081	0.501	0.238–1.057	0.230	0.617	0.303–1.256	0.295
Smoke									
No	1			1			1		
Yes	1.729	0.888–3.368	0.107	0.703	0.213–2.318	0.562	2.774	1.013–7.596	0.047
Hypertension									
No	1			1			1		
Yes	0.560	0.388–0.809	0.002	0.727	0.434–1.216	0.225	0.678	0.419–1.098	0.114
DM									
No	1			1			1		
Yes	0.684	0.430–1.087	0.108	1.292	0.736–2.269	0.372	0.952	0.540–1.680	0.866
Hemoglobin	0.943	0.798–1.114	0.487	1.011	0.804–1.271	0.927	0.870	0.697–1.086	0.218
Uric acid	0.894	0.763–1.048	0.167	0.999	0.811–1.230	0.991	0.936	0.756–1.158	0.541
Albumin	0.618	0.314–1.215	0.163	0.630	0.254–1.562	0.318	0.384	0.167–0.883	0.024
γ -GTP	1.002	0.998–1.006	0.291	1.006	1.001–1.010	0.010	1.004	0.998–1.010	0.161
Creatinine	0.315	0.115–0.859	0.024	0.339	0.109–1.058	0.063	0.194	0.043–0.874	0.033
Cholesterol	1.001	0.996–1.006	0.642	0.993	0.986–1.000	0.054	1.002	0.995–1.008	0.616

OR, odds ratio; CI, confidence interval; ECW/TBW, extracellular water/total body water; DM, diabetes mellitus; γ -GTP, γ -glutamyl transpeptidase.

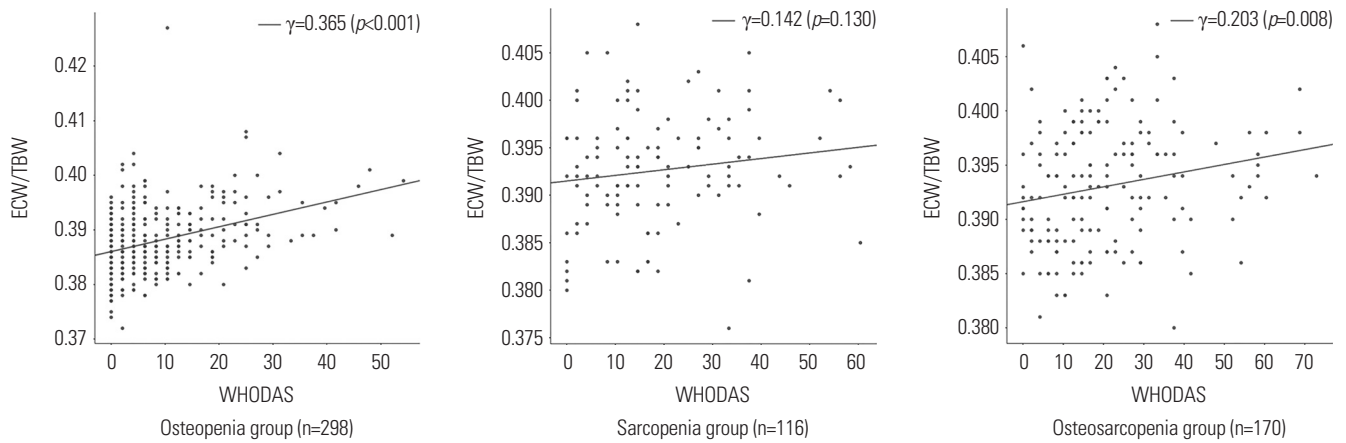


Fig. 1. Scatter plots of the association between WHODAS scores and ECW/TBW. ECW/TBW, extracellular water/total body water; WHODAS, World Health Organization Disability Assessment Schedule.

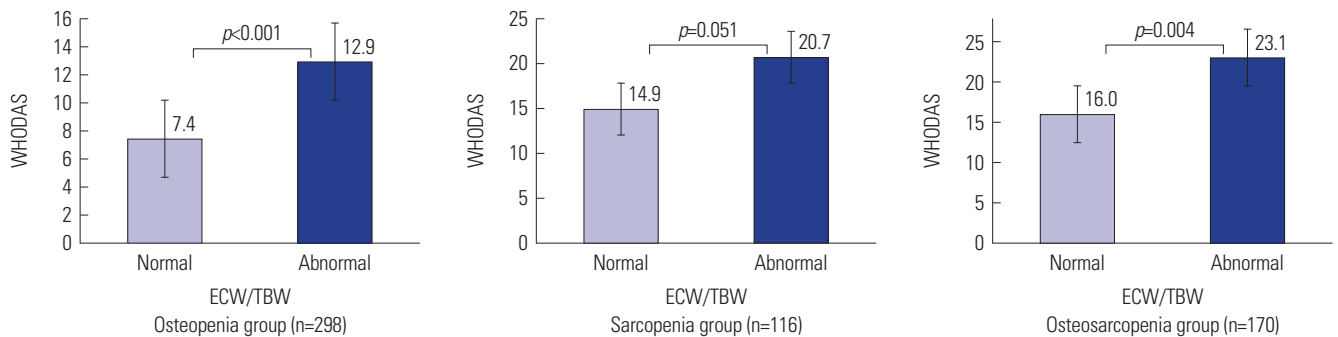


Fig. 2. Bar charts of associations between mean WHODAS scores and ECW/TBW. ECW/TBW, extracellular water/total body water; WHODAS, World Health Organization Disability Assessment Schedule.

tion between WHODAS and the edema index (ECW/TBW) after adjusting for sex, age, marital status, economic status, smoking history, hypertension, diabetes, and blood test results (hemoglobin, albumin, γ -GTP, cholesterol, creatinine, etc.). The analysis results are presented in Table 3. In the osteopenia group, the edema index (ECW/TBW) was significantly higher in the abnormal group than in the normal group ($B = 4.646$, $p = 0.001$) and was also significant in the group with only sarcopenia ($B = 5.097$, $p = 0.016$) and in the group with OS ($B = 5.653$, $p = 0.043$).

DISCUSSION

This study is the first to investigate the association between degree of disability and the edema index (ECW/TBW) among older adults living in the community with osteopenia, sarcopenia, and OS. We found that the degree of disability and the edema index were significantly related in all three groups and that individuals with higher edema index values had higher disability scores.

Among the subjects, 33.7% of the subjects had only osteopenia, 13.1% had only sarcopenia, and 19.2% had OS. In patients with hip fractures, the prevalence of each group (normal, osteoporosis only, sarcopenia only, and OS) was reported to be

21.6%, 41.5%, 9.6%, and 27.2%, respectively.¹² In a cross-sectional study of 680 older people living in the community,²² the proportion of osteopenia was nearly 40%, and another study²³ found that 10.4% of male and 15.1% of female had OS. Although the prevalence of OS varies, patients with OS consistently were more susceptible to fractures, reduced quality of life, increased disability, and increased mortality.^{12,22,23} In another study in Korea,¹⁵ after adjusting for covariates, the scores for disability, frailty, and depression were also highest in osteopenia, and there was a significant difference.

BIA is a useful and accurate tool for evaluating body composition.^{24,25} Body composition can additionally be measured by DEXA, magnetic resonance imaging, and computed tomography imaging, but BIA has the advantage of being cost-effective and not using radiation. BIA can also be used easily and inexpensively in the local community. Moreover, BIA is easy to use for reliably evaluating TBW volume, ECW volume, and intracellular water volume.²⁶⁻²⁸

In addition, the edema index (ECW/TBW) ratio, which is an important and sensitive index for changes in body water, can be calculated.²⁹ The edema index has recently been studied as a biomarker for aging. This index is related to age, body mass index, dry weight, and blood pressure. In addition, the edema index measures the "quality" of lean body mass. It is also known

Table 3. Multiple Regression Analysis of the Association between Disability (WHODAS 12 Value) and Edema Index (ECW/TBW) in Groups with Osteopenia, Sarcopenia, and Osteosarcopenia

Variables	Osteopenia (n=298)				Sarcopenia (n=116)				Osteosarcopenia (n=170)			
	B	SE	Standardized b	p value	B	SE	Standardized b	p value	B	SE	Standardized b	p value
ECW/TBW	4.646	1.316	0.166	0.001	5.097	2.091	0.154	0.016	5.653	2.768	0.166	0.043
Sex	3.419	2.072	0.098	0.100	5.153	3.314	0.118	0.121	-1.756	5.070	-0.033	0.730
Age	0.631	0.105	0.297	<.0001	0.488	0.182	0.179	0.008	0.474	0.254	0.167	0.064
Spouse	-0.037	1.313	-0.001	0.978	0.157	2.008	0.005	0.938	2.725	2.764	0.083	0.326
Economic (middle)	-4.815	1.268	-0.173	<0.001	-5.812	1.956	-0.187	0.003	-7.727	2.640	-0.239	0.004
Economic (rich)	-6.394	1.827	-0.160	0.001	-6.800	2.951	-0.147	0.022	-10.004	3.981	-0.209	0.013
Smoke	-2.600	2.487	-0.048	0.296	4.246	4.403	0.059	0.336	-4.658	5.772	-0.068	0.421
Hypertension	1.385	1.180	0.050	0.241	-1.296	1.929	-0.041	0.502	-2.494	2.608	-0.076	0.340
DM	3.252	1.532	0.089	0.034	1.322	2.180	0.037	0.545	3.336	3.126	0.084	0.288
Hemoglobin	-0.911	0.544	-0.088	0.095	-0.259	0.838	-0.020	0.758	-0.578	1.167	-0.042	0.621
Uric acid	0.223	0.525	0.019	0.671	-0.476	0.875	-0.038	0.587	-0.112	1.209	-0.008	0.926
Albumin	4.242	1.958	0.095	0.031	7.017	3.082	0.139	0.024	8.003	4.163	0.159	0.056
γ-GTP	0.016	0.015	0.049	0.284	0.010	0.013	0.048	0.438	0.021	0.034	0.048	0.538
Creatinine	0.010	0.016	0.028	0.526	0.010	0.024	0.026	0.680	0.009	0.032	0.024	0.771
Cholesterol	2.070	2.868	0.035	0.471	6.658	6.028	0.080	0.270	2.761	8.955	0.029	0.758

WHODAS, World Health Organization Disability Assessment Schedule; ECW/TBW, extracellular water/total body water ratio; DM, diabetes mellitus; γ-GTP, γ-glutamyl transpeptidase.

Reference values for categorical data: ECW/TBW (normal), sex (male), spouse (yes), economic status (poor), smoking (no), hypertension (no), diabetes (no).

to be helpful in diagnosing sarcopenic obesity, which corresponds to a state of high fat and low muscle mass. Therefore, by routinely using BIA to easily evaluate the edema index ratio, it may be possible to detect and intervene early in the community population at risk of health problems. In particular, this indicator could be used as an objective evaluation indicator for health programs because it well represents water intake and nutritional status in older adults.³⁰

The edema index (ECW/TBW) is an indicator of systemic edema, and the normal range can be defined in various ways. In this study, the cut-off point was 0.391, which was suggested in a study conducted on Japanese people who are racially similar to those in Korea.¹⁷ That study was conducted on people with locomotive syndrome (a syndrome with a combination of sarcopenia, osteoporosis, and arthritis), and the disease group was similar to that in our study. In their study, ECW/TBW was important in classifying locomotive syndrome, and there was a correlation with the degree of disability in people with osteopenia, sarcopenia, and OS. Thus, this indicator could be conveniently used to predict the degree of disability for those affected with these diseases. It had been reported that ECW/TBW values in various diseases were also related to cognitive function and treatment success rate.^{31,32}

WHODAS 12, a questionnaire that evaluates the degree of disability, evaluates disability due to disease or injury in six domains (cognition, mobility, self-care, getting along, life activities, and participation). In particular, in previous studies on OS,¹⁵ the degree of disability evaluated by this questionnaire tool was also closely associated with frailty and depression in older adults, so this questionnaire could be used to evaluate the degree of

disability in OS. In addition, in this study, the disability score and the edema index (ECW/TBW) were significantly correlated in each of the three disease groups but not in the normal group, making it possible to predict disability simply as an index measured by BIA.

This study has a few limitations. First was that it was cross-sectional and was insufficient to explain the temporal relationship between edema index (ECW/TBW) values and WHODAS 12 values. For example, due to a high degree of disability, there were difficulties in behaviors closely related to the edema index value, such as beverage and nutritional intake, so the edema index value might be abnormal. In addition, since the edema index was highly associated with nutritional status,³⁰ a better study could be made if the correction was made together. However, nutritional status could be corrected to some extent by correcting for variables closely related to nutritional status in blood tests. Also, subjects were not well-represented because they lived in three communities selected by consent for the study. Despite these limitations, studies targeting these disease groups have shown that the edema index is related to disease prognosis and disability, supporting the results from our study.

In conclusion, the edema index (ECW/TBW) value can be used to predict the degree of disability in osteopenia and sarcopenia, which are common diseases in older adults. Importantly, the edema index, which is highly associated with edema or malnutrition, can be obtained easily and objectively used as an evaluation index and method for health programs targeting these disease groups.

AUTHOR CONTRIBUTIONS

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