

Original article

# The utility of a phase angle analysis in patients with severe motor and intellectual disabilities

Motomu Yoshida<sup>a</sup>, Kimio Asagiri<sup>a</sup>, Suguru Fukahori<sup>a,\*</sup>, Yoshiaki Tanaka<sup>a,c</sup>,  
Naoki Hashizume<sup>a</sup>, Shinji Ishii<sup>a</sup>, Nobuyuki Saikusa<sup>a</sup>, Naruki Higashidate<sup>a</sup>,  
Daisuke Masui<sup>a</sup>, Naoko Komatsuzaki<sup>a</sup>, Hiroto Nakahara<sup>a</sup>, Minoru Yagi<sup>a</sup>,  
Yushiro Yamashita<sup>b</sup>

<sup>a</sup> Department of Pediatric Surgery, Kurume University School of Medicine, 67 Asahi-machi, Kurume, Fukuoka 830-0011, Japan

<sup>b</sup> Pediatrics and Child Health, Kurume University School of Medicine, 67 Asahi-machi, Kurume, Fukuoka 830-0011, Japan

<sup>c</sup> Division of Medical Safety Management, Kurume University School of Medicine, 67 Asahi-machi, Kurume, Fukuoka 830-0011, Japan

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## Abstract

**Purpose:** The purpose of the present study was to evaluate whether evaluating the phase angle (PhA), in a bioelectrical impedance analysis (BIA) is useful for estimating the nutritional status of severe motor and intellectual disabilities (SMID) patients.

**Subjects and methods:** This retrospective study included 31 SMID patients (mean age:  $33.9 \pm 13.5$  years, median age: 29 years (range: 18–58 years), male/female: 23/8). First, each of the parameters from the total study population and the male and female SMID patients were compared with those of healthy Asian subjects. Second, correlation analyses were conducted to investigate the correlation between the PhA and the other BIA parameters (appendicular skeletal muscle mass index (ASMI), appendicular muscle mass (AMM), extracellular water (ECW)/total body water (TBW)) as well as subjective global assessment and serum nutritional markers. Finally, all patients were divided into 2 groups according to their albumin (Alb) ( $<3.5$  or  $\geq 3.5$ ) values and PhA of the 2 groups were compared.

**Results:** The mean PhA and ASMI were a considerably low, whereas ECW/TBW was considerably high in comparison to the healthy Asian subjects. Significant negative correlations were observed between the PhA and ECW/TBW, whereas there were significant positive correlations between PhA and AMM, ASMI, total protein and albumin levels. Furthermore, PhA of Alb  $\geq 3.5$  group was significantly higher than that of Alb  $<3.5$  group.

**Conclusions:** The present study indicated that SMID patients demonstrate the low PhA, which were similar to sarcopenia and a certain proportion of them also potentially have nutritional disturbances.

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**Keywords:** Phase angle; Severe motor and intellectual disabilities; Bioelectrical impedance analysis

## 1. Introduction

Several body composition analyzing modalities are applied to evaluating the body compartments in the clinical setting. These include dual energy X-ray absorptiometry (DEXA), magnetic resonance imaging, and

\* Corresponding author. Fax: +81 942 31 7705.

E-mail address: [s\\_fukahori@med.kurume-u.ac.jp](mailto:s_fukahori@med.kurume-u.ac.jp) (S. Fukahori).

computed tomography. However, they have not been accepted as mainstream techniques due to their cost or the necessity of radiation exposure. Recently, bioelectrical impedance analyses (BIAs) has been used as an alternative, noninvasive method of analyzing the body composition. BIAs are now used in daily nutritional assessments [1,2]. BIA principally allows for the estimation of the components of the body structure by measuring the biological impedance against a subtle alternating current. A multi-frequency BIA can measure the total body water (TBW), intracellular water (ICW) and extracellular water (ECW) by applying the frequency-based difference of the transit current. The ECW/TBW has been the standard parameter for evaluating the body water balance and has also been reported as a useful parameter both for determining the nutritional status and for predicting the life prognosis in the critically ill patients [3]. Furthermore, the skeletal muscle mass, which is an important factor for diagnosing sarcopenia [4], can be calculated based on the TBW value.

The Phase angle (PhA) is the BIA parameter that is most frequently applied in the clinical setting. It reflects both the amount and the quality of soft tissue, and is currently regarded as a composite measure of tissue resistance and reactance [5]. The PhA increases according to the structural completeness of the cell membrane and the improvement of the cellular function, and decreases when plasma luminal structural damage of the cell is present. It also causes a decrease in the selective transmission function [5]. In a pure cell membrane mass, the PhA is 90 degrees, while that in pure electrolyte water is 0 degrees. In healthy subjects, the PhA typically range from 8° to 15° [6]. Thus, the PhA is suggested to be a good indicator of cellular health and a high PhA value reflects the high cellularity and the integrity and the function of the cell membrane [6]. Moreover, this parameter has also been used as a nutritional indicator that correlated with the nutritional parameters such as serum transthyretin (TTR) and has gained popularity because it has been shown to be highly predictive of an impaired clinical outcome and increased mortality in a variety of diseases [7].

In the pediatric field, the presence of severe motor and intellectual disabilities (SMID) has been recognized as a critical disorder that requires intensive nutritional support due to the presence of neurological and/or metabolic disorders, and because it is associated with a high incidence of complications such as gastroesophageal reflux disease and oropharyngeal discoordination. SMID patients frequently require surgical procedures such as anti-reflux surgery and tracheostomy and pediatric surgeons face various problems in their perioperative management, most notably, in managements associated with their insufficient nutrition at the referring institution.

Although it should be fundamental to accurately evaluate their nutritional status, it is often difficult to calculate it from physical measurements due to their severe scoliosis. Another nutritional assessment technique, which combines the evaluation of temporal weight changes and the hematological/nutritional index has often been attempted for SMID patients. However, such techniques may be less accurate because the height-for-age and weight-for-age growth standards of SMID patients are lower than those of the reference population and the TTR value is often affected by non-nutritional factors such as chronic inflammation. Thus, a nutritional assessment that utilizes the BIA might be well-suited to SMID patients. To the best of our knowledge, no previous reports have assessed the nutritional status of SMID patients by analyzing the PhA. However, several clinical reports regarding the application of the PhA to the assessment of the nutritional status of other subjects have been found [1,2,7,8].

The purpose of the present study was to evaluate whether the PhA is a useful parameter for estimating the nutritional status of SMID patients. We investigated the relationship between the PhA and other BIA parameters, the subjective global assessment (SGA) parameters and serum nutritional markers levels.

## 2. Patients and methods

This present retrospective study included 31 SMID patients  $\geq 18$  years (male,  $n = 23$ ; female,  $n = 8$ ; mean age,  $33.9 \pm 13.5$  years; median age: 29 years (range: 18 to 58 years)) who were admitted for surgical treatment in Kurume University Hospital between June 2013 and March 2016.

Regarding the causal disorders of SMID, one had a genetic anomaly, 1 had a chromosomal anomaly, 2 had congenital parencephalia, 2 had congenital cytomegalovirus infection, 13 had perinatal brain injury, 8 had acquired brain injury and 4 were unknown. Eleven patients had undergone respiratory tract surgical procedures (tracheostomy: 3, laryngotracheal separation: 7 and total laryngectomy: 1) and 16 had gastrostomy.

All of the patients were bedridden and 29 patients required tube feeding (nasogastric tube: 13 patients or gastrostomy tube: 16 patients). There were only 2 patients who were fed orally. The patients who were suffering from decompensated heart, lung, kidney or liver failure or the involuntary loss or gain of  $>5\%$  body weight in the previous 3 months (which affected the BIA data) were excluded from the present study. Informed consent was obtained from the patient's families before they were enrolled in the present study. All of the patients underwent a baseline nutritional assessment, which included laboratory measurements of the SGA parameters, including their age, height, weight, body mass index (BMI) and the measurement of the

serum levels of nutritional markers, including the total protein (TP), albumin (Alb), cholinesterase (ChE) and TTR.

Prior to the BIA, all of the enrolled patients were fasted for more than 2 h and did not receive any parenteral nutrition. They were then placed in the supine position in a thermoneutral environment at a temperature of 28 °C. Their arms were separated from the trunk and both legs were separated from each other. The InBody S20 device (Biospace, Tokyo, Japan) was originally used for the BIA measurements. The BIA was conducted with 8 surface electrodes and the obtained data were automatically analyzed and the following parameters were calculated: the PhA, the body water ratio (ECW/TBW) and the appendicular muscle mass (AMM).

The PhA was determined at single frequencies (50 kHz) and was calculated using the sum of the impedance and reactance of the right arm, trunk, and right leg and according to the following formula:  $\text{PhA } (^\circ) = (\text{Reactance/Resistance}) \times (180^\circ/\pi)$ .

The ECW/TBW represents not only the individual parts of the body (such as the arms, trunk, and legs) but also the whole body. In a healthy subject, the ratio of the intracellular water level and the extracellular water level is maintained. The normal range of the ECW/TBW (edema index) is considered to be 0.36–0.39. A ratio of between 0.39 and 0.40 indicates “slight edema”, while a ratio of >0.40 indicates edema [9]. The AMM was calculated as the sum of the muscle mass of the arms and the legs. The absolute AMM was converted to an appendicular skeletal muscle mass index (ASMI) by dividing the height in meters squared ( $\text{kg/m}^2$ ). ASMI values of <7.0  $\text{kg/m}^2$  in males and

<5.8  $\text{kg/m}^2$  in females were considered to indicate a low muscle mass [10–13].

First, the value of each of the SGA (age, height, weight and BMI), the BIA (PhA, ECW/TBW, AMM and ASMI) and serum nutritional parameters (TP, Alb, TTR and ChE) were compared among total study population, and among the male and female patients. Three of the BIA parameters (PhA, ECW/TBW and ASMI) were compared to those of healthy Asian subjects [6,9,12]. Second, correlation analyses were conducted between the PhA and other BIA parameters including ECW/TBW, AMM and ASMI and the serum levels of nutritional markers. Finally, all of the patients were divided into 2 groups according their Alb (<3.5 or  $\geq 3.5$  g/dL) levels. The PhA was then compared between the 2 groups.

Comparisons between 2 groups were made using Pearson’s Chi square test and the Mann–Whitney *U* test. The obtained data were presented as the mean  $\pm$  standard deviation and range. *P*-values of <0.05 were considered to indicate statistical significance. All of the statistical analyses were performed using the JMP software program (SAS Institute Inc., Cary, NC, USA).

### 3. Results

The mean SGA, BIA and serum nutritional parameters of the total study population, male and female are shown in Table 1. In comparison of the mean SGA parameters, the mean age, height and weight of female patients were tended to be lower than those of the male patients although no significant difference was observed in these parameters between genders. In the same manner, regarding the mean BIA data, the mean PhA,

Table 1  
The parameters in the 3 groups of SMID patients.

	Total	Male	Female	<i>p</i> value
No. of patients (No.)	31	23	8	
<i>SGA parameter</i>				
Age (years)	33.9 $\pm$ 13.5	36.0 $\pm$ 14.2	27.8 $\pm$ 9.33	0.1418
Height (cm)	143.0 $\pm$ 11.7	144.4 $\pm$ 10.9	139.1 $\pm$ 13.9	0.4158
Weight (kg)	30.8 $\pm$ 8.37	31.2 $\pm$ 9.18	29.7 $\pm$ 5.80	1.0000
BMI ( $\text{kg/m}^2$ )	15.0 $\pm$ 3.35	14.9 $\pm$ 3.70	15.4 $\pm$ 2.19	0.4426
<i>BIA data</i>				
Phase Angle (°)	3.26 $\pm$ 0.93	3.36 $\pm$ 0.99	2.97 $\pm$ 0.71	0.4036
ECW/TBW	0.40 $\pm$ 0.027	0.40 $\pm$ 0.025	0.40 $\pm$ 0.033	0.5718
AMM (kg)	6.98 $\pm$ 3.84	7.30 $\pm$ 3.51	6.07 $\pm$ 4.80	0.2687
ASMI ( $\text{kg/cm}^2$ )	3.29 $\pm$ 1.62	3.42 $\pm$ 1.46	2.89 $\pm$ 2.08	0.2497
<i>Serum nutrition marker</i>				
Total protein (g/dL)	7.06 $\pm$ 0.61	7.06 $\pm$ 0.68	7.07 $\pm$ 0.35	0.9820
Albumin (g/dL)	3.73 $\pm$ 0.44	3.76 $\pm$ 0.49	3.65 $\pm$ 0.25	0.4840
Transthyretin (mg/dL)	22.1 $\pm$ 4.97	22.4 $\pm$ 5.68	21.5 $\pm$ 2.19	0.7604
Cholinesterase (U/L)	334.0 $\pm$ 97.1	325.8 $\pm$ 106.9	357.8 $\pm$ 59.7	0.2886

SMID: severe motor and intellectual disabilities, SGA: subjective global assessment, BIA: bioelectrical impedance analysis, BMI: body mass index, ECW/TBW: extracellular water/total body water, AMM: appendicular muscle mass, ASMI: appendicular skeletal mass index.

AMM and ASMI of the female patients were tended to be lower than those of the male patients. However, there was no significant difference in these data between genders. Meanwhile, when comparing the serum nutritional parameters between male and female SMID patients, no significant difference and tendency were observed in any of the parameters between genders.

The mean PhA and ASMI of the total study population and the male and female SMID patients were considerably low, whereas the mean ECW/TBW values were considerably high in comparison to healthy Asian subjects (Fig. 1A–C).

In the correlation analysis to investigate the correlation between the PhA and other parameters including SGA and BIA parameters and the serum levels of nutritional markers, significant negative correlations were observed between the PhA and ECW/TBW values ( $p < 0.0001$ ); whereas significant positive correlations were observed between the PhA and the AMM, ASMI, TP and Alb levels ( $p < 0.0001$ ,  $p < 0.0001$ ,  $p = 0.0328$  and  $p = 0.0105$ , respectively) (Table 2).

Regarding the comparison analysis of the PhA in the Alb  $\geq 3.5$  and Alb  $< 3.5$  groups, the PhA of the Alb  $\geq 3.5$  group was significantly higher than that of the Alb  $< 3.5$  group ( $3.55 \pm 0.89^\circ$  vs.  $2.36 \pm 0.52^\circ$ , respectively;  $p = 0.0007$ ) (Fig. 2).

#### 4. Discussion

To the best of our knowledge, the present study might be the first study to evaluate the PhA of SMID

Table 2

The analysis of correlations between the PhA and the other parameters in SMID patients.

Variables	Pearson's correlation coefficient	<i>p</i> value
<i>SGA parameters</i>		
Age	-0.1413	0.4482
Height	-0.1429	0.8474
Weight	0.1990	0.2833
BMI	0.1188	0.5244
<i>BIA parameters</i>		
ECW/TBW	-0.7681	<0.0001
AMM	0.6899	<0.0001
ASMI	0.7750	<0.0001
<i>Serum nutrition markers</i>		
Total protein	0.3912	0.0295
Albumin	0.4605	0.0091
Transthyretin	0.1237	0.5148
Cholinesterase	0.2672	0.1462

SMID: severe motor and intellectual disabilities, SGA: subjective global assessment, BIA: bioelectrical impedance analysis, BMI: body mass index, ECW/TBW: extracellular water/total body water, AMM: appendicular muscle mass, ASMI: appendicular skeletal mass index.

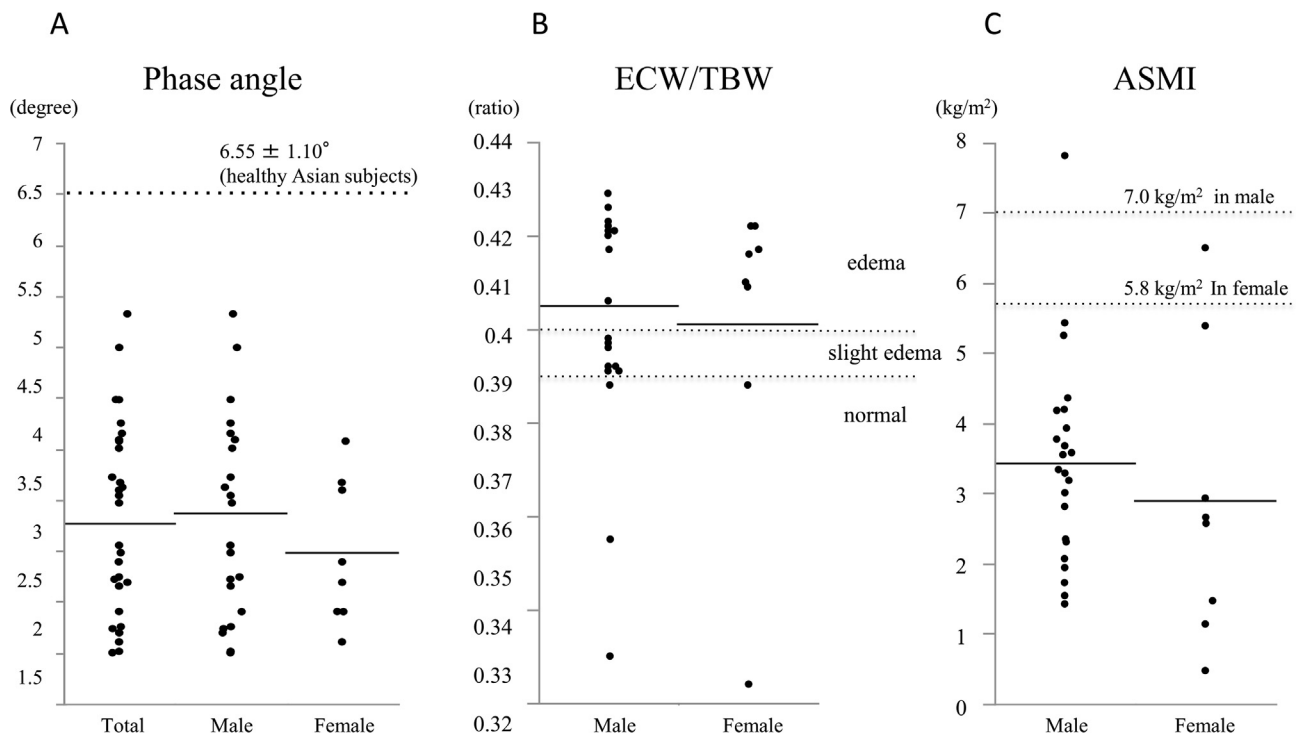


Fig. 1. The mean PhA and ASMI of total study population, and the male and female SMID patients were considerably low (A and B), whereas the mean ECW/TBW values were considerably high in comparison to healthy Asian subjects (C).

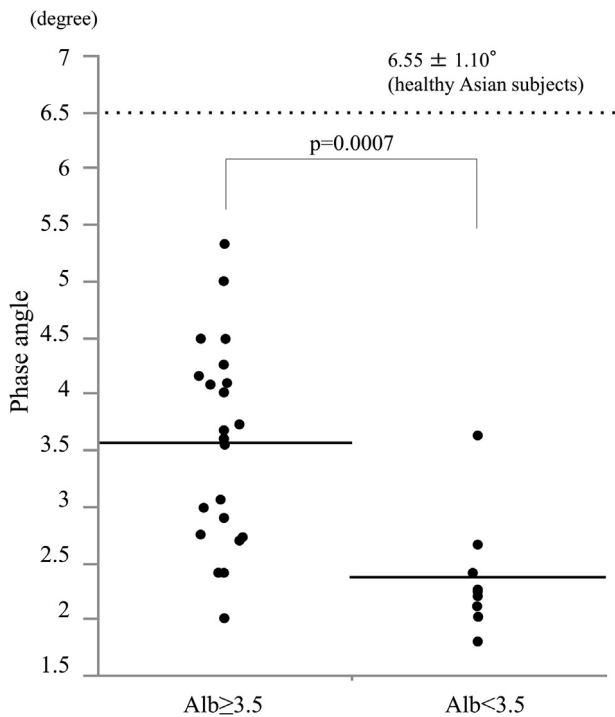


Fig. 2. Regarding the comparison analyses of the PhA in the Alb  $\geq 3.5$  and Alb  $< 3.5$  groups, the PhA of Alb  $\geq 3.5$  group was significantly higher than that of the Alb  $< 3.5$  group ( $3.55 \pm 0.89^\circ$  vs.  $2.36 \pm 0.53^\circ$ , respectively;  $p = 0.0007$ ).

patients by utilizing a BIA. Interestingly, the PhA has been found to be affected by several clinical factors, including race, gender and age. A study that employed a crude analysis of 1967 healthy adult subjects (age: 18–94y, male/female: 832/1135, race: whites (46%), African Americans (22%), Asians (14%), Hispanics or other races (18%)) to compare the PhA in different races showed significant differences: Asians,  $6.55 \pm 1.10^\circ$ ; whites,  $6.82 \pm 1.13^\circ$ ; multiracial subjects,  $7.00 \pm 1.01^\circ$ ; African Americans,  $7.21 \pm 1.19^\circ$ ; Hispanics,  $7.33 \pm 1.13^\circ$ ; and other races,  $7.45 \pm 0.98^\circ$  [6]. Although the mean PhA value of the Asian subjects was the smallest, the cause of the difference was not described. The PhA of SMID patients in the present study demonstrated lower value than the healthy Asian subjects. It is hypothesized that the poor physical activity of the SMID patients was likely to have influenced the electrical properties of their bodies, in particular their small amount of skeletal muscle or low BMI, which expresses smaller amounts of cells, is suspected to have resulted in a lower PhA in comparison to healthy subjects.

Regarding the relationship between the PhA and gender, several studies have reported the PhA to be significantly higher in male subjects than it is in female subjects. Gunn et al. described a significant gender-based difference in the PhA ( $5.1 \pm 1.2^\circ$ : male and  $4.5 \pm 0.9^\circ$ : female,  $p < 0.001$ ) [8]. Barbosa-Silva et al. also reported that the overall mean PhA was  $6.93 \pm 1.15^\circ$ ,

$7.48 \pm 1.10^\circ$  in male subjects, while that in female subjects was  $6.53 \pm 1.01^\circ$ , and the PhA in male subjects was significantly higher than that in female subjects for all age categories [6]. In the present study, there was no significant gender-based difference in PhA, AMM and ASMI although those parameters in female tended to show lower values than those of males, indicate that these different results in PhA from the previous study might be due to the smaller amount of skeletal muscle in SMID patients than that in the healthy subjects regardless of gender.

Concerning the relationship between the PhA and age, there was a significant linear decrease in the PhA according to age in both genders. Previous reports also showed a significant decrease in the PhA with age after the PhA peaks at between 20 and 40 years of age in healthy elderly subjects and healthy adults [6,14,15]. Barbosa-Silva et al. indicated that the decrease in the PhA value with increasing age might reflect the cell function and the general health conditions in addition to the body composition [6]. The present study found that there was no significant correlation between the age and PhA in SMID patients, which was different from the results of these previous reports. It is speculated that the cell function and the general health conditions of the SMID patients might already have declined since early in their life, similar to those seen in healthy elderly subjects due to their poor overall physical activity.

PhA analyses are also known to be useful for evaluating the nutritional status. There was a significant association between a low PhA and the nutritional risk, the length of hospital stay and the mortality rate. In patients with pancreatic cancer, the PhA has been shown to be a better predictor of mortality than the traditional nutrition index [6], which indicates that the PhA has a higher correlation with the survival rate rather than the nutrition index [16] or weight loss [17], because the change in the PhA that occurs before cachexia appears earlier than weight loss [18].

A low PhA indicates the presence of malnutrition and reflects the development of edema due to acute inflammation or hypoalbuminemia [2]. A previous study investigated the relationship between the PhA and the serum levels of nutritional markers and found that patients with Alb levels of  $< 3.5$  g/dL demonstrated a lower PhA than patients with Alb levels of  $\geq 3.5$  g/dL. In the present study, a significant positive correlation was also found between the PhA and the TP and Alb levels. However, the PhA values of the SMID patients were apparently lower than those of the healthy patients, whereas the TP and Alb levels of both the SMID patients and the healthy subjects were similar. Furthermore, the present study demonstrated that the PhA of SMID patients with serum Alb levels of  $< 3.5$  g/dL was significantly lower than that of patients with levels of  $\geq 3.5$  g/dL, which was a similar result to that observed

in healthy subjects; however, the PhA of SMID patients was lower than that of healthy subjects. Thus, from the present results, the PhA value was as useful for assessing the nutritional status of SMID patients as it was for healthy subjects. The PhA cut-off values for diagnosing malnutrition are reported to be  $5.0^\circ$  in males and  $4.6^\circ$  in females, respectively [1]. The PhA values in the present SMID patients were below these cut-off values. Thus, it might be necessary to set a lower malnutrition cut-off value for SMID patients.

In addition to the PhA, the ECW/TBW value has been evaluated in several previous BIA-related studies and is recognized as being useful factors for the assessment of the nutritional status or the prediction of the life prognosis in the critically ill patients [3]. Previous studies have indicated that malnutrition is characterized by changes in the integrity of the cellular membrane and that fluid shifts due to an increase in the amount of extracellular water. Lee et al. reported that there was a significant negative correlation between the ECW/TBW and the Alb and hemoglobin levels and that the value was consistently increased in subjects with a poor nutritional status [3]. The presence of both a low PhA and a high ECW/TBW value strongly suggests the presence of malnutrition and predicts a poor prognosis in critically ill patients. The ECW/TBW values of the present SMID patients were higher than those of healthy samples [1,6,8]; 61% of them were  $>0.40$ , which indicated that the body cell mass of SMID patients was low due to an increased amount of extracellular water, which changed from intracellular water. The present ECW/TBW results suggest the disturbed water homeostasis due to their distinctive characteristics such as brain atrophy, low bone mineral density and muscular atrophy. Additionally, a certain proportion of SMID patients were potentially in a state of chronic malnutrition.

Malnutrition is considered to be an associated factor of sarcopenia. Sarcopenia has been described as an age-related decline in the skeletal muscle mass and the muscle function, which may result in reduced physical capabilities and an impaired cardiopulmonary function as well as high healthcare expenditure. The Asian Working Group for Sarcopenia recommended ASMI (kg)/height ( $m^2$ ) cutoff values of  $7.0 \text{ kg}/m^2$  for males and  $5.4 \text{ kg}/m^2$  for females [12]. Based on this definition, all of the SMID patients in the present study would have been diagnosed with sarcopenia. Furthermore, the ASMI values of the SMID patients were extremely low in comparison to those in healthy subjects. Based on these results, the clinical condition of the SMID patients in the present study was likely to be similar to that of patients with sarcopenia.

In summary, the mean PhA and ASMI values in SMID patients were considerably lower than those in healthy Asian subjects, while the mean ECW/TBW val-

ues were considerably higher, which reflects their smaller amount of skeletal muscle or low BMI due to their poor physical activity and the disturbed water homeostasis due to their distinctive characteristics, while in some patients, the presence of malnutrition was also observed. Thus, the present study suggested that the values of PhA as well as ASMI and ECW/TBW likely to reflect the nutritional status of SMID patients despite of their lower or higher values compared with those of the healthy subjects.

The PhA was not correlated with age. This result was not consistent with the results of previous reports which indicated that aging still affects the values of PhA in SMID patients, which is speculated that their skeletal muscle mass is already low from young age similar to that in patients with sarcopenia.

A significant strong negative correlation was observed between the PhA value and the ECW/TBW, while a moderate significant positive correlation was observed between the PhA value and the ASMI, TP and Alb values. The significant difference in the PhA values between the SMID patients with albumin levels of  $<3.5$  and  $\geq 3.5$  g/dL, indicated that the PhA still provides a sensitive reflection of the nutritional status of SMID patients despite of the low PhA values of the SMID patients.

The present study is associated with some limitations due to a wide age distribution, various health conditions and the small sample size and the fact that it was a single center study. Thus, a further multicenter study with a large number of age and health matched SMID patients should be performed to verify the effectiveness of BIA.

In conclusion, the present study demonstrated that the PhA values of SMID patients were considerably low thus reflecting a depressed cell function, and were similar to those observed in sarcopenia patients. This suggests the possibility of a nutritional disturbance in a certain proportion of SMID patients. The study also suggested that the calculation of the PhA in a BIA was as useful for evaluating the nutritional status of SMID patients as it was in healthy subject.

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