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Original Article

Validation of bioimpedance phase angle in lower extremity of male patients with chronic spinal cord injury

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Abstract. [Purpose] This study aimed to evaluate the relationship between lower extremity phase angle and muscle thickness/echo intensity in males with chronic spinal cord injury. It also compared bioelectrical impedance analysis measurements to investigate skeletal muscle degeneration between individuals with spinal cord injury and healthy controls. [Participants and Methods] This cross-sectional study included 12 male patients with chronic spinal cord injury and 14 healthy male controls. We used bioelectrical impedance analysis and ultrasonography to measure the lower extremity phase angle and muscle thickness/echo intensity of the rectus femoris muscle, respectively. We also compared the bioelectrical impedance analysis measurements between individuals with spinal cord injury and healthy controls. [Results] Lower extremity phase angle was strongly correlated with muscle thickness and echo intensity of the rectus femoris muscle in individuals with spinal cord injury. All measures differed significantly between individuals with spinal cord injury and healthy controls. [Conclusion] These findings suggest that lower extremity phase angle is a valuable skeletal muscle indicator in spinal cord injury. Furthermore, bioelectrical impedance analysis revealed degeneration of the lower extremity skeletal muscles in individuals with chronic spinal cord injury.

Key words: Spinal cord injury, Ultrasonography, Electric impedance

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INTRODUCTION

Spinal cord injury (SCI) is characterized by early skeletal muscle atrophy, fat infiltration, and muscle fibrosis. The muscle mass of patients with SCI, represented by the cross-sectional area (CSA), is reportedly approximately 33% lower in the thigh muscles at 6 weeks post-injury, with no subsequent change in the CSA[1)]. Similarly, the CSA decreases by approximately 31% in the rectus femoris (RF) during the maintenance phase[2)]. Fatty infiltration of skeletal muscles in SCI replaces atrophied myofibers with adipocytes and collagen in the skeletal muscle, which have experienced prolonged denervation[3, 4)]. Moreover, adipose tissue accumulation in the skeletal muscles of the lower extremity is reportedly as much as four times greater in individuals with chronic SCI than in healthy individuals[1–3)].

Muscle thickness and echo intensity are measured using ultrasound imaging devices to evaluate muscle mass and quality[5)]. Muscle thickness strongly correlates with the physiological CSA of skeletal muscle measured using magnetic resonance imaging (MRI), which is considered the gold standard for measuring muscle mass and a reliable index thereof[6, 7)]. Echo intensity correlates with intramuscular adipose and fibrotic tissues as identified through muscle biopsy[8)]. Furthermore, echo intensity correlates with muscle extracellular fat measured using MRI[9)], also considered an indicator of intramuscular noncontractile tissue. The whole-body phase angle (PhA) can be measured using bioelectrical impedance analysis (BIA) and serves as a unique measure of skeletal muscle[10)]. The PhA serves as an indicator of cell membrane structure. A lower PhA

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value suggests reduced cellular integrity[11–13]. Additionally, the PhA is computed from reactance (Xc) and resistance (Rz), the electrical resistance values of the body, which remain useful even in severe cases, unlike estimations such as BIA that rely on algorithms based on sex, age, and body composition[14].

The PhA is reportedly associated with both muscle mass and quality[15–17], in healthy older patients, garnering attention as a novel new evaluation index to assess muscle function. However, no reports on specific diseases have been found in the index of skeletal muscle assessment in PhA, and further validation is needed. Although reports of the PhA in chronic SCI have revealed significantly lower PhA compared to healthy participants[18], the relationship between lower PhA and trait changes in paralyzed muscles is unknown. Therefore, in chronic SCI patients with severe paralysis of the lower extremities, we measured muscle thickness and echo intensity of the thigh by ultrasonography and investigated their relationship to lower extremity-specific phase angle (PhA_L) localized to the paralyzed area. Furthermore, a comparison of BIA, PhA and PhA_L between the SCI and healthy control (HCG) groups, verified the usefulness of the PhA_L as a measure of paralytic muscle evaluation. The PhA is a useful parameter in critically ill patients and is therefore expected to be correlated with muscle thickness and echo intensity, as has been reported for healthy older participants[15].

PARTICIPANTS AND METHODS

This study was an observational cross-sectional study of patients with chronic SCI and healthy participants. In the selection of participants, only male participants were recruited in order to minimize the influence of gender-related variables on the BIA and ultrasound measurements. Participants with SCI were recruited from specialized gyms dedicated to SCI rehabilitation or local wheelchair sports organizations. Eligible participants were male individuals with SCI of at least 1 year duration, characterized by residual paralysis in the lower extremity. The exclusion criteria were independent ambulation capacity and a manual muscle test (MMT) score of >3 for knee extension. Furthermore, individuals with SCI-bearing cardiac pacemakers or other artificial implants were excluded owing to the infeasibility of conducting BIA measurements. The ASIA impairment scale and MMT scores, which were essential information for this study, were obtained from affiliated organizations. The HCG comprised male health care providers, with the exclusion criteria encompassing any history of orthopedic ailments involving the lower extremity. The sites where measurements were taken were a specialized gym for SCI and a university laboratory for HCG.

This study adhered to the principles outlined in the Declaration of Helsinki, with the study protocol receiving thorough review and approval from the International University of Health and Welfare, (approval number: 20-Ifh-081). Informed consent was obtained from all participants before their involvement in the study. Participants were provided with a detailed explanation of the study's objectives, procedures, potential risks, and benefits.

Ultrasound examinations were performed using a SONIMAGER MX1α ultrasound device (Konita Minolta Co., Tokyo, Japan) coupled with a 3–11 MHz linear-array probe. The ultrasound device was set to a gain of 25 dB. A physical therapist with 15 years of experience who routinely uses ultrasound imaging devices in research activities and in the field of sports took the measurements. Participants assumed a supine position, and measurements were recorded per established methodologies[19]. The short-axis image of the RF was captured at a 39% point distal to the anterior superior iliac spine, situated above the patella. Muscle thickness was assessed from the superficial to the deep fascia of the RF, positioned just above the apex of the superior border of the femur. Echo intensity was measured according to previously established protocols[20] and was subjected to analysis using ImageJ (National Institutes of Health, Bethesda, MD, USA). The region of interest excluded the fascia and encompassed the maximal RF extent. Echo intensity was computed as the average value of the RF quantified in 256 increments using an 8-bit grayscale. Measurements were repeated twice for the left and right RF muscles, with the average value serving as the representative metric. In advance, we assessed the reliability of the measurement method using intraclass correlation coefficients (ICCs) (1, 2) in advance. The measurement method was reliable, with an ICC (1, 2) of 0.999 for muscle thickness and 0.941 for echo intensity.

Bioelectrical impedance analysis was performed using the InBody S10 multi-frequency system (InBody Japan, Tokyo, Japan). The InBody S10 permits utilization in a supine position, thereby accommodating individuals with standing difficulties[21]. The InBody S10 employs 8-point contact electrodes to directly measure the extracellular and intracellular water content at distinct frequencies (5 kHz, 50 kHz, and 250 kHz). The height and weight of participants were initially measured, and the electrodes were then applied to their extremities while in a supine posture. These bioelectrical impedances were employed for the computation of various metrics, including the PhA, PhA_L, skeletal muscle mass index (SMI), lower extremity-specific skeletal muscle index (SMI_L), total body water (TBW), lower extremity-specific total body water (TBW_L), intracellular water (ICW), lower extremity-specific ICW (ICW_L), extracellular water (ECW), lower extremity-specific ECW (ECW_L), ECW to TBW ratio (ECW/TBW), and lower extremity-specific ECW/TBW ratio (ECW/TBW_L). Additionally, the measured values of Xc and Rz at 50 kHz were extracted to estimate the PhA_L. SMI_L was determined by dividing the muscle mass at the specific site by the square of the height (kg/m^2)[14, 22], and the TBW_L was normalized using the same methodology.

The relationship between the PhA, muscle thickness of the RF, and echo intensity of the RF in individuals with chronic SCI was analyzed using Pearson's correlation coefficient after confirming normality. Additionally, two patterns were employed to analyze the PhA for the entire body and lower extremity. To distinguish variations between individuals with chronic SCI and the HCG, the Mann–Whitney U test was applied to identify distinctions in each measurement between the groups. Moreover,

the Wilcoxon signed-rank sum test was used to compare the PhA and PhA_L. The data were managed and analyzed using the SPSS software (version 27.0; IBM Corp., Armonk, NY, USA), and statistical significance was set at $p<0.05$.

RESULTS

Table 1 shows the attributes of SCI and HCG, and there were no differences between the two groups. Table 2 presents the demographic profiles of the individuals affected by SCI. The ASIA impairment scale indicated four patients as grade A, six as grade B, and two as grade C. The MMT scores for the lower extremity were 0–2 levels for SCI and 4–5 levels for HCG.

The mean and standard deviation of SCI ultrasound examination was 0.99 ± 0.57 cm for muscle thickness and 113.6 ± 22.8 for echo intensity. The PhA was strongly correlated with the muscle thickness ($r=0.66$, $p<0.01$) and echo intensity of the RF ($r=-0.80$, $p<0.01$). In addition, the PhA_L was strongly correlated with the muscle thickness ($r=0.72$, $p<0.01$) and echo intensity of the RF ($r=-0.72$, $p<0.01$).

A comparison of outcomes between individuals with SCI and HCG is presented in Table 3. The results showed significant differences in all measures ($p<0.01$) between the groups (Table 3).

Upon comparing the PhA and PhA_L, there was a significant difference ($p<0.01$) in the SCI group with the PhA of 3.86 ± 0.91° and the PhA_L of 2.58 ± 1.22°; in the HCG group there was no significant difference with the PhA of 6.09 ± 0.64° and the PhA_L of 6.23 ± 0.84°.

DISCUSSION

Our findings demonstrate a robust and statistically significant connection between the PhA and muscle thickness, an index of muscle mass, and echo intensity, a marker of muscle quality, among individuals with chronic SCI. The PhA serves as an indicator of cellular nutrition and the aging process. Prior studies have established its associations with physical performance[23, 24], physical activity, and nutritional status[25]. The PhA also exhibits correlations with muscle strength and skeletal muscle mass in healthy older individuals[16]. Yamada et al.[15] observed analogous correlations between the PhA and both the muscle thickness and echo intensity of the RF in healthy older adults, suggesting the potential utility of the PhA as a composite index reflecting the quantity and quality of skeletal muscle. In this study, the PhA was significantly and positively

Table 1. SCI and HCG attributes

	SCI n=12	HCG n=14
Age (years)	43.8 ± 13.2	43.3 ± 12.6
Height (cm)	172.6 ± 5.9	172.0 ± 6.6
Weight (kg)	65.3 ± 8.1	67.3 ± 8.3
BMI (kg/m^2)	22.0 ± 3.4	22.7 ± 2.3

Values are means ± standard deviations.
SCI: spinal cord injury; HCG: healthy control group.

Table 2. Characteristics of the participants with SCI

	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m^2)	Years past injury	Neurological level	ASIA impairment scale	MMT Knee joint extension
A	73	174	72	24	43	L3	C	2
B	61	168	77	27	26	C6	C	2
C	54	184	59	17	33	C6	B	0
D	48	170	68	24	11	C6	B	0
E	41	165	57	20	12	C6	B	0
F	45	173	67	22	27	C7	A	0
G	39	165	79	29	20	C6	B	0
H	38	170	58	20	9	T11	B	1
I	36	184	70	21	19	C5	A	0
J	36	173	59	19	2	T11	A	0
K	33	173	64	21	18	C6	B	0
L	21	173	51	17	3	T12	A	0

SCI: spinal cord injury; BMI: body mass index; MMT: manual muscle test.

Table 3. Differences in each parameter of ultrasound and BIA comparing the participants with SCI and healthy controls

	SCI n=12	HCG n=14	
PhA (°)	3.86 ± 0.91	6.09 ± 0.64	**
PhA_L (°)	2.58 ± 1.22	6.23 ± 0.84	**
Xc (ohm)	12.45 ± 4.09	25.86 ± 5.16	**
Rz (ohm)	298.68 ± 63.93	235.94 ± 28.8	**
SMI (kg/m^2)	6.43 ± 0.80	7.56 ± 0.50	**
SMI_L (kg/m^2)	2.32 ± 0.32	2.89 ± 0.50	**
TBW (L)	31.73 ± 3.55	36.43 ± 5.22	**
TBW_L (L)	5.45 ± 0.79	6.65 ± 0.8	**
ICW (L)	18.96 ± 2.29	23.06 ± 1.92	**
ICW_L (L)	3.21 ± 0.48	4.09 ± 0.48	**
ECW (L)	12.78 ± 1.31	14.25 ± 1.49	*
ECW_L (L)	2.25 ± 0.31	2.55 ± 0.36	**
ECW/TBW (%)	40.25 ± 0.87	38.49 ± 1.20	**
ECW/TBW_L (%)	41.25 ± 1.29	38.30 ± 1.01	**

Values are means ± standard deviation.
Mann-Whitney U test: **p<0.01, *p<0.05.
BIA: bioelectrical impedance analysis; SCI: spinal cord injury; HCG: healthy control group; PhA: whole-body phase angle; PhA_L: lower extremity-specific PhA; Xc: reactance; Rz: resistance; SMI: skeletal muscle mass index; SMI_L: lower extremity-specific SMI; TBW: total body water; TBW_L: lower extremity-specific TBW; ICW: Intracellular water; ICW_L: lower extremity-specific ICW; ECW: extracellular water; ECW_L: lower extremity-specific ECW; ECW/TBW_L: lower extremity-specific ECW/TBW.

correlated with both the muscle thickness and echo intensity of the RF, indicating that the PhA is an indicator of skeletal muscle quantity and quality in individuals with chronic SCI. Furthermore, the relationship between muscle thickness and echo intensity was confirmed using the PhA_L, measured at specific sites. Although the PhA has been used as an indicator of general conditions[26], the PhA by the site shows promise for evaluating skeletal muscles with limited paralysis sites, such as paraplegia and hemiplegia.

A comparison between the SCI group and HCG revealed that the PhA was 2.23° lower and the PhA_L 3.26° lower in the SCI group than in the HCG. Aldobali et al.[18] reported that the cut-off point for the PhA in male individuals with SCI was ≤4.7°. The mean value for the SCI in our study was 3.86°, which suggests that this was a population with high disease severity. The comparison between the PhA and PhA_L revealed that the PhA_L was significantly lower in individuals with SCI; however, there was no significant difference between the PhA and PhA_L in individuals in the HCG. Given that the lower extremity muscle mass is 40–50% of the total body muscle mass, the PhA_L is unlikely to be lower than the PhA. Collectively, the PhA_L could reflect the skeletal muscle status owing to paralysis of the lower extremity.

In addition, we examined the factors that contribute to the PhA_L being lower in the SCI group than the HCG, based on the 50 kHz Xc and Rz that make up the PhA_L. The PhA is the angle derived from the time shift of the current and voltage when an alternating current is applied to the capacitor. It is calculated by $\tan\theta=Rz/Xc$ where Rz and Xc is measured with the BIA[14]. That is, the PhA decreases with a decrease in Xc or increase in Rz.

The Rz is the resistance of body water with intra- and extracellular fluids as conductors and increases in muscle tissue with high water content[27]. In this study, the SCI group had higher Rz and lower TBW_L than the HCG. Low TBW_L is caused by decreased skeletal muscle, which retains large amounts of intracellular fluid, as inferred from the results for muscle thickness and SMI_L. The significant correlation between PhA and echo intensity in this study suggests that the Rz may have been increased because of increased resistance due to displacement by adipose and fibrous tissue at the myocyte interstitial sites. The increase in Rz is due to decreased muscle mass and fat infiltration of skeletal muscle, which explains the relationship between PhA_L and muscle thickness/echo intensity in this study.

The Xc is the capacitive resistance of the cell membrane, which acts as a capacitor and indicates cell membrane degradation[27]. Li et al.[28] found that Xc and PhA were significantly lower in disabled participants than those in non-disabled participants and reported that these changes were related to muscle structure and cell membrane integrity. Similar results were obtained in this study, with lower Xc in the SCI group compared to the HCG, presumably due to cell membrane deterioration caused by prolonged paralysis and immobility. Furthermore, ECW/TBW also indicates cell membrane degradation and is highly correlated with PhA[29]. The increase in ECW/TBW due to aging or worsening nutritional status is caused by a higher proportion of ECW caused by a decrease in intracellular water (ICW)[30]. The reference value of ECW/TBW in healthy individuals was approximately 38%[31]. In this study, individuals with SCI showed an ECW/TBW of approximately 40% and

ECW/TBW$_L$ of 41%, which were higher than those of the HCG and reference values, respectively. In this study, a lower Xc and greater ECW/TBW, which are indicators of cell membrane degradation, were observed in individuals with SCI. These factors suggest that the PhA$_L$ of the SCI group was lower than that of the HCG.

In conclusion, this study suggest that the PhA correlated with muscle thickness and echo intensity, as assessed by muscle mass and quality in chronic SCI. Furthermore, comparison with the HCG suggested that PhA$_L$ may be able to reflect the plasmatic state of paralyzed skeletal muscle better than PhA. However, the PhA has been found to be affected by several clinical factors, including race, gender, and age[32]. This study has some limitations due to a wide age distribution, a male-only target population, and a small sample size. Thus, further study with a large number of age- and sex-matched SCI patients should be performed to verify the effectiveness of PhA. Furthermore, the skeletal muscle in this study was evaluated by muscle mass/muscle quality of RF using ultrasound imaging alone, and measurement methods such as MRI and dual-energy X-ray absorptiometry should be considered to obtain a complete picture of the skeletal muscle of the lower extremity. Furthermore, this was a cross-sectional study and was limited in its capacity to monitor the evolving skeletal muscle degeneration process. In future studies, we intend to examine the usefulness of the PhA by continuing to investigate the degeneration of paralyzed skeletal muscles among individuals with SCI using BIA. The PhA can provide valuable insights into skeletal muscles in patients with severe diseases through direct measurements, in contrast to estimates derived from the SMI, which are primarily based on data from healthy individuals[14]. This study shows that the PhA using BIA is useful for the clinical examination and evaluation of muscle changes after SCI. because the BIA is noninvasive and easy to apply, eliminating the need for a measurement environment or techniques such as MRI or dual-energy X-ray absorptiometry. Our findings open new avenues for future research in the field of SCI. Subsequent studies could explore the relationship between PhA and specific clinical outcomes in SCI patients.

Conflict of interest

The authors declare that there is no conflict of interest.

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