scientific reports

Check for updates

OPEN

Usefulness of body composition assessment by bioelectrical impedance vector analysis in subacute post-stroke patients in rehabilitation

Alessandro Guerrini[1,2], Mariacristina Siotto[1]✉, Carola Cocco[1], Marco Germanotta[1], Valeria Cipollini[1], Laura Cortellini[1], Arianna Pavan[1], Stefania Lattanzi[1], Sabina Insalaco[1], Yeganeh Manon Khazrai[2] & Irene Giovanna Aprile[1]

Bioelectrical Impedance Vector Analysis (BIVA) is a valuable tool for evaluating hydration and body composition, but its application in subacute post-stroke patients remains unexplored. This study aimed to fill this gap by analyzing BIVA in a cohort of 87 subacute post-stroke patients (42 women, mean age 69 ± 12) undergoing rehabilitation. At admission (T0), diagnosis of malnutrition with GLIM criteria and of sarcopenia with EWGSOP2 was done, and patients were analyzed with BIVA. The change in modified Barthel Index (mBIT1-mBIT0) was assessed to evaluate the improvement in functional recovery. BIVA revealed that both adult patients (< 65 years, *n* = 29) and elderly patients (≥ 65 years, *n* = 58) exhibited high body fluid overload and low muscle mass. Additionally, BIVA revealed a significant rightward shift of the bioimpedance vectors in malnourished (*n* = 37) versus non-malnourished patients (T2 = 56.9, *p* < 0.001, D = 1.68) and in sarcopenic (*n* = 24) versus non-sarcopenic patients (T2 = 36.4, *p* < 0.001, D = 1.5). Lastly, the BIVA distinguished patients with greater improvement (*n* = 53) from patients with lower improvement (*n* = 34) (T2 = 10.6, *p* = 0.007, D = 0.7). In conclusion, BIVA is an effective, easy-to-use tool for evaluating hydration, nutritional status, and recovery in post-stroke rehabilitation.

Keywords Body composition, BIVA, BIA, Hydration, Stroke, Rehabilitation, Nutritional status

Stroke is one of the leading causes of death, morbidity, and disability worldwide, significantly impacting healthcare systems[1]. Stroke survivors may experience malnutrition and sarcopenia[2,3], both of which significantly impact clinical outcomes and functional recovery during the often extended rehabilitation period[2,4–10].

Malnutrition (undernutrition) is defined by the European Society for Clinical Nutrition and Metabolism (ESPEN) as an imbalance in nutrient intake that leads to changes in body and cellular composition, resulting in decreased functional capacity[11]. A meta-analysis of 78 studies[2] found that malnutrition is prevalent in all phases of stroke, affecting 37% of patients during the early subacute phase and up to 29% of patients during subacute phase[12]. Sarcopenia, which is the progressive decline in skeletal muscle mass and strength, is another condition affecting stroke patients, frequently associated to ageing, chronic malnutrition, and the stroke itself[3].

The importance of a correct diagnosis of malnutrition and sarcopenia upon admission to a rehabilitation center is often not adequately considered in the multidisciplinary approach managing post-stroke patients[13]. In this context, an accurate evaluation of body composition at admission of a rehabilitation unit is crucial for the early identification of sarcopenia, malnutrition, and other body composition changes that can significantly affect recovery[10,14,15].

Even if Computed tomography (CT) and Dual-Energy X-ray Absorptiometry (DEXA) are the gold standard methods to assess body composition, they are expensive, require specialized personnel, and often are not present in rehabilitation centers[15]. Bioelectrical Impedance Analysis (BIA) is a methodology commonly used in different clinical setting being easy to use, safe, cheap and non-invasive[15]. For this reason, is frequently employed to assess body composition in post-stroke patients in rehabilitation setting[16,17].

[1]IRCCS Fondazione Don Carlo Gnocchi ONLUS, 50143 Florence, Italy. [2]Department of Science and Technology for Humans and the Environment, Università Campus Bio-Medico di Roma, Via Álvaro del Portillo, 21, 00128 Rome, Italy. ✉email: msiotto@dongnocchi.it

BIA measures the opposition of the body-tissues to alternating current, namely the whole-body Impedance[18]. The two raw parameters deriving from this analysis are Resistance (Rz) and Reactance (Xc). Rz is inversely correlated to the water content in biological tissues, while Xc depends on the capacitance properties of the cell membrane, providing insights into cellular health, integrity and density[19,20]. From Rz and Xc it is possible to directly calculate the Phase Angle (PhA), which is related to cellular health and muscle quality[21,22]. Lower values of PhA were typically observed in subjects with severe pathological conditions and have been related to worse outcomes, such as increased mortality risk, disease progression and prolonged hospital stay[22,23]. Conversely, higher PhA values are indicative of better overall health, greater muscle strength and function[20,24]. Several studies have shown its prognostic utility in several diseases[22,23]. Moreover PhA has been identified as a useful marker of malnutrition and sarcopenia in post-stroke patients[10,25–27], as well as a valuable predictor of their functional independence and recovery[14,26,28–30].

BIA analysis allows to evaluate other body composition parameters, through predictive equations that incorporate the raw parameters along with sex, age, height and weight[18]. While BIA predictive equations are commonly used for body composition assessment, they can lead to estimation errors because they are highly accurate only when the subjects' characteristics match those of the population for whom the equations were developed[31,32]. In addition, the accuracy of body composition estimates can also be significantly influenced by altered hydration states and other physiological condition[33]. In contrast, the direct analysis of Rz, Xc and PhA, known as Bioelectrical Impedance Vector Analysis (BIVA), has gained attention for its ability to provide additional insights into hydration status and body composition, without the potential biases associated with BIA predictive equations [22,23]. In BIVA, the Rz and Xc of subjects, standardized by their height in meters, are plotted on a Rz-Xc graph[34], creating a bioimpedance vector which can be visualized and analyzed, with a inter-rater variability very low even in patients with diseases[22,33,35]. BIVA is particularly valuable in situations where body composition estimation is compromised due to fluid imbalance or other conditions[22,36]. These characteristics makes BIVA a highly versatile tool suitable for a broader range of clinical scenarios[33]. In fact, several studies highlighted the effectiveness of BIVA in qualitatively assessing hydration and body composition, not only in athletes[37], but also in elderly patients[38,39], in patients undergoing hemodialysis[40,41], in critically ill individuals[42], in cancer patients[43,44] and in those affected by obesity[22]. Moreover, BIVA has been used as an easy approach to identify patients with malnutrition or sarcopenia[45–51]. However, it is important to consider that age, sex and ethnicity, are factors affecting BIVA, due to different hydration and body composition[33].

Despite the widespread use of BIVA in clinical and athletic contexts, no data have been yet published on subjects with a stroke insult, with the exception of one study on a small sample of patients during the acute phase[52]. The application of BIVA in a post-stroke rehabilitation setting could be extremely helpful, as it allows for an early and easy characterization of body composition and nutritional status in post stroke patients admitted to rehabilitation centers after acute-phase hospitalization. As previously mentioned, in fact, these patients are at risk of experiencing sarcopenia, malnutrition and other body composition changes, all of which can affect recovery.

This study aims to fill this gap by analysing the usefulness of BIVA in qualitatively assessing body composition and characterizing malnutrition and sarcopenia in subacute post-stroke patient starting the rehabilitation treatment. Moreover, we aim to investigate if BIVA can effectively characterize patients based on the level of their functional recovery.

Methods

Study design and participants

The study is an observational prospective study aimed to analyze the nutritional status in post-stroke patients. Patients were consecutively enrolled at the "Santa Maria della Provvidenza" center of the Fondazione Don Carlo Gnocchi, in Rome, between September 2020 and April 2023 ("NUTRISTROKE" study, clinical trial identifier: NCT04923165).

Patients were selected based on the subsequent criteria: (i) a first ischemic or hemorrhagic stroke, as determined by computed tomography (CT) or magnetic resonance imaging (MRI); (ii) age between 18 and 85; (iii) the stroke insult occurred less than six months before; (iv) sufficient cognitive and language skills to understand the directions for using the assessment scales and to sign the informed consent. The exclusion criteria were the following: (i) a previous stroke; (ii) behavioral and cognitive disorders, as well as impaired compliance, which interfere with active therapy or comprehending and writing informed consent; (iii) the presence of pacemakers (which may interfere with bioimpedance measures).

The Ethical Committee of the Fondazione Don Carlo Gnocchi in Milan, Italy, authorized the study protocol on February 12th, 2020 and with a non-substantial amendment on October 14th, 2020 (Prot.n.22/2020/CE_FdG/FC/SA_14/10/20). All patients provided written informed consent.

Rehabilitation treatment

The rehabilitation protocol was outlined in our previous work[53]. Specifically, the patients followed a six-week rehabilitation treatment that included traditional physical therapy for 45 min for six days a week. Passive, active-assisted, and active mobilizations, exercises for restoring muscle strength, stretching, functional and task-oriented training, proprioceptive exercises, postural passages and transfers, sitting and standing training, motor coordination and balance training, walking training, and activities of daily living recovery training were all included in the rehabilitation treatment. To promote neuroplasticity and improve upper limb motor recovery, patients also performed task-oriented exercises such as reaching and grasping movements (e.g., reaching and picking up a glass or other objects), as well as activities of daily living (e.g., transfers, dressing, brushing/combing hair, depending on the subject's ability).

Additionally, robotic treatment of the upper limb was administered to each patient five times a week for 45 min at a time. The following robotic devices were employed: (i) Amadeo (Tyromotion, Austria); (ii) Pablo (Tyromotion, Austria); (iii) Motore (Humanware, Italy); (iv) Diego (Tyromotion, Austria) as detailed in previous studies[54,55]. Patients used robotic upper limb devices that provided visual and auditory feedback while performing motor and cognitive exercises.

Demographic, clinical and anthropometric measurements

We recorded clinical, anamnestic and demographic information on admission (T0).

The Cumulative Illness Rating Scale (CIRS), a 56-point scale, was used to quantify the burden of disease[56].

Weight and height data were included in anthropometric measures. Body weight was measured at T0: a calibrated scale (Seca 750, Seca Hamburg, Germany) was used to weigh the patients who could stand, while a chair weighing scale (Wunder DE5, Wunder Sa.Bi. srl; Milan, Italy) was used for the patients who couldn't. The weight information was given in kilogrammes (kg), with accuracy to the closest 0.1 kg. For every patient who was able to stand, the height was measured at T0, with results reported in meters (m). For individuals unable to stand, height was measured by assessing knee height using a flexible tape measure. Finally, the Body Mass Index was calculated dividing the weight for the squared of the height (BMI, kg/m^2).

Bioelectrical impedance analysis (BIA) and bioelectrical impedance vector analysis (BIVA)

Whole-body BIA of the patients enrolled were assessed at T0 using a Single-Frequency Bioelectrical Impedance Analysis device (BIA 101 Anniversary Sport Edition, Akern, Firenze, Italy). BIA allows the evaluations of body composition parameters applying an alternating sinusoidal electric current of 800 μA at an operating frequency of 50 kHz, obtaining the BIA-derived parameters Resistance (Rz) and Reactance (Xc)[18]. Rz reflects the opposition to the flow of an alternating electrical current through biological tissues and Xc depends on the capacitance properties of the cell membrane. Rz and Xc together represent the Impedance (Z) of biological tissues[57]. The BIA-derived PhA can then be calculated from the ratio between Rz and Xc quantified as arctangent (Xc/R)*180°/π[18]. Rz and Xc are employed within regression models (predictive equations) to estimate body composition components such as fat mass, muscle mass and fluids, or are directly analyzed by BIVA. With BIVA, the bioelectrical Rz and Xc, standardized for the height of the measured subject (h) generate a vector within a Cartesian plane (Rz-Xc graph), with the Rz/h on the abscissa and the Xc/h on the ordinate[34]. Bioimpedance vectors obtained can subsequently be analyzed on the basis of their position, length and direction (which corresponds to the PhA), providing information about the patient's hydration status, body soft tissues and body cell mas[34]. Specifically, the evaluations of BIVA parameters is allowed by comparing patient's bioimpedance vectors with the 50th, 75th, and 95th bivariate percentiles (tolerance ellipses) of a reference population[58]. Vector displacement along the major axis of the tolerance ellipses indicates changes in total body water, with longer vectors suggesting dehydration and shorter vectors indicating overhydration or edema[59]. Rightward shifts parallel to the minor axis signify that soft tissue mass and body cell mass are decreased respect to normal values, while leftward shifts indicate the opposite[37,59]. The vectors of healthy subjects are usually positioned within the 75th tolerance ellipses[22]; in contrast, vectors positioned to the right or outside of the 75th percentile tolerance ellipses are indicative of patients with alterations of hydration status[59] and soft tissue wasting[40].

The "Piccoli" software (Piccoli A, Pastori G. BIVA software. Department of Medical and Surgical Sciences, University of Padova, Italy, 2002) was used to perform BIVA. In this study, we employed two distinct tolerance reference: for the adult population (< 65 years), we utilized the reference ellipses proposed by Campa et al.[35], while for the elderly population (≥ 65 years), we applied the ellipses designed by Saragat et al.[60].

BIA was conducted applying 4 certified electrodes (BIATRODES, Akern, Firenze, Italy), with two pairs of electrodes placed at 5 cm apart at the metacarpal and metatarsal sites of the non-hemiparetic wrist and ankle. All patients were examined in a supine position, with their limbs equally spaced. Before the measurement, the skin at the contact points was cleaned to prevent alterations. Patients with fever or hypothermia were not analyzed because body temperature may alter bioelectric resistance. Patients' hydration status was clinically assessed before the BIA evaluation, and patients presenting local edema or severe dehydration were excluded. Additionally, patients with pacemakers were excluded. Operators were instructed to properly acquire data before starting measurements to minimize estimation errors. Moreover, to establish the variability and reliability of BIVA parameters in our patient's population, the technical error of measurement (TEM) for BIVA data (Rz, Xc, and PhA) was computed with test-retest method. Data were obtained by two different examiners (inter-observer assessment) performed on 10 post-stroke patients out of the population of this study. A TEM percentage below 2% is generally considered an acceptable threshold for inter-observer variability[61].

Malnutrition and sarcopenia assessment at admission

The evaluation of malnutrition was done following the GLIM guidelines[62]. Five criteria are included in GLIM to identify adult malnutrition in a clinical context[62]. These criteria were split into two categories: etiologic (lower food intake or assimilation or any chronic gastrointestinal disorders that adversely impacts patient's food assimilation and an inflammatory condition) and phenotypic (non-volitional weight loss, low BMI, and low muscle mass). Patients with at least one phenotypic and one etiologic requirement at the same time, were considered malnourished.

Sarcopenia was assessed according to the EWGSOP2 guidelines[63], by the simultaneous presence of low values of muscle strength and low muscle mass quantity. Muscle strength was performed with a hand-held digital dynamometer (Citec, C.I.T Techincs, Haren, The Netherlands). Specifically, the maximum isometric strength of the hand and forearm muscles of the non-hemiparetic hand was measured[64]. Patients were evaluated while seated, with their elbows bent at a 90° angle, their shoulders adducted, and their forearms neutrally positioned without any assistances. The mean value reported in kilograms (kg) was calculated after the patients completed three maximal isometric contractions with short rests in between. According to the EWGSOP2, probable sarcopenia was defined as handgrip strength below 27 kg for men, and below 16 kg for women[63]. Muscle mass quantity was estimated using BIA: the appendicular skeletal muscle mass (ASMM) divided by the patient's height squared (ASMM/h^2; kg/m^2) was assessed as a parameter of muscle mass. For low muscle mass quantity, the cut-off for sarcopenia, according to EWGSOP2, is < 5.5 kg/m^2 for women and < 7 kg/m^2 for men[63].

Rehabilitation outcomes

Patients, performance in activity of daily living (ADL) were evaluated both at T0 and after six-weeks rehabilitation treatment (T1) by the modified Barthel Index (mBI). The mBI is an ordinal scale with a range of 0 to 100 composed by ten items that evaluate the patient's ability to perform several tasks, including eating, personal hygiene, clothes, bathing, bladder control, bowel control, toilet transfers, stair climbing, and ambulation/wheelchair use[65].

Recovery was assessed the change in the patients' mBI values assessed at T0 and T1 (ΔmBI = mBIT1-mBIT0). After treatment, patients were classified in two groups, on the basis of ΔmBI: if the ΔmBI was higher than or equal to 10 points, patients were considered to have a greater improvement, and otherwise patients were considered to have a lower improvement[66,67].

Statistical analysis

Demographic and clinical characteristics of patients were shown a as mean and standard deviation for numerical data, and as counts and percentages, form numerical ones.

The Shapiro-Wilk test was employed to assess normality, and non-parametric tests were used when necessary.

The Wilcoxon signed-rank test was employed to investigate changes in rehabilitation outcomes by comparing data at T0 and at T1 for ADL performance (mBI).

To compare the BIVA data from our sample with those from a reference healthy population, we plotted their bioimpedance vectors on two gender-specific tolerance ellipses: one tailored for adults (< 65 years)[35] and another specifically designed for the elderly population (≥ 65 years)[60]. In addition, the mean bioimpedance vectors for women and men were transformed into bivariate Z-scores, that represents the number of standard deviations from the mean values of the two reference populations chosen.

To compare the bioimpedance vectors between patients grouped as: (i) with or without malnutrition; (ii) with or without sarcopenia; (iii) with greater or lower recovery (clinically significant improvement: ΔmBI ≥ 10; no clinically significant improvement: ΔmBI < 10), we analyzed the bivariate 95% confidence ellipses of their mean vectors; statistically significant differences between the mean vectors of the groups were assessed using the multivariate extension of the Student's t-test for unpaired data, known as the two-sample Hotelling's T^2 test. Mahalanobis distances (D) were calculated to quantify the difference among mean bioimpedance vectors, interpreted according to Stevens's guidelines[68]: 0.25–0.49: small; 0.5–0.99: medium; ≥1: large. To compare raw BIA parameters between the previously mentioned groups, we used the Mann-Whitney U test. Chi-squared test was used to investigate whether there were significant differences by sex between groups.

For all the statistical analyses, a *P* value below 0.05 was considered significant. Statistical analysis was performed using SPSS (IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp).

Results

Participants and baseline characteristic

We enrolled 91 patients, 4 patients dropped out, and a final sample of 87 subject was analyzed. The baseline characteristics of the sample group, including anthropometric measurements, demographic and clinical features, disability assessment, nutritional status assessment, and raw BIA parameters, are detailed in Table 1. This study evaluated 87 subacute post-stroke patients, (women $n = 42$, mean age 69 ± 12 years). Among these patients, ischemic stroke was prevalent (76%) and the means days from stroke onset were 100 ± 52. Malnutrition according to GLIM criteria were found in 37 patients (43%; women $n = 22$). Sarcopenia was diagnosed in 24 patients (28%¸ women $n = 14$). There were no significant differences in the proportion of malnutrition and sarcopenia between sexes, neither between ischemic and hemorragic.

Whole-body BIA reproducibility in stroke

The technical error of measurement (TEM) data for Rz, Xc and PhA of the whole-body were provided in supplementary material (Supplementary Table 1). All raw BIA parameters exhibited a TEM percentage below 2%.

BIVA: comparison with the healthy reference's values

Bioimpedance vectors of the women and men of the sample at T0 were plotted on the corresponding BIVA tolerance ellipses (Fig. 1).

BIVA revealed that many patients at admission had higher body fluid overload and lower amounts of soft tissue compared to healthy subjects' reference values. In fact, almost all bioimpedance vectors, both of men and women, were positioned in the fourth quadrant, below the minor axis and at the right of the major axis of the tolerance ellipses. In addition, 60% of men vectors and 74% of women vectors were to the right at the bottom, and outside of the 75th tolerance ellipses. These results were further supported by the Rz-Xc z-score analysis (Fig. 2): gender-specific mean bivariate z-scores for both adults ($n = 29$) and elderly ($n = 58$) were positioned on the lower right quadrant and outside the 75th tolerance ellipses.

Baseline Characteristics	Sample group (*n* = 87)
Age (years)	69 ± 12
Women	42 (48%)
Men	45 (52%)
Antropometric value	
Weight (kg)	69.6 ± 17.3
Height (m)	1.66 ± 0.11
BMI (kg/m^2)	24.9 ± 4.9
Index stroke type	
Ischemic	66 (76%)
Hemorrhagic	21 (24%)
Smoking	45 (52%)
Comorbidities	
Hypertension	74 (85%)
Type 2 diabetes	26 (30%)
Dyslipidemia	37 (43%)
Heart disease	12 (14%)
Dysphagia	29 (33%)
Cumulative illness rating scale (CIRS)	
CIRS severity	2.7 ± 0.4
CIRS comorbidity	5.7 ± 1.7
Days from stroke onset to enrollment	100 ± 52
Performance in activity of daily lliving (ADL)	
Modified barthel index (mBI) (0-100)	45 ± 19
Upper limb motor performance	
Fugl-meyer assessment for the upper extremity scale (FMA-UE)	30 ± 22
Limb's muscle strength	
Motricity index upper extremity (MI-UE)	46 ± 32
Motricity index lower extremity (MI-LE)	52 ± 28
Malnutrition GLIM	37 (43%)
Sarcopenia	24 (28%)
BIA	
Rz (ohm)	515.3 ± 105.3
Xc (ohm)	41.3 ± 9.5
PhA (°)	4.7 ± 1.1

Table 1. Baseline (T0) characteristics of the sample group (*n* = 87).

BIVA, malnutrition, and Sarcopenia

At admission, we observed significant differences in PhA values and bioimpedance vectors between patients with and without malnutrition or sarcopenia. Specifically, we detected lower PhA values in patients with malnutrition (4.32 ± 0.92° vs. 4.94 ± 1.21°, $p = 0.025$) and sarcopenia (3.90 ± 0.90° vs. 4.97 ± 1.10°, $p < 0.001$) compared to those without these conditions.

BIVA showed a significant difference in the confidence ellipses between malnourished and non-malnourished patients ($T^2 = 56.9$, $F = 28.1$, $p < 0.001$, $D = 1.68$) and between sarcopenic and non-sarcopenic patients ($T^2 = 36.4$, $F = 18.0$, $p < 0.001$, $D = 1.5$) (Fig. 3). Notably, the two-sample Hotelling's T^2 test revealed that patients with malnutrition or sarcopenia were characterized by a large ($D \geq 1$) rightward shift of their impedance vectors compared to patients without malnutrition or sarcopenia. We didn't find any differences in PhA values or in the confidence ellipses between patients who experienced haemorrhagic or ischemic stroke.

Effect of rehabilitation

As expected, patients' performance in ADL significantly improved after rehabilitation treatment. Specifically, the mean scores of mBI (61 ± 25 vs. 45 ± 19, $p < 0.001$) was higher at T1 with respect to T0.

The mean ΔmBI assessed in our sample was 16 ± 15. Fifty-three patients (60%; 23 women) exhibited greater improvement based on the ΔmBI cut-off points, while 34 patients (40%; 20 women) exhibited lower improvement. No significant differences in age were observed between the two recovery groups. Furthermore, Chi-square test revealed no significant differences in the proportions of men and women across the recovery outcome groups, or between ischemic and hemorrhagic.

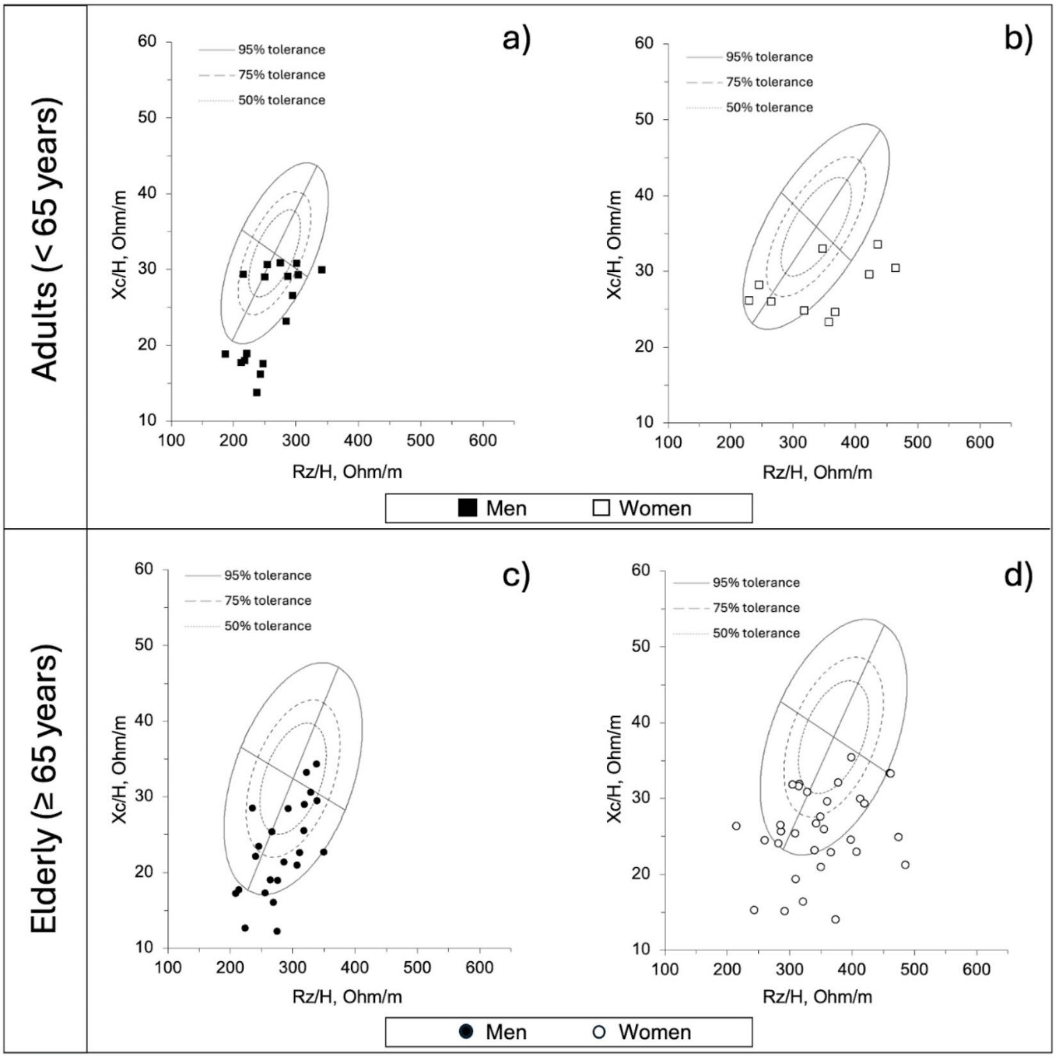

Fig. 1. Men (**a** and **c**) and women (**b** and **d**) bioimpedance vectors plotted on the gender-specific ellipses references (Campa et al. 2023 for adults, and Saragat et al. 2014 for elderly). Filled circles and squares: men; hollow circles and squares: women.

BIVA at admission and recovery after rehabilitation

At admission, PhA values of patients were significantly higher in those who showed greater improvement compared to those with lower improvement ($5.00 \pm 1.12°$ vs. $4.32 \pm 1.10°$, $p = 0.010$). Furthermore, in the two group of patients, we found that also the mean bioimpedance vectors were significantly different (Fig. 4): specifically, in patients who experienced a better recovery there was a medium leftward shift of the vectors ($T^2 = 10.6$, $F = 5.2$, $p = 0.007$, $D = 0.7$).

Discussion

This is the first study which analyzes the body composition of subacute patients with stroke undergoing rehabilitation using BIVA. Our findings demonstrated that BIVA at admission provides valuable information regarding the hydration and nutritional status of post-stroke patients. Furthermore, BIVA at admission not only distinguished patients based on the presence or absence of malnutrition or sarcopenia, but also effectively differentiated those who would have higher or lower ADL recovery after the rehabilitation program.

We evaluated the BIVA parameters of our sample by comparing individual bioimpedance vectors and the mean bivariate Z-score with the updated bioelectrical impedance vector references for the healthy adults[35] and healthy elderly[60]. These updated ellipses were designed to enhance the accuracy and utility of BIVA in body composition assessments[35]. Our findings revealed that the majority of the bioimpedance vectors of our sample were located below the minor axis, to the right, and outside the 75th tolerance ellipses. These placements indicates a significant shift towards higher extracellular fluid levels (body fluid overload) and reduced soft tissue mass when compared to healthy reference populations[22,36,59]. These results were further confirmed by the Rz-Xc Z-score analysis, which revealed that the mean bivariate Z-scores of both sexes were positioned in the lower-right (fourth) quadrant and outside the 75th percentile tolerance ellipses. Such vector positions on

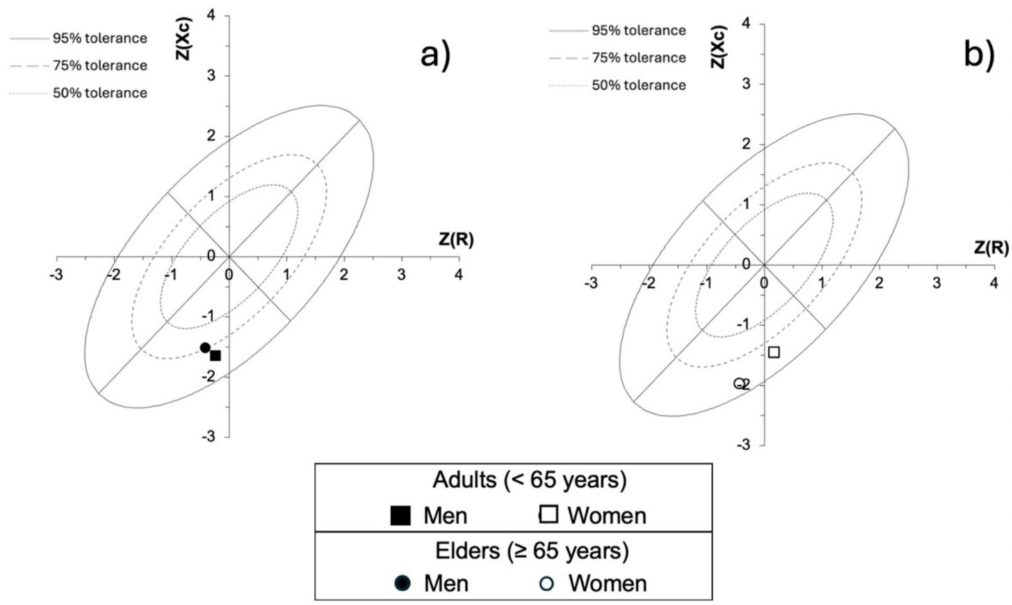

Fig. 2. Men (**a**) and women (**b**) mean bioimpedance vectors (bivariate z-scores) plotted on the Rz-Xc Z-score graph (Campa et al. 2023 for adults, and Saragat et al. 2014). Filled circles and squares: men; hollow circles and squares: women.

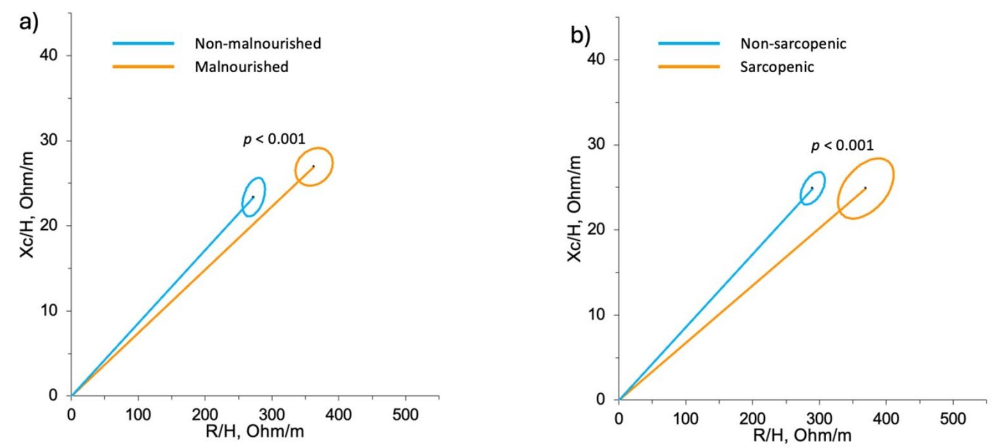

Fig. 3. Comparison of the bioimpedance vectors with 95% confidence ellipses between patients: (**a**) with or without malnutrition (GLIM criteria) and (**b**) with or without sarcopenia (EWGSOP2 criteria). *p* value refers to the statistically significant difference found using the two-sample Hotelling's T^2 test.

the Rz-Xc graph have been consistently associated with alterations in hydration status and soft tissue wasting[40]. Furthermore, patients with bioimpedance vectors plotted in the fourth quadrant and outside the 75th percentile ellipses were found to be at higher risk of malnutrition, sarcopenia, or cachexia[51,59,69]. Since this is the first study assessing BIVA parameters in a sample of patients with sub-acute stroke, it is not possible to compare our findings with those of other studies. However, we believe that the results presented herein accurately reflect the baseline characteristics of our sample and, more broadly, of post-stroke patients undergoing rehabilitation treatment: at T0 many of our patients were characterized by malnutrition (43%) or sarcopenia (28%); the PhA values at T0 of our sample were lower with respect to the references values of healthy population for the same age group[35], suggesting less muscle mass quantity and quality, and lower status of cells capable of contributing to strength expression[24,70]; lastly, following a stroke, most patients in this study had difficulty in walking or were already bedridden, which likely contributed to muscle wasting, loss of muscle strength, and soft tissue

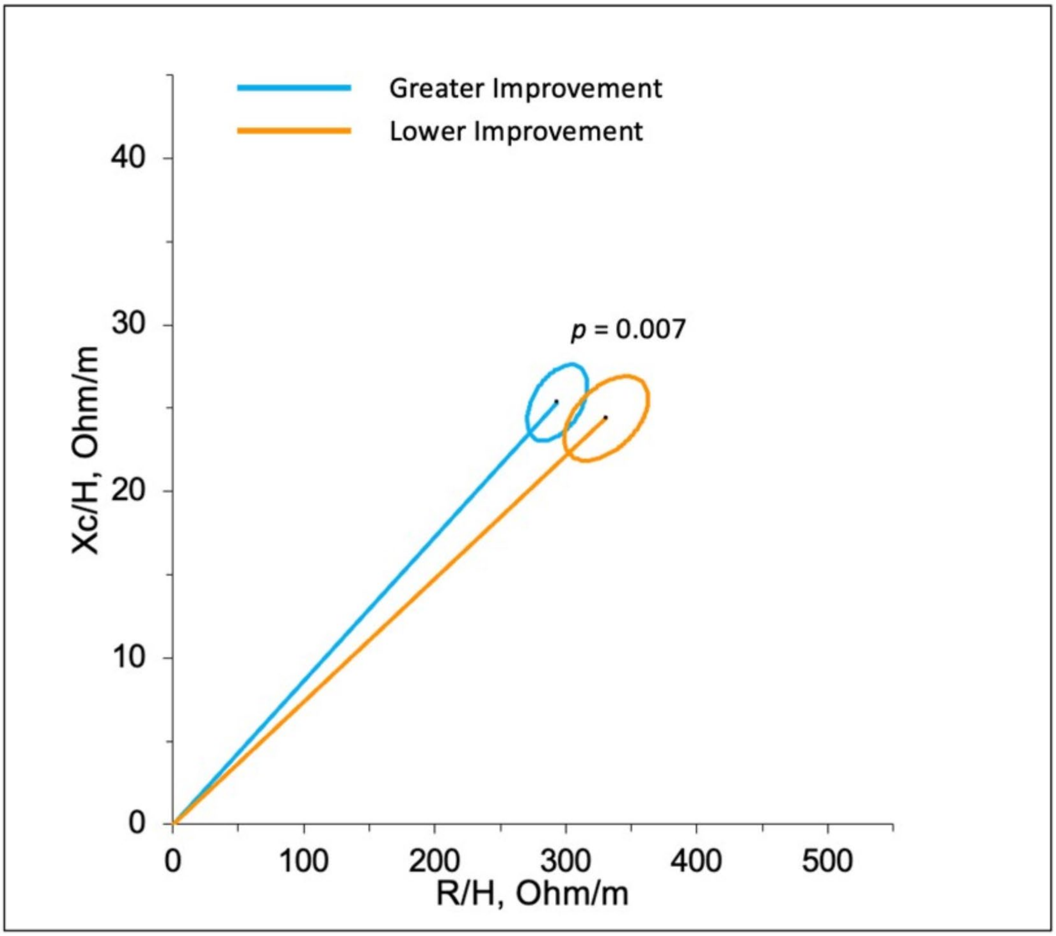

Fig. 4. Comparison of the bioimpedance vectors with 95% confidence ellipses between patients with greater improvement (ΔmBI ≥ 10) or lower improvement (ΔmBI < 10) recovery. *p* value refers to the statistically significant difference found using the two-sample Hotelling's T^2 test.

changes[71,72]. Rehabilitation is crucial for improving patient outcomes, especially given poor initial conditions. Indeed, our patients showed significant improvements in their performances activities of daily living (ADL), limb's motor performance, and muscle strength following the rehabilitation treatment.

Another interesting finding of this study emerged from the inter-group comparison analyses. Patients who were malnourished, sarcopenic, or had lower improvement in ADL, showed lower PhA values compared to those who were not malnourished, not sarcopenic, or had higher recovery, consistent with findings from other clinical studies[10,25,26]. BIVA revealed that patients with malnutrition and sarcopenia were characterized at admission by rightward shift of their bioimpedance vectors on the Rz-Xc graph compared to those without these conditions. Previous studies in other clinical settings have reported similar findings in patients with malnutrition[38,39,41,49,50] or those with sarcopenia[45–48].

Our findings also revealed that BIVA effectively differentiated patients with higher ADL recovery from those with lower recovery after the rehabilitation program. To date, no studies had yet evaluated the relationship between BIVA and post-stroke recovery. Specifically, we observed that patients with improved recovery exhibited a noticeable leftward shift in their bioimpedance vectors at admission, indicating that these patients had a higher amount of soft tissues and muscle mass[22,40] and this can probably contribute to the process of recovery. BIVA appears to be a valuable tool that complements and enhances the usefulness of BIA for monitoring the body composition of post-stroke patients undergoing rehabilitation. Several studies showed that BIA muscle mass parameters[8–10,73–75], together with the BIA-derived PhA[14,25,28,29] were positively related with the outcomes rehabilitation. We have also recently demonstrated that BIA can differentiate segmental muscle quality between the affected and unaffected sides, as well as detect improvements in muscle quality on the hemiparetic side following rehabilitation[53]. However, for a complete body composition assessment, we suggest to consider also data from BIVA. In fact, it is important to clarify that there are still insufficient valid equations for estimating body muscle mass by BIA for every population and bioelectrical technology[32]. Moreover, although the clinical utility of PhA has been widely discussed, other important information provided by raw bioelectrical parameters may be overlooked[23]. In fact, the analysis of the bioimpedance vector provides insights into body hydration, nutrition and muscle health[22,34], offering a more comprehensive body composition assessment compared to PhA alone[22,23]. Additionally, BIVA is free from any potential biases associated with BIA predictive equarions[35] and could be utilized at the onset of post-stroke rehabilitation therapy for immediate body composition assessment, enabling the creation of more tailored and effective treatment plans.

The experience gained from this study in diagnosing malnutrition with the GLIM criteria in post-stroke patients was instrumental in defining the nutritional status assessment of a multicenter study protocol in a large cohort of patients with stroke during rehabilitation treatment (trial registered at ClinicalTrials.gov with identifier number: NCT06547827).

One limitation of this study arises from the recruitment of a restricted sample only from a single rehabilitation center. Another limitation is that only foot-to-hand bioimpedance devices operating at a frequency of 50 kHz can be utilized for BIVA. Therefore, it must be considered that different types of bioimpedance devices are not suitable for BIVA analysis. Further investigations on a larger sample through multicenter trials should be programmed to confirm the data presented herein.

In conclusion, this study provides the first evidence of the application of BIVA in assessing body composition among subacute post-stroke patients undergoing rehabilitation. BIVA allows an easy and immediate evaluation of hydration and nutritional status of these patients, significantly complementing the traditional BIA approach. Moreover, we showed that BIVA is able to differentiate patients based on a higher recovery, making it a future potential prognostic tool.

Data availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Received: 2 September 2024; Accepted: 30 December 2024
Published online: 13 January 2025

References

1. GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and its risk factors, 1990–2019: A systematic analysis for the global burden of disease study 2019. *Lancet Neurol.* **20**, 795–820 (2021).
2. Huppertz, V. et al. Impaired nutritional condition after Stroke from the Hyperacute to the chronic phase: A systematic review and meta-analysis. *Front. Neurol.* **12**, 780080 (2021).
3. Scherbakov, N., Sandek, A. & Doehner, W. Stroke-related sarcopenia: Specific characteristics. *J. Am. Med. Dir. Assoc.* **16**, 272–276 (2015).
4. Lee, Y. C. & Chiu, E. C. Nutritional status as a predictor of comprehensive activities of daily living function and quality of life in patients with stroke. *NeuroRehabilitation* **48**, 337–343 (2021).
5. Nishioka, S. et al. Nutritional improvement correlates with recovery of activities of daily living among malnourished elderly stroke patients in the convalescent stage: A cross-sectional study. *J. Acad. Nutr. Diet.* **116**, 837–843 (2016).
6. Shimazu, S. et al. Frequent and personalized nutritional support leads to improved nutritional status, activities of daily living, and dysphagia after stroke. *Nutrition* **83**, 111091 (2021).
7. Sabbouh, T. & Torbey, M. T. Malnutrition in stroke patients: risk factors, assessment, and management. *Neurocrit. Care* **29**, 374–384 (2018).
8. Ohyama, K. et al. Correlation between skeletal muscle mass deficit and poor functional outcome in patients with acute ischemic stroke. *J. Stroke Cerebrovasc. Dis.* **29**, 104623 (2020).
9. Matsushita, T., Nishioka, S., Taguchi, S. & Yamanouchi, A. Sarcopenia as a predictor of activities of daily living capability in stroke patients undergoing rehabilitation. *Geriatr. Gerontol. Int.* **19**, 1124–1128 (2019).
10. Siotto, M. et al. Relationship between nutritional status, food consumption and sarcopenia in post-stroke rehabilitation: Preliminary data. *Nutrients* **14**, 4825 (2022).
11. Cederholm, T. et al. ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin. Nutr.* **36**, 49–64 (2017).
12. Cereda, E. et al. Nutritional status in older persons according to healthcare setting: A systematic review and meta-analysis of prevalence data using MNA®. *Clin. Nutr.***35**, 1282–1290 (2016).
13. Di Vincenzo, O. et al. The assessment of the risk of malnutrition (undernutrition) in stroke patients. *Nutrients* **15**, 683 (2023).
14. Irisawa, H. & Mizushima, T. Correlation of body composition and nutritional status with functional recovery in stroke rehabilitation patients. *Nutrients* **12**, E1923 (2020).
15. Borga, M. et al. Advanced body composition assessment: From body mass index to body composition profiling. *J. Investig Med.* **66**, 1–9 (2018).
16. Gheri, C. F., Scalfi, L., Luisi, M. L. E. & Di Vincenzo, O. Bioelectrical impedance analysis (BIA) phase angle in stroke patients: A systematic review. *Clin. Nutr.* **43**, 63–72 (2024).
17. Nakanishi, N. et al. Measuring and monitoring skeletal muscle mass after stroke: A review of current methods and clinical applications. *J. Stroke Cerebrovasc. Dis.* **30**, 105736 (2021).
18. Kyle, U. G. et al. Bioelectrical impedance analysis–part I: Review of principles and methods. *Clin. Nutr.* **23**, 1226–1243 (2004).
19. Thomasset, M. A. Bioelectric properties of tissue. Impedance measurement in clinical medicine. Significance of curves obtained. *Lyon Med.* **94**, 107–118 (1962).
20. Lukaski, H. C. & Talluri, A. Phase angle as an index of physiological status: Validating bioelectrical assessments of hydration and cell mass in health and disease. *Rev. Endocr. Metab. Disord.* **24**, 371–379 (2023).
21. Akamatsu, Y. et al. Phase angle from bioelectrical impedance analysis is a useful indicator of muscle quality. *J. Cachexia Sarcopenia Mus.* **13**, 180–189 (2022).
22. Norman, K., Stobäus, N., Pirlich, M. & Bosy-Westphal, A. Bioelectrical phase angle and impedance vector analysis–clinical relevance and applicability of impedance parameters. *Clin. Nutr.* **31**, 854–861 (2012).
23. Bellido, D., García-García, C., Talluri, A., Lukaski, H. C. & García-Almeida, J. M. Future lines of research on phase angle: Strengths and limitations. *Rev. Endocr. Metab. Disord.* **24**, 563–583 (2023).
24. Campa, F. et al. Effect of resistance training on bioelectrical phase angle in older adults: A systematic review with meta-analysis of randomized controlled trials. *Rev. Endocr. Metab. Disord* **24**, 439–449 (2023).
25. Sato, Y., Yoshimura, Y. & Abe, T. Phase angle as an indicator of baseline nutritional status and sarcopenia in acute stroke. *J. Stroke Cerebrovasc. Dis.* **31**, 106220 (2022).
26. Bise, T. et al. Association between BIA-derived phase angle and sarcopenia and improvement in activities of daily living and dysphagia in patients undergoing post-stroke rehabilitation. *J. Nutr. Health Aging*. **26**, 590–597 (2022).
27. Yoshimura, Y. et al. Phase angle is associated with sarcopenic obesity in post-stroke patients. *Clin. Nutr.* **42**, 2051–2057 (2023).
28. Abe, T. et al. Impact of phase angle on physical function in patients with acute stroke. *J. Stroke Cerebrovasc. Dis.* **30**, 105941 (2021).

29. Abe, T., Yoshimua, Y., Imai, R. & Sato, Y. A combined assessment method of phase angle and skeletal muscle index to better predict functional recovery after acute stroke. *J. Nutr. Health Aging.* **26**, 445–451 (2022).
30. Park, S., Kim, J., Kim, Y. & Kim, M. W. Correlation of body composition via bioelectrical impedance analysis and motor function and recovery of upper extremity in patients undergoing stroke rehabilitation. *Brain Neurorehabilit.* **15**, 2 (e20) (2022).
31. Ward, L. C. Bioelectrical impedance analysis for body composition assessment: Reflections on accuracy, clinical utility, and standardisation. *Eur. J. Clin. Nutr.* **73**, 194–199 (2019).
32. Campa, F. et al. High-standard predictive equations for estimating body composition using bioelectrical impedance analysis: A systematic review. *J. Transl Med.* **22**, 515 (2024).
33. Catapano, A. et al. Impedance analysis to evaluate nutritional status in physiological and pathological conditions. *Nutrients* **15**, 2264 (2023).
34. Piccoli, A., Rossi, B., Pillon, L. & Bucciante, G. A new method for monitoring body fluid variation by bioimpedance analysis: The RXc graph. *Kidney Int.* **46**, 534–539 (1994).
35. Campa, F. et al. New bioelectrical impedance vector references and phase angle centile curves in 4367 adults: The need for an urgent update after 30 years. *Clin. Nutr.* **42**, 1749–1758 (2023).
36. Lukaski, H. C., Diaz, V., Talluri, N., Nescolarde, L. & A. & Classification of hydration in clinical conditions: Indirect and direct approaches using bioimpedance. *Nutrients* **11**, 809 (2019).
37. Marini, E. et al. Phase angle and bioelectrical impedance vector analysis in the evaluation of body composition in athletes. *Clin. Nutr.* **39**, 447–454 (2020).
38. Slee, A., Birc, D. & Stokoe, D. Bioelectrical impedance vector analysis, phase-angle assessment and relationship with malnutrition risk in a cohort of frail older hospital patients in the United Kingdom. *Nutrition* **31**, 132–137 (2015).
39. Santomauro, F. et al. Bioelectrical impedance vector analysis and mini nutritional assessment in elderly nursing home residents. *J. Nutr. Health Aging* **15**, 163–167 (2011).
40. Piccoli, A., Codognotto, M., Piasentin, P. & Naso, A. Combined evaluation of nutrition and hydration in dialysis patients with bioelectrical impedance vector analysis (BIVA). *Clin. Nutr.* **33**, 673–677 (2014).
41. Muñoz-Pérez, E., Espinosa-Cuevas, M. D. L. Á., Miranda-Alatriste, P. V., Correa-Rotter, R. & Atilano-Carsi, X. Combined assessment of nutritional status in patients with peritoneal dialysis using bioelectrical impedance vectors and malnutrition inflammation score. *Nutr. Hosp.* **34**, 1125–1132 (2017).
42. Lima, J., Eckert, I., Gonzalez, M. C. & Silva, F. M. Prognostic value of phase angle and bioelectrical impedance vector in critically ill patients: A systematic review and meta-analysis of observational studies. *Clin. Nutr.* **41**, 2801–2816 (2022).
43. Limon-Miro, A. T. et al. Bioelectric impedance vector analysis (BIVA) in breast cancer patients: A tool for research and clinical practice. *Med. (Kaunas)* **55**, 663 (2019).
44. Nwosu, A. C. et al. Bioelectrical impedance vector analysis (BIVA) as a method to compare body composition differences according to cancer stage and type. *Clin. Nutr. ESPEN.* **30**, 59–66 (2019).
45. de-Mateo-Silleras, B. et al. Bioimpedance analysis as an indicator of muscle mass and strength in a group of elderly subjects. *Exp. Gerontol.* **113**, 113–119 (2018).
46. Rossini-Venturini, A. C. et al. Association between classic and specific bioimpedance vector analysis and sarcopenia in older adults: A cross-sectional study. *BMC Sports Sci. Med. Rehabil.* **14**, 170 (2022).
47. Jiang, F. L. et al. Distribution of bioelectrical impedance vector analysis and phase angle in Korean elderly and sarcopenia. *Sens. (Basel)* **23**, 7090 (2023).
48. Marini, E. et al. The potential of classic and specific bioelectrical impedance vector analysis for the assessment of sarcopenia and sarcopenic obesity. *Clin. Interv Aging* **7**, 585–591 (2012).
49. Bonaccorsi, G. et al. Risk of malnutrition in a sample of nonagenarians: Specific versus classic bioelectrical impedance vector analysis. *Nutrition* **32**, 368–374 (2016).
50. Norman, K. et al. Disease-related malnutrition but not underweight by BMI is reflected by disturbed electric tissue properties in the bioelectrical impedance vector analysis. *Br. J. Nutr.* **100**, 590–595 (2008).
51. Sugizaki, C. S. A. et al. Comparison of bioelectrical impedance vector analysis (BIVA) to 7-point subjective global assessment for the diagnosis of malnutrition. *J. Bras. Nefrol.* **44**, 171–178 (2022).
52. Yoo, C., Kim, J., Yang, Y., Lee, J. & Jeon, G. Bioelectrical impedance analysis for severe stroke patients with upper extremity hemiplegia. *J. Phys. Ther. Sci.* **28**, 2708–2712 (2016).
53. Guerrini, A. et al. Muscle quality improvement in subacute post-stroke patients after rehabilitation: Usefulness of segmental phase angle from bioelectrical impedance analysis. *Clin. Nutr.* **43**, 224–231 (2024).
54. Aprile, I. et al. Upper limb robotic rehabilitation after stroke: A multicenter, randomized clinical trial. *J. Neurol. Phys. Ther.* **44**, 3–14 (2020).
55. Aprile, I. et al. Upper limb robotics in rehabilitation: An approach to select the devices, based on rehabilitation aims, and their evaluation in a feasibility study. *Appl. Sci.* **9**, 3920 (2019).
56. Hudon, C., Fortin, M. & Vanasse, A. Cumulative illness rating scale was a reliable and valid index in a family practice context. *J. Clin. Epidemiol.* **58**, 603–608 (2005).
57. Khalil, S. F., Mohktar, M. S. & Ibrahim, F. The theory and fundamentals of bioimpedance analysis in clinical status monitoring and diagnosis of diseases. *Sens. (Basel)* **14**, 10895–10928 (2014).
58. Piccoli, A. et al. Bivariate normal values of the bioelectrical impedance vector in adult and elderly populations. *Am. J. Clin. Nutr.* **61**, 269–270 (1995).
59. Piccoli, A. Bioelectric impedance measurement for fluid status assessment. *Contrib. Nephrol.* **164**, 143–152 (2010).
60. Saragat, B. et al. Specific bioelectrical impedance vector reference values for assessing body composition in the Italian elderly. *Exp. Gerontol.* **50**, 52–56 (2014).
61. Perini, T. A. & de Oliveira, G. L. Technical error of measurement in anthropometry. *Rev. Bras. Med. Esporte* **11**, 1 (2005).
62. Cederholm, T. et al. GLIM criteria for the diagnosis of malnutrition : A consensus report from the global clinical nutrition community. *Clin. Nutr.* **38**, 1–9 (2019).
63. Cruz-Jentoft, A. J. et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. **48**, 16–31 (2019).
64. Innes, E. Handgrip strength testing: A review of theliterature. 120–140 (2002).
65. Castiglia, S. F. et al. The culturally adapted Italian version of the barthel index (IcaBI): Assessment of structural validity, inter-rater reliability and responsiveness to clinically relevant improvements in patients admitted to inpatient rehabilitation centers. *Funct. Neurol.* **22**, 221–228 (2017).
66. Hsieh, Y. W. et al. Establishing the minimal clinically important difference of the Barthel Index in stroke patients. *Neurorehabil. Neural Repair.* **21**, 233–238 (2007).
67. Golicki, D. et al. Comparing responsiveness of the EQ-5D-5L, EQ-5D-3L and EQ VAS in stroke patients. *Qual. Life Res.* **24**, 1555–1563 (2015).
68. Stevens, J. P. *Applied Multivariate Statistics for the Social Sciences*. (2002).
69. Castillo-Martínez, L. et al. Cachexia assessed by bioimpedance vector analysis as a prognostic indicator in chronic stable heart failure patients. *Nutrition* **28**, 886–891 (2012).
70. Rosa, G. B. et al. Limb-specific isometric and isokinetic strength in adults: The potential role of regional bioelectrical impedance analysis-derived phase angle. *Clin. Nutr.* **43**, 154–162 (2024).

71. Fazzini, B. et al. The rate and assessment of muscle wasting during critical illness: A systematic review and meta-analysis. *Crit. Care* **27**, 2 (2023).
72. Dittmer, D. K. & Teasell, R. Complications of immobilization and bed rest. Part 1: Musculoskeletal and cardiovascular complications. *Can. Fam Phys.* **39**, 1428–1432 (1993).
73. Jang, A., Bae, C. H., Han, S. J. & Bae, H. Association between length of stay in the intensive care unit and sarcopenia among hemiplegic stroke patients. *Ann. Rehabil Med.* **45**, 49–56 (2021).
74. Park, J. G., Lee, K. W., Kim, S. B., Lee, J. H. & Kim, Y. H. Effect of decreased skeletal muscle index and hand grip strength on functional recovery in subacute ambulatory stroke patients. *Ann. Rehabil Med.* **43**, 535–543 (2019).
75. Guerrini, A. et al. Body cell mass from bioelectrical impedance analysis in patients with stroke undergoing rehabilitation. *Appl. Sci.* **13**, 3965 (2023).

Author contributions
Conceptualization, A.G., M.S., and I.G.A.; methodology, A.G., M.S., C.C. and M.G.; software, M.G.; validation, M.S., C.C., M.G.; formal analysis, A.G., M.S.; investigation, A.G., C.C., V.C., L.C., A.P., S.I.; data curation, A.G., M.S., and M.G.; writing—original draft preparation, A.G. ; writing—review and editing, M.S., C.C., M.G., , M.K., and I.G.A.; visualization, V.C., L.C., A.P., S.I., M.S., M.K., and I.G.A.; supervision: I.G.A. All authors have read and agreed to the published version of the manuscript.

Funding
This study was partially supported and funded by the Italian Ministry of Health—Ricerca Corrente. This work was also supported by the Italian Ministry of Research, under the complementary actions of the NRRP "Fit-4MedRob-Fit for Medical Robotics" Grant (# PNC0000007).

Declarations

Competing interests
The authors declare no competing interests.

Institutional review board statement
The study was conducted in accordance with the Declaration of Helsinki and approved by Ethics Committee of Fondazione Don Carlo Gnocchi, Milan on February 12th, 2020, and with a non-substantial amendment on October 14th, 2020 (Prot.n.22/2020/CE_FdG/FC/SA_14/10/20). Informed consent was obtained from all subjects involved in the study.

Additional information
Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-024-84968-y.

Correspondence and requests for materials should be addressed to M.S.

Reprints and permissions information is available at www.nature.com/reprints.